Do we need to validate existing methods for risk assessment of nanomaterials?

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Ca. 1.000+ nanotechnology based products on the market*

Increasing production, use and disposal of nanomaterials

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Increasing exposure to society and the environment

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Increasing occupational, consumer and environmental health risks

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Increasing impact along the whole life cycle of ENMs

* Source: Project on Emerging Nanotechnologies (PEN), AOLNEWS, Gallery: Nano-Products Are Everywhere Mar 24, 2010

- **Last 10 years of nanosafety research shows that current measurement + testing methods:**

  - not accurate
  - hardly reproducible
  - mostly not validated
  - high variation of biological responses
  - endpoints + dose levels often not appropriate
  - many false negatives + positives

Source: Hunt and Riediker 2011: Building expert consensus on problems of uncertainty and complexity in nanomaterial safety, NanoImpactNet

Non-validated methods ➢ high uncertainty of knowledge:

- hazard
- exposure
- dose-response
- bioavailability
- bio-persistence
- accumulation
- transport and fate

Due to method uncertainties, current RA and LCA are uncertain:

- not based on scientifically sound data
- not supported by robust validated methods

➢ RA and LCA methods not reliable

Why do current measurement and testing methods hardly match nanomaterials?

- capture not unique physicochemical properties
- biological responses strongly related to these properties
- nano-bio-interactions highly depend on test media and environment conditions

OECD list of endpoints for pc properties:

- • Agglomeration/ aggregation
- • Water solubility/ Dispersability
- • Crystalline phase
- • Dustiness
- • Crystallite size
- • Representative Electron Microscopy (TEM) picture(s)
- • Particle size distribution – dry and in relevant media
- • Specific surface area
- • Zeta potential (surface charge)
- • Surface chemistry (where appropriate)
- • Photocatalytic activity
- • Pour density
- • Porosity
- • Octanol-water partition coefficient, where relevant
- • Redox potential
- • Radical formation potential
- • Other relevant pc properties and material characterization information

From: Guidance Manual for the Testing of manufactured Nanomaterials: OECD's Sponsorship Programme; Fist Revision [ENV/JM/MONO(2009)20/REV].

New research confirms:

- fundamental importance of nanomaterial characteristics (surface metrics, charge, chemistry, dispersion, agglomeration/aggregation, surface adsorption ("corona") for biological effects
- type of test media and environment crucial
- translation of results from one to another NP form of the same nanomaterial inappropriate
- hazard differs from hazard associated with dissolved forms of the same material (as used in classical tox-tests)

Johnston et al. 2009

Why validated methods?

- If your methods are not validated, only you will know how good your method and results are!
- Validated methods tested in many laboratories on the same samples showing that the method is robust to produce comparable results in different labs and with different operators!
- Regulators and manufacturers can be sure that they compare "apples to apples"!
- Only validated methods prove compliance with regulatory standards!

Validated methods help:

- to obtain high quality and comparability of analytical results
- to get acceptable accuracy and precision
- to identify false positives or false negatives
- to assist method standardization and compliance with standards
- to allow accreditation of control laboratories
- to support classification and product labeling
- to facilitate registration + authorization (REACH)
- to provide EU wide harmonization of quality control systems

Validated methods based on:

- calibration
- recovery (labeling) experiments
- method inter-comparison (RR)
- investigation of robustness (RR)
- definition of parameters to be validated
- comparability of results

http://www.labcompliance.com/tutorial/methods/default.aspx

Validated methods improve:

- Accuracy
- Precision
- Specificity/selectivity
- Limit of detection
- Limit of quantitation
- Linearity and range
- Robustness (interlaboratory studies)
- Applicability to a wide range of different samples with specific properties and specific environmental and test conditions

U.S. EPA, Guidance for methods development and methods validation for the Resource Conservation and Recovery Act (RCRA) Program, Washington, D.C. (1995).,

Validation of methods includes:

- the whole assessment chain from design, fabrication, sampling, storage, transport and sample preparation until detection and quantification
- dispersion/agglomeration/aggregation control in test media
- exposure dose and condition control
- control of robustness by round robins to get a reproducible measure of uncertainty and variability of results

Urgent need

1
- Test, validate and further develop existing methods for fabrication, characterization and hazard assessment

2
- Develop reference methods and materials for synthesis, sampling/sample preparation, measurement, labeling, dispersion control and biological testing towards further standardization

3
- Develop reliable RA + LCA applicable to nanomaterials

NanoValid is addressing these needs:

Synthesize reproducibly stable nanomaterials and test conditions

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Validate existing measurement + testing methods

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Develop new reference methods + materials applicable to ENMs

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Develop reliable RA and LCA approaches for ENMs

NanoValid

- NanoValid: Large-scale integrating collaborative project
- Title: “Development of reference methods for risk and life cycle assessment of engineered nanomaterials”
- Project number: 263147
- Consortium: 29 +1 partners from 17+1 countries
- Total budget: 13.3 mio. €
- Requested EC contribution: 9.6 mio. €
- Duration: 2011 to 2015
- Coordinator: Rudolf Reuther, NordMiljö AB, SE
- Project officer: Nicolas Segebarth, EU Commission
- Contact: www.nanovalid.eu

NanoValid: Consortium

Type of organization	Partners
University	University of Tampere **FI,** University of Salzburg **AT,** University of Zaragoza **ES,** University of Namur **BE**, University of Lublijana **SI**, Federal University of Minas Gerais **BR**, McGill University **CA**
Private-public research institution	Fraunhofer Gesellschaft **DE**, Helmholtz-Centre for Environmental Research **DE**, University of Birmingham **UK**, National Institute for R&D in Micro-technologies **RO,** National Institute for Chemical Physics and Biophysics **EE,** Indian Institute for Toxicology Research **IN,** Centre for Cellular and Molecular Biology **IN**
Governmental body	Federal Institute for Occupational Safety and Health **DE**, Federal Institute for Materials Research and Testing **DE**, German Institute for Standardization **DE**, National Institute of Metrology, Standardization and Industrial Quality **BR**, Swiss Federal Institute of Aquatic Science and Technology **CH**, National Research Centre for the Working Environment **DK**, US Environmental Protection Agency **US** (associated by LOI)
SME	Nanologica **SE,** Grimm Aerosol Technologies **DE,** Straticell **BE,** QUANTIS **CH,** Institute of Nanotechnology **UK,** Nordmiljö **SE**
Large industry	Centro Ricerche FIAT, **IT,** ARKEMA **FR,** Veneto Nanotech **IT,**

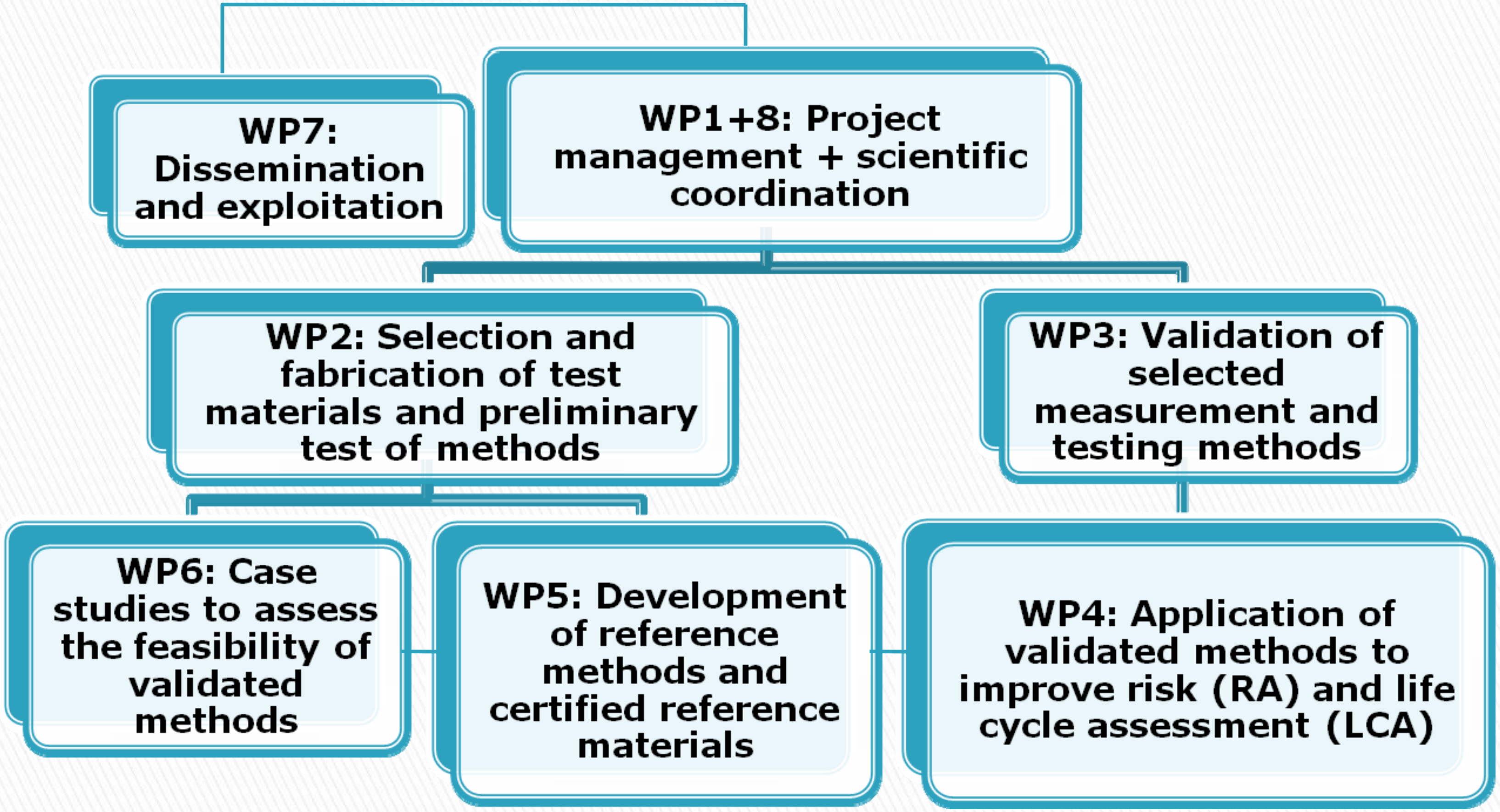
NanoValid: Countries

Austria (1)	India (2)
Belgium (3)	Romania (1)
Brazil (2)	Slovenia (1)
Canada (1)	Spain (1)
Denmark (1)	Sweden (2)
Estonia (1)	Switzerland (1)
Finland (1)	United Kingdom (2)
France (1)	United States (1) (associated by LOI)
Germany (6)	
Italy (2)	

NanoValid: Test Materials

Priority 1	Priority 2
metals (**Ag, Au** and Pd)	quantum dots (CdSe, CdS, CeO_2)
metal oxides (**SiO_2, TiO_2**, ZnO, CuO)	ceramics, nanoclays
CNT (SWCNT, MWCNT)	salts (Ca-phosphate, PbS)
fullerenes	nanocellulose
	polystyrene, dendrimers

NanoValid work plan

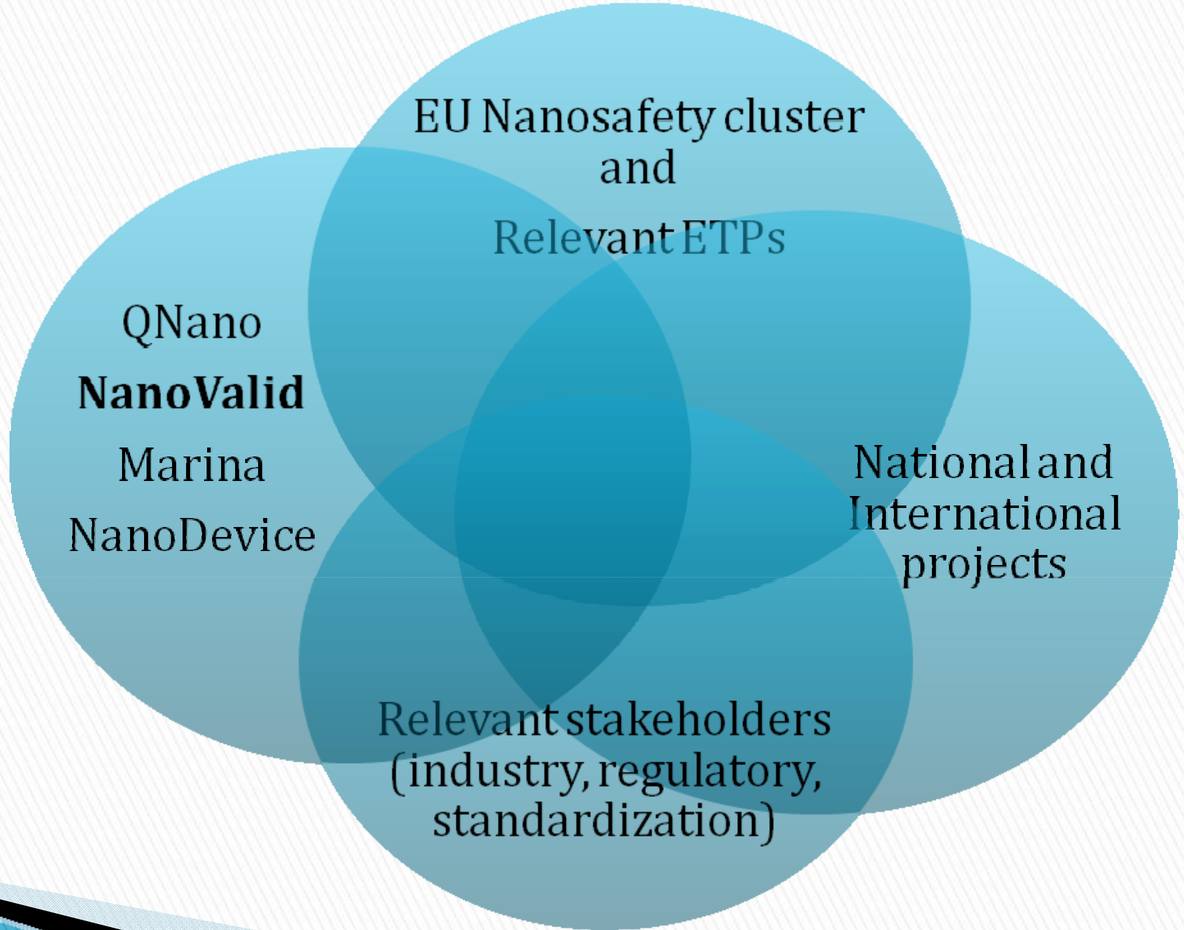


Step 5 (WP6)

Assess feasibility of validated and established reference methods under "real" conditions

- **Case study 1:** assess **occupational exposure** of manufacturing
- **Case study 2:** develop **online monitoring** of airborne exposure
- **Case study 3:** study **environmental** behavior, fate + impact
- **Case study 4:** assess **accidental risks** associated with transport
- **Case study 5:** develop **risk reduction strategies** for handling
- **Case study 6:** improve nanosafety in the **automotive industry**.

Thank you!


EU Nanosafety cluster
and
Relevant ETPs
QNano
NanoValid
Marina
NanoDevice
National and
International
projects
Relevant stakeholders
(industry, regulatory,
standardization)