Sample preparation for solubility of nanomaterials risk assessment

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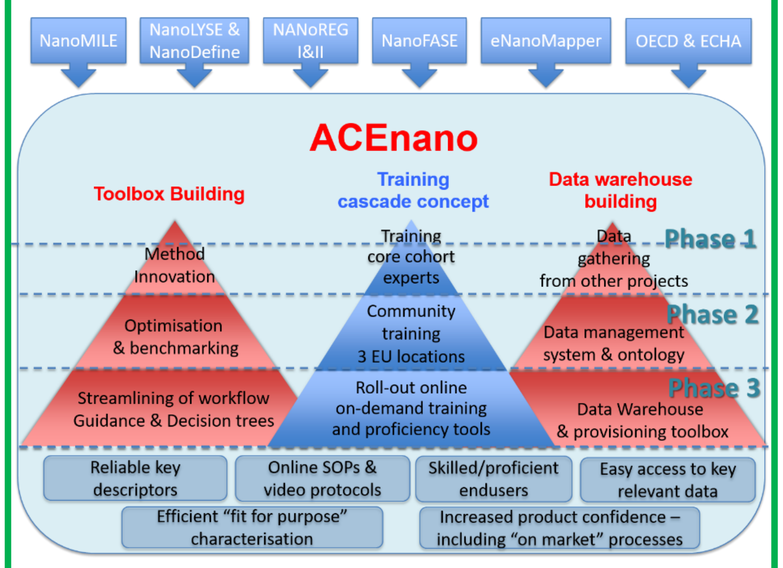
Engineered nanomaterials are being produced in exponentially increasing quantities, due to their unique physical and chemical properties and the improved performance of final products, and therefore spur technological and economic progress. However, **assessment of potential risks** associated with nanomaterials in an **industry-friendly manner**, is still lagging behind considerably. Solubility of nanomaterials has been identified in the nanosafety research community as a potential key property to be assessed and included in a cost efficient analysis that will facilitate decision-making in choice of techniques and support quality control, labelling and anti-counterfeiting. Here we present the development of a **wellplate based preparation system** for **automated nanomaterials mixing and incubation** for 24 assays in parallel for consecutive feeding into an analysis system, e.g. an ICP-MS.

ACEnano vision: Confidence, adaptability & clarity

The vision of the European H2020 research project ACEnano is to introduce confidence, adaptability and clarity into nanomaterial (NM) risk assessment by:

- Innovation in NM physicochemical characterization methods
- Delivery of a robust tiered approach in characterization
- Development of widely implementable analytical tools, with a simple and facile contextual description
- Initiation of a reliable NM grouping framework
- Support for stakeholders and users

Visit: www.acenano-project.eu



3. The plate can be put on a plate shaker (prevention of particle settlement):

Hours to days

Plate shaker

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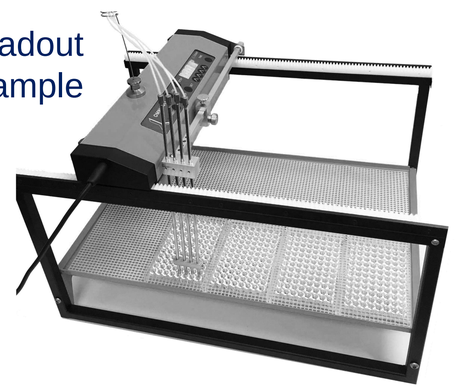
4. An autosampler can pierce the readout well of interest in order to recover the sample and transport to the analysis system

Auto sampling



5. Solubility can be assessed with a single-particle ICP-MS (ion concentration and particle size measurement)

Analysis: ICP-MS

2. When introducing the plate into the Minca reader, mixing is done automatically (pneumatics) in <1 second

Mixing & incubation

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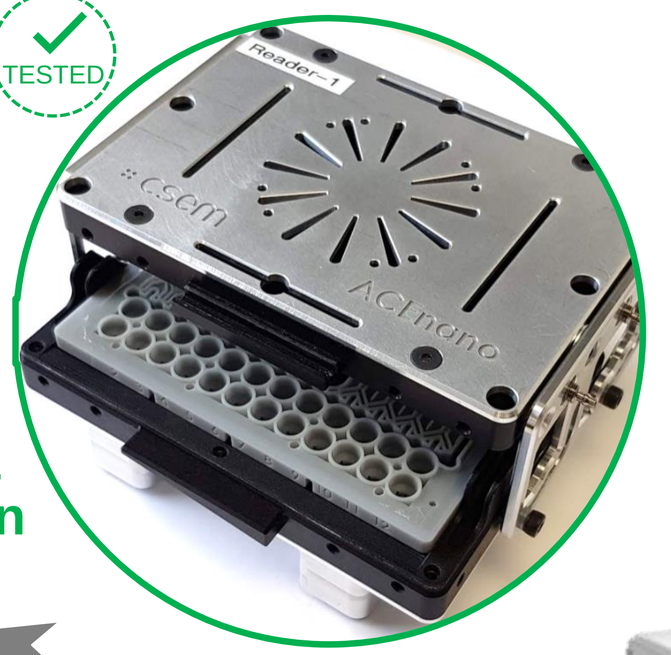

Robotic / manual pipetting

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1. ANSI-SLAS sized microfluidics plate can be filled manually or with a robot: 24x binary A & B (1:1)

Automation for solubility monitoring of nanomaterials

NM solubility has been identified in the nanosafety research community as a potential key property to be assessed.

NM dissolution and dissolution rate is essential in two respects: (i) it's a direct control of the concentrations of NMs and of the time that the NMs reside in the solvent, and (ii) it determines the concentrations of dissolved species that originate from the nanomaterials[1].

A new approach is being developed in ACEnano that will be included in a conceptual toolbox in order to facilitate decision-making in choice of techniques and support quality control, labelling and anti-counterfeiting, focusing on:

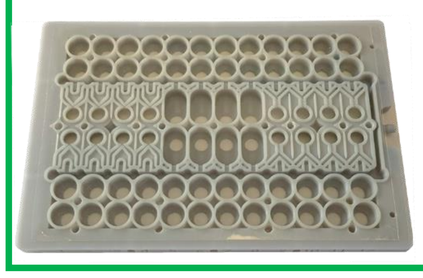
- Providing a **reliable** and **fast** tool
- Drastically **reducing time-consuming manual handling** and **human error**: Automated sample preparation unit for mixing and incubation of NM in solutions of interest
- Single particle inductively coupled plasma mass spectrometry (ICP-MS) analysis: **Ion concentration** & **particle size** measurement

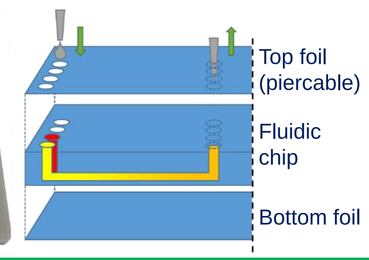
[1]: SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), Risk assessment of products of nanotechnologies, 19 January 2009

Microfluidic plate: 24 assays parallel mixing & incubation

A microfluidic chip has been developed in a standard ANSI-SLAS 96 wellplate format. The chip features **24 parallel assays** for binary 1:1 mixing (A: NM in solution, B: solvent of interest).

- Manual or robotic pipetting, max. 300 µl/well
- In-plate mixing and incubation
- Max. **550 µl mixure**, can be recovered with autosampler through piercable top foil
- Single-use disposable plate (injection molded)

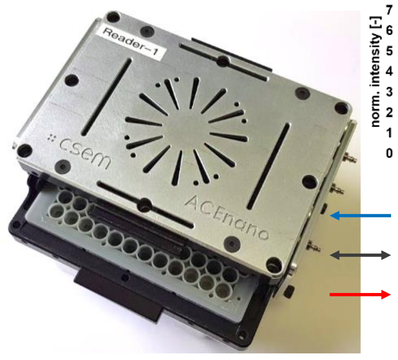


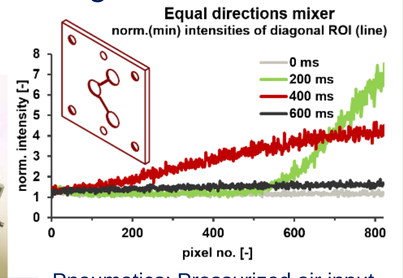


CSEM Minca: Versatile reader with pneumatics & optics

A compact reader (15x10x6 cm^3) has been developed and tested.

- Pneumatic mixing of 24 assays in <1 s
- Integrated absorbance readout: Laser-based (2 wavelengths differential mode) for reactivity or concentration monitoring





Pneumatics: Pressurized air input

Control: Laptop, Simple GUI

Optics: 24-channel differential absorbance reader, e.g. for concentration measurement

Conclusions & Outlook

Manual sample preparation for NM solubility assessment is time consuming and error-prone. A **microfluidic chip** (ANSI-SLAS standard size) for **automatic mixing** and incubation of 24 parallel assays has been developed with a compact and versatile pneumatic activation system. Efficient mixing (<1 s) and incubation has been **successfully tested (cycle steps 1-3)**. Next are tests including probing with an autosampler and consecutive analysis with ICP-MS (steps 4-5).