

NanoExplore – A pilot study to demonstrate the feasibility of a harmonized approach for monitoring exposure to engineered and incidental nanoparticles and their potential health effects

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Background and Objectives

The increased **production and handling of nanomaterials (NMs)** have raised concerns regarding the potential of unforeseen health effects, especially among **exposed workers**. Implementing **epidemiological investigations on longitudinal cohorts** is key to ensure workers safety. Therein, **biomarkers** are useful in early detection of exposure-related health alterations.

The objectives of the NanoExplore pilot study are to:

- Assess the **feasibility of a harmonized approach** across participating countries (Switzerland, Italy, Spain and Germany)
- Validate a set of **exposure and effect biomarkers**, and evaluate their associations with air concentrations in terms of causal inference after reducing, whenever possible, exposure

A device to monitor external exposure

Device developed by **RAMEM (Madrid, Spain)** comprising 3 modules in one case:

- A **nanoparticle sensor (Partector 2)** for the real-time measurement of particle physical properties in the nanometer range (number concentration, size and Lung-Deposited Surface Area [LDSA]).
- An Optical Particle Counting (OPC) module to measure mass concentrations in real-time for particulate matter with sizes inferior to 1 (PM1), 2.5 (PM2.5) and 10 µm (PM10).

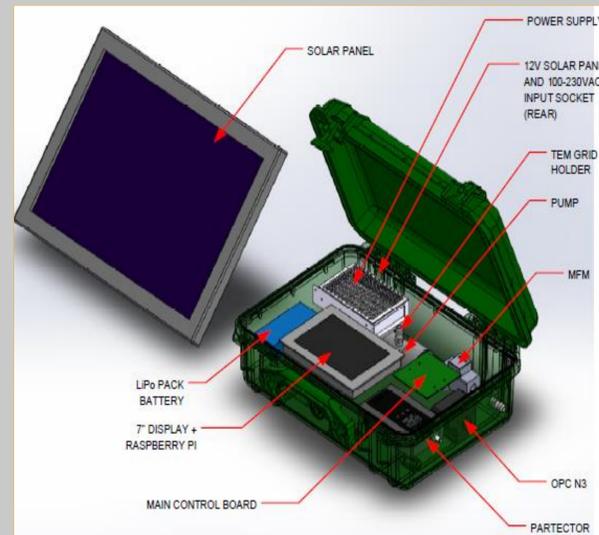


Figure 1: Image by courtesy of RAMEM.

- A TEM-grid module with polycarbonate filters to collect airborne particles and analysis of particles' chemical profile, average size distribution and shape.

Design, Population and Methodological approach

➢ **International multi-center prospective cohort across Switzerland, Italy, Spain and Germany**

➢ **Two-step consecutive sampling procedure:**

1. Recruitment of **companies** manufacturing and/or handling engineered NMs, and/or concerned with incidental NM exposure
2. Recruitment of **volunteer workers** within these companies

'Exposed' group (n = 80): Workers who are occupationally exposed to engineered and incidental NMs.
'Internal control' group (n = 40): Workers who are not occupationally exposed to NMs, from the same companies
'Universal control' group (n = 40): Workers from Consortium institutions in Switzerland, Italy, Spain and Germany

➢ **Two field campaigns conducted with a 6-month interval, aiming at assessing associations between workers' external exposure and individual biomarkers of exposure and effect:**

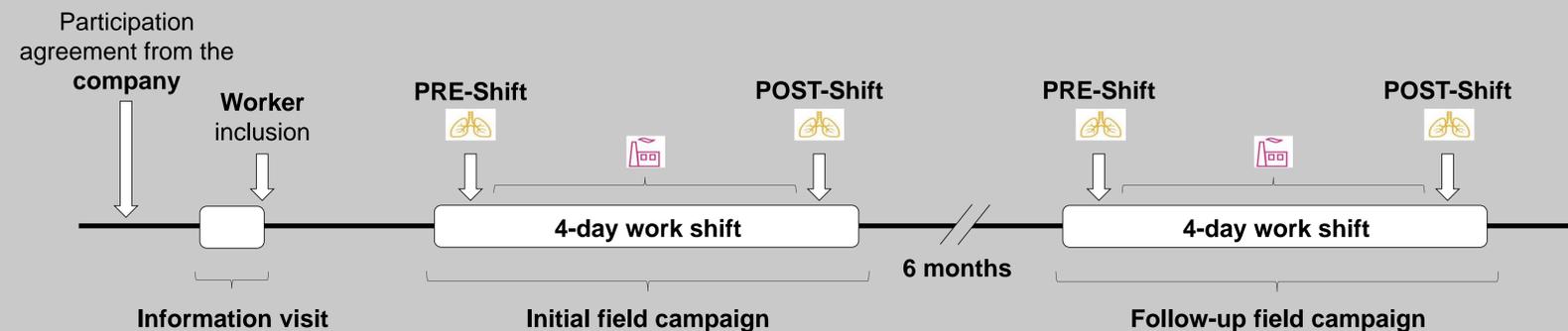


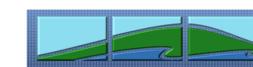
Figure 2: Pilot study design, consisting of two field campaigns conducted with a 6 month-interval. An information visit conducted beforehand will serve to collect company-related information, inform and enroll volunteer participants.

Individuals' biomarkers of oxidative stress (e.g. 8-isoprostane, MDA, oxidative potential), inflammation (e.g. interleukins, TNF-α) and DNA damage (e.g. 8-OHdG) will be analyzed from biological matrices (urine, Exhaled Breath Condensate [EBC] and Expired Air [EA]) collected at the beginning (PRE-shift) and end (POST-shift) of a working week.

External exposure monitoring

Ongoing progress and Agenda

- The present integrated protocol has been accepted by referent **ethical committees** in Italy (Prot. N°368525) and Switzerland (CER-VD N°2020-01098), and ongoing in Spain and Germany
- Field **campaigns for the 'Universal Control' group (n = 43)** are completed in Switzerland (Unisanté; October 2020; n=16) and Italy (University of Torino; October-November 2020; n=27)
- Company **recruitment** is ongoing in Spain, Italy, Switzerland and Germany
- Initial **field campaigns for 'Internal Control' and 'Exposed' groups** within recruited companies are planned for May – July 2021 (Italy, Spain), with follow-up campaigns in Fall 2021.



NanoExplore is partly funded by the European Commission Life with grant agreement LIFE14 ENV/GR/000285

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