NanoExplore Project Summary

Integrated approach for exposure and health effects monitoring of engineered nanomaterials in workplaces and urban areas

Layman's report

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NanoExplore

Project Details

Project location : Greece, Spain, Switzerland, Italy, Germany, UK
Project start date : September 2018
Project end date : September 2022
Total budget : €2.2 million
EC financial contribution : 60%

Project website:
https://www.lifenanoexplore.eu/

Project Coordinator:
ALCON Consultant Engineers Ltd (Greece)

Project Partners

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Problem Targeted

There is an urgent need to provide stakeholders with an integrated approach to generate robust data on the levels of exposure and related health effects of nanomaterials, supporting the risk assessment of those substances.

Nanotechnology is a fast growing and promising technology due to its potential to develop new add-values products. Nanomaterials are defined as solid substances with a number size distribution of 50% being particles with at least one dimension of 1-100 nm. Their unique characteristics (e.g. small size or high surface area to volume ratio) can cause negative (eco)toxicological effects as, for example, the biological uptake. Different exposure routes have to be taken into account and in terms of ultrafine dust the inhalation route might be the most relevant. The increased production, handling and availability of nanomaterials on the market brings innovative applications, but can also lead to personal exposure with the potential for unforeseen biological effects. In particular, workers in companies manufacturing and handling nanomaterials are likely to have regular exposures to engineered nanomaterials and incidental ultrafine dusts. For comprehensive occupational safety, it is essential to quantify the exact exposure to nanomaterials and to know their toxicological profile in order to be able to derive adequate safety measures for the workers.

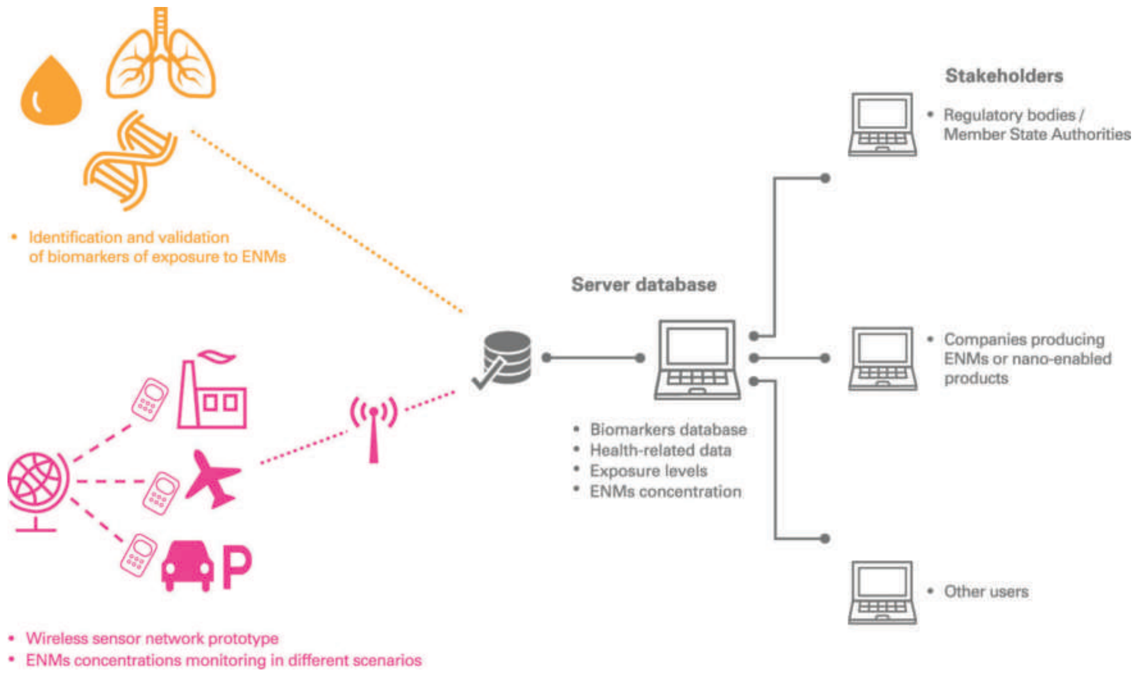
NanoExplore Solution

The overall aim of the NanoExplore project is to develop and demonstrate the feasibility of an integrated approach to conduct biomonitoring studies, characterise exposure levels and identify possible health effects deriving from exposure to engineered nanomaterials (ENMs) in indoor workplaces and urban areas.
The two key aspects of the project include:

- **Development of new approaches to control the release of ENMs**
- **Enhancement of knowledge on the presence of ENMs in the environment and workplaces**

NanoExplore promotes a harmonised approach to overcome current data gaps and barriers limiting the implementation of the REACH regulation. It uses human bio-monitoring data in the protection of human health and the environment to deal with particles in the nanometer range by combining long series of robust data on the concentration of ENMs measured by a wireless sensor network (WSN) of monitoring devices, appropriate biomarkers, and a tailored designed data management application. This approach addresses current environmental, health, and safety questions about ENMs. It also provides stakeholders from government, industry, NGOs, or the general public, with reliable data on the concentration and effects of nanoparticles

Figure 1. Development of the web-based platform



Project Development

The project has been coordinated by ALCON Consultant Engineers. The project includes partners from all the spectrum of disciplines needed for a successful implementation of the project. The key project activities were delivered into three stages, as shown in the figure below.

A. Preparatory actions

A series of preparatory actions were implemented to define the key concepts and develop the conceptual design for the project.

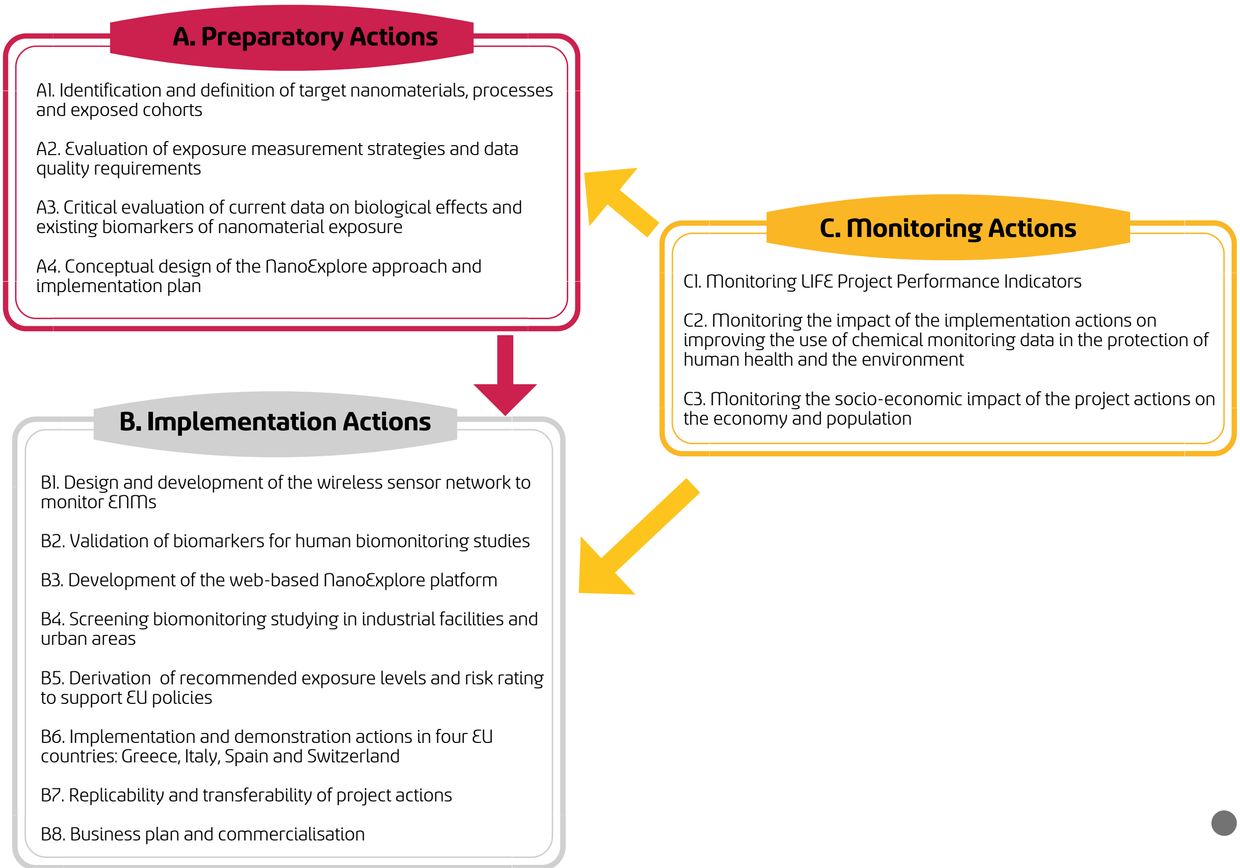
B. Implementation actions

Implementation actions allowed partners to meet the objectives of the project.

C. Monitoring of the impact of the project actions

A series of actions were implemented to monitor the performance of the project in accordance with established performance indicators.

Figure 2. Overview of the phases of the project



Project Results

The main outcome of NanoExplore is an integrated system for assessment, monitoring and surveillance of the exposure and effects deriving from exposure to engineered nanomaterials (ENM) in indoor workplaces and urban areas. The tangible project results include:

Outcome 1. Selection of eight candidate biomarkers panel of exposure and effect of ENMs on pulmonary and cardiovascular system for health surveillance.

Table 1. Exposure and effect biomarkers

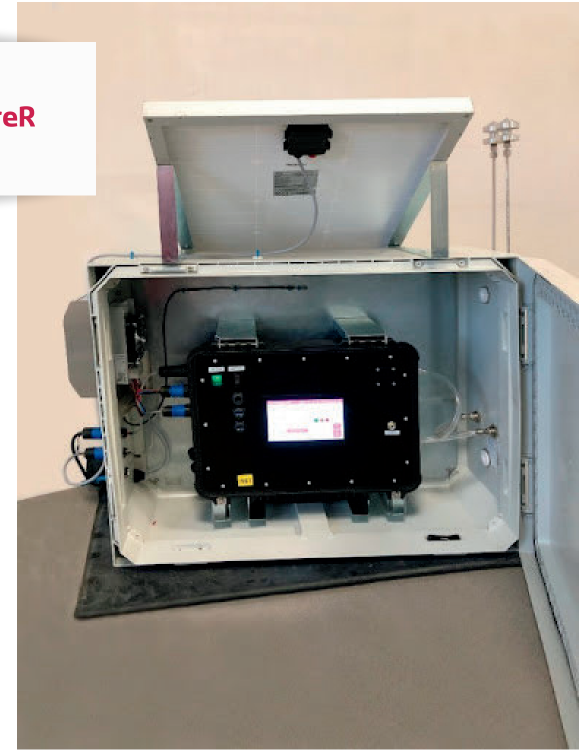
Biomarker	Biological matrix	Biomarker description	Analytical method
Metals mass concentration Ag, Cu, Ti, Zn, Ce, Si, Fe, Al, Ca,[EB1] Moa*	Urine	Metals concentration	ICP-MS
8-isoprostaneb	Urine	Oxidative stress	ELISA
Malondialdehyde (MDA)b	Urine	Oxidative stress	Thiobarbituric Acid Reactive Substances assay (Colorimetric)
8-Oxo-2'-deoxyguanosine (8OHdG)b	Urine	DNA oxidative damage	ELISA
Total Antioxidant Power (TAP)b	Urine	Antioxidant capacity	Cupric ion reducing antioxidant capacity assay (Colorimetric)
Creatinineb	Urine	Clinical biomarker for renal excretion also used for volume normalization in the spot urine samples	Spectrophotometric method (Kinetic Jaffé procedure)
Particle size and number concentrationa	EBC	Estimation of particle deposited dose	Nanoparticle Tracking analysis (NTA)
Metals mass concentration Ag, Cu, Ti, Zn, Ce, Si, Fe, Al,Ca, Moa*	EBC	Estimation of lung deposited dose	ICP-MS
8-Oxo-2'-deoxyguanosine (8OHdG)b	EBC	DNA oxidative damage	ELISA
8-isoprostaneb	EBC	Oxidative stress	ELISA
Malondialdehyde (MDA)b	EBC	Oxidative stress	Thiobarbituric Acid Reactive Substances Assay (Colorimetric)
Tumor necrosis factor (TNF-α)b	EBC	Pro-inflammatory multifunctional cytokine; it plays important roles in different cellular events such as cell survival, proliferation, differentiation, and death	Real time PCR- linked ELISA
Interleukin 1 beta (IL-1β)b	EBC	Pro-inflammatory cytokine key mediator of the inflammatory response	Real time PCR- linked ELISA
Interleukin 6 (IL-6)b	EBC	Pro-inflammatory cytokine secreted by macrophages in response to specific microbial molecules (PAMPs)	Real time PCR- linked ELISA
Interleukin 10 (IL-10)b	EBC	Immuno-suppressive cytokine which reduces the recruitment of effector T cells and counteracts the effects of TNF-α and IL-1β.	Real time PCR- linked ELISA
Interleukin 17 (IL-17)b	EBC	Pro-inflammatory cytokine essential for host defense against bacteria and fungi. It is important in autoimmune disease	Real time PCR- linked ELISA
Leukotriene B4 (LTB4)b	EBC	Bronchial tract activation, permeability and local inflammation	ELISA
High-Sensitivity C-Reactive Protein (Hs-CRP)b	EBC	Low grade systemic inflammation	Real time PCR- linked ELISA
Surfactant protein-D (SPD)b	EBC	Regulation of pulmonary host defense and inflammation; type II alveolar epithelial cells integrity	ELISA
Krebs von den Lungen glycoprotein 6 (KL6)b	EBC	Potential biomarkers of interstitial lung disease; activation of pro-fibrotic cascade	ELISA
Nitrotyrosineb	EBC	Nitrosative stress	ELISA
Oxidative potential in exhaled air (OPEA)b	Exhaled air	Oxidative stress	OPEA analyser + FOX colorimetric test (6 min including sampling)

Notes: a Exposure biomarkers.
b Effect biomarkers.
*Measured only in workers exposed to metal containing ENMs.

[EB1]Ca is largely affected by diet intake. Not useful. The same is for Si (milligrams/liter).

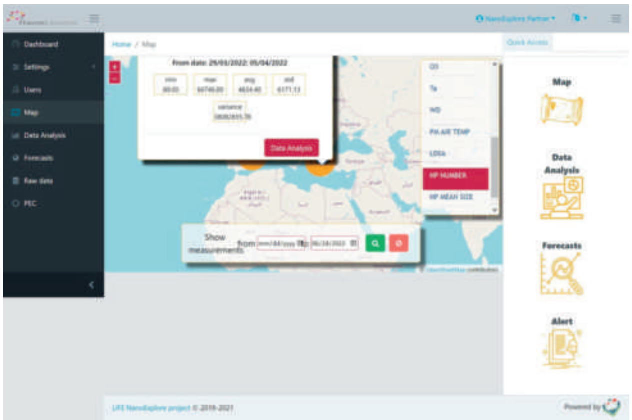
Outcome 2. A functional wireless sensor network prototype of 8 unattended, low-cost, portable and battery powered devices.

Indoor NanoExploreR



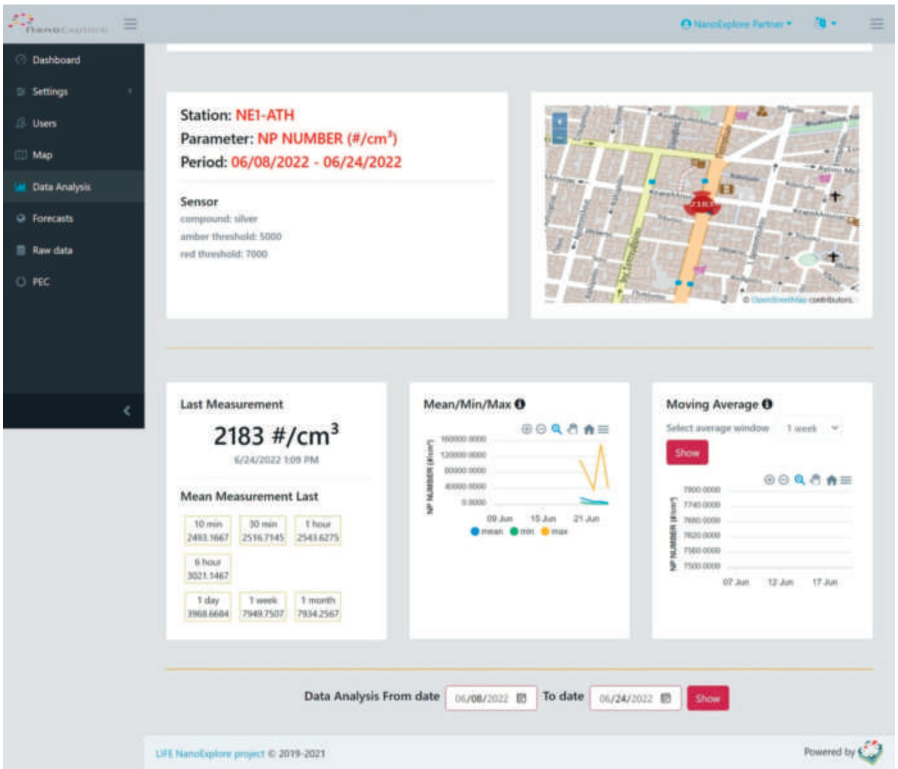
Outdoor NanoExploreR

Outcome 3. Development of an online software application to support the processing, analysis and interpretation of data on ENMs concentration



Main screen of tailored software for controlling the NanoExploreR Wireless Sensor

The software permits switching on and off the sensors, data acquisition, data transfer to Web platform, measurement configuration, automatic measurement planification, etc. The traffic-light indicator gives information about exposure levels.



- **Outcome 4.** Development of a harmonised protocol for the first international collaborative study of human biomonitoring studies.

- **Outcome 5.** Determination of reference values of biomarkers selected.

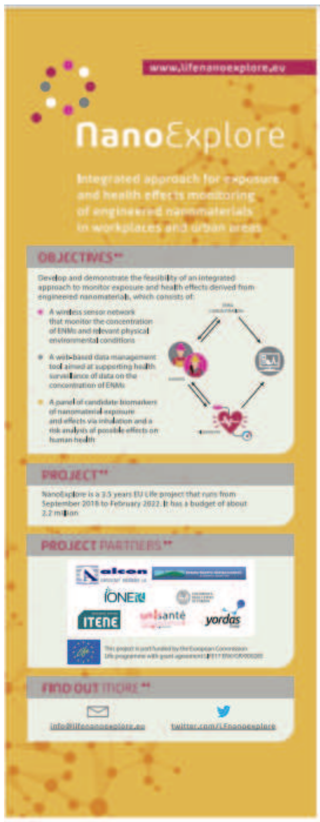
- **Outcome 6.** Derivation of Occupational Exposure Levels (OELs) for workers, from a priority list of 12 ENMs through calculation of the Human Equivalent Concentration (HEC) and by considering the uncertainty factors. Moreover, four occupational exposure bands (OEBs) have been proposed for the nanomaterials risk assessment, according to two parameters: dustiness and the way of use.

- **Outcome 7.** Development of a map of exposure scenarios and calculation of the risk characterisation ratios RCR by comparing the levels of exposure measured with the proposed nanoOELs and nanoOEBs.

- **Outcome 8.** Published guidance on the use of human biomonitoring and exposure data for REACH implementation and epidemiological purposes.

- **Outcome 9.** Dissemination of the knowledge base and project results during three project workshops, three webinars and one international conference.

NanoExplore Poster



NanoExplore Banner

Environmental Impact

The key environmental issues targeted with this project are related to the increased worldwide use of ENMs in products, the lack of information on current exposure levels on both workers and the population, and the scarcity of ENM's potential negative effects data on human health and the environment.

The environmental benefits of the project include:

1. Reduction of environmental pollution from ENMs
2. Reduction of costs to remediate or compensate for environmental damage
3. Reduction of risks related to environmental damages

The characterisation of the baseline data is very challenging due to the lack of available information, especially related to data on the following aspects of ENMs:

- Production volumes
- Types of uses
- Amount of emissions
- Pathways/environmental fate
- Exposure
- Geographical distribution of emissions
- Extent of damage caused to the environment by exposures to ENMs
- Monitoring data

Despite these data gaps, we can clearly identify that the key environmental benefits of NanoExplore are to address several of those data gaps, by increasing the information on exposure levels and gathering toxicological data.

The impact of the project has been assumed at '15% average reduction' of exposures and is stated to mainly stem from reduced releases of ENMs in the environment (and to a lesser extent to market withdrawal) due to proper selection of risk management measures, such as selection of cost effective filters and handling procedures.

Environmental Performance in numbers:

- Number of sensors installed: **8**
- Change in the amount of environmentally hazardous nanomaterials of **PM 2.5** and **PM 10** releases in industrial and urban areas: **7%** in industrial sites, 3% in urban areas (according to annual European inventories)
- Reduction or substitution of dangerous substances: **8%**
- Enhancement of the performance of risk management measures (RMMs)
- Awareness-raising through the application of the RMMs in industry and the overall dissemination of project results

A secondary impact of the project, which is a result of the reduction of releases of ENMs, is the improvement of water quality, which however cannot be quantified in the framework of the present project.

Table 2. Environmental Performance Summary

Parameters	Medium term (2 y)	Long term (5 y)
Changes in the amount of environmentally hazardous nanomaterials. PM2.5 and PM10 releases in industrial and research workplaces	7% reduction of the released amount	15% reduction of the released amount
Enhancement of the performance of risk management measures	8% reduction of the released amount	20% reduction of the released amount
Total reduction	15% reduction of the released amount	35% reduction of the released amount

Transferability of Results

Several actions have been taken to transfer the results of the project at the EU level. Some of these transferability activities include:

- Transfer of the human monitoring protocols to relevant institutions in EU countries other than those represented by the project.
- Development of a good practice manual for human biomonitoring of ENMs considering the specificities of areas other than those represented in the project. The manual has been shared at regional, national and EU level through chemical associations, occupational medicine related institutions and public centres with responsibilities in guarantee a high level of safety for all citizens.
- Identification of supporting institutions to promote the dissemination of the approach, including tools and services needed to sustain dissemination. Among the supporting institutions, the following bodies have been identified: ministries of health, ministries of environment, universities, local administrations (regions, provinces, city councils), trade associations and private foundations or other institutions interested in the outcomes of the project.
- Dissemination of the ideas and the results of the project through the 8 partners' 11 scientific publications so far, participation in international conferences such as NanoTox, International Symposium on Biological Monitoring in Occupational and Environmental Health, as well as continuous publication of informative leaflets, booklets, banners, and newsletters and through the NanoExplore website. Presentations, brochures, newsletters, publications and other material can be found here: www.lifenanoexplore.eu

Conclusion

The activities of NanoExplore resulted in the implementation of a network of sensors for indoor and urban environments for monitoring exposure in workplaces and public areas. This achievement was the first international collaborative study of human biomonitoring studies, where the partners developed a harmonised protocol.

The harmonised protocol includes:

- Determination of reference values of selected biomarkers
- Derivation of Occupational Exposure Levels (RELs) for workers and of four OEBs for the nanomaterials risk assessment
- Guidance on the use of human biomonitoring and exposure data for REACH implementation and epidemiological purposes

The transferability of project achievements is guaranteed through the consideration of various development conditions, such as network and guidelines for human biomonitoring. The tools developed as part of this project are applicable to other chemicals, taking into account technical issues, economic factors, regulatory aspects, acceptance of relevant stakeholders (international and across different industrial sectors).

Through the dissemination activities, professionals in the fields of nanotechnology and other fields were trained to enable replicability of the results beyond the project. Tools to support replicability are delivered as an e-learning platform with flexible access and workshops for interactive exchange.

Contact

Project Coordinator: Dr. Athena Progiou

Address : 18, Troias str., 11257 Athens GR

Tel.: +302108223083

E-mail: ap@axonenviro.gr; nano@al-fa.gr

www.lifenanoexplore.eu

Project Partners

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