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Nanoreg: New standard operating procedures to evaluate the effectiveness of risk management measures

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INTRODUCTION

1. INTRODUCTION

Background Information

- In the occupational context, it has been demonstrated that **workers have the potential to be exposed to uniquely ENMs** with novel sizes, shapes, and chemical properties, at levels far exceeding ambient concentrations.

- As nanotechnology applications move from research laboratories to industrial and commercial settings, the **likelihood of workplace exposure** and industrial releases will tend to increase.

- Studies conducted so far under several initiatives revealed that a **significant release of submicron sized particles**, including single particles, aggregates and agglomerates (< 1000 nm) and embedded in a solid matrix (i.e. polymers) , can be expected during the production and downstream use of ENMs.

1. INTRODUCTION

Background Information

Examples of operations that may lead to direct contact and emission of ENMs from workplace operations are:

- Production, handling or use of ENMs in powder form or dispersed in liquids.
- Packing / Bag filling from laboratory to industrial scale facilities
- Abrasive machining of materials containing ENMs (e.g. milling, polishing, sanding, etc.).
- Processes that are not completely contained.
- Interfaces between contained and open process steps (e.g., loading and un-loading, sampling, etc.
- Waste disposal

Emission Source	NPs Type	Measured levels range
Primary / SD1		
Liquid-phase reaction	PGNP	4.0×10^4 to 11.0×10^6
Flame spraying	PGNP	4.7×10^3 to 1.0×10^6
CVD	PGNP	Non-significant
Top-down (milling)	ENPs / PGNP	
Secondary NP aerosol / SD2		
Weighing of powders	ENPs	$2.0X10^4$ to $7.0x10^4$
Harvesting	ENPs	$2.0X10^4$ to $5.0x10^4$
Manual packaging (Bagging)	ENPs / PGNP	$20.0x10^4$
Bag emptying of powders	ENPs	Significant increase
Melt Blending	ENPs / PGNP	$> 1.0x10^5$
SD3a / SD3b		
Spraying of liquid	ENPs	$2.0x10^8$
Spraying (gas)	ENPs	$1.6x10^5$ to $2.0x10^{10}$
Injection Molding	ENPs	$> 8.0x10^5$
Brushing and rolling	ENPs	$> 6.0x10^5$
Sonication of nanodispersions	ENPs	$> 8.0x10^6$
Tertiary NP aerosol / SD4		
Abrasion of nanoproducts	PM / EMNP	$8.0x10^3$ to $2.0x10^4$
Drilling	PM / EMNP	$4.0x10^4$
Grinding	PM / EMNP	$3.0x10^3$ to $1.0x10^6$

1. INTRODUCTION

State of the art and basics on risk management

- knowledge, data, and test methods on common risk management measures for NMs are still very limited, which implies a **severe knowledge gap** on the effectiveness of currently available RMMs during nanomaterial production and handling processes

- Several research projects, including NanoMICEX (FP7-280713), GUIDEnano (FP7-604387)or NanoRISK (LIFE12 ENV/ES/178), are working to help bridge this gap by providing:
    - Reliable data on the effectiveness of personal protective equipment (PPE) and engineering controls (ECs) when dealing with NMs in dry form and/or dispersed in liquid)
    - Innovative tools to support the selection of proper controls to reduce the exposure to ENMs in the workplace

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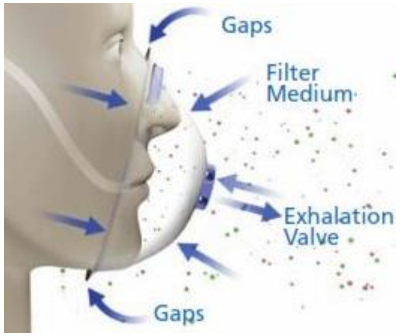
1. INTRODUCTION

State of the art and basics on risk management

- The performance factors "level of protection" studied under relevant initiatives are based on the testing requirements defined under current standards, telling us quantitatively how capable the product is in reducing the risk (directly or indirectly).

Measures	RMM Type	Performace
Respiratory protective equipment (RPE)	Filtering Facepiece (FFP)	Total Inward Leakage (TIL)
	Half-Face mask (HM) Full-Face mask (FM)	Inward Leakage (IL) Total Inward Leakage (TIL) Nominal protection factor (NPF)
Dermal protective equipment	Chemical protective gloves (DPE-Gloves	Permeation Penetration Nominal protection factor (NPF)
	Protective clothing	Total Inward Leakage (TIL) Nominal protection factor (NPF)
Eye protection	Safety glasses Safety googles	Total Inward Leakage (TIL)
Ventilation	Local Exhaustive ventilation	Capture efficiency (Cf)



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2. Effectiveness of common RMMs against ENMs

Most of the research activities related with the evaluation of the effectiveness of RMMs have been limited to RPE, and only a limited number of studies have reported information on the effectiveness of chemical protective gloves, protective clothes and/or technical measures.

- **Respiratory protective equipment (RPE)**

PPEs	Type	ENM	Size (nm)	Efficiency (ENMs)	Certified efficiency	Reference
Filtering facepiece respirators (FFP)	N95 (free of oil aerosols)	NaCl	20-500	P95 > 85 %	≥ 95 %	Gao S, et al. 2015
	P95 (oil resistant)			N95 > 91 - 99 %		
	N95	NaCl	10-400	98.79 - 99,10%	≥ 95 %	Vo E, et al. 2015.
	P100			99.77 - 99,98%	≥ 99.97 %	
	FFP1	NaCl	93-1600	93.60 - 95.00%	≥ 78 %	Lee SA, et al. 2016
	FFP2			91.90 - 93.50%	≥ 92 %	
	FFP3			86,50 - 93.90%	≥ 98%	
	N95	NaCl	7 - 289	96,90%	≥ 95 %	Ramirez JA, et al. 2016
	N95			94,70%		
	N95	NaCl	8 - 400	98,47%	≥ 95 %	Rengasamy et al; 2011b,
	P100			99,23%	≥ 99.97 %	
	FFP2			65,30%	≥ 92 %	
	FFP3			97,80%	≥ 98%	
	N95 A	NaCl	10 - 600	94 - 95,00%	≥ 95 %	BaŁazy, A. et al. 2006
	N99	NaCl	< 0,1 µm	95,50 - 97.40	≥ 99 %	Eninger, R. M., et al.. 2008.
	N95 B			96,60%	≥ 95 %	
Half-mask respirator	N95	NaCl	10-400	>99,49%	≥ 95 %	Vo E, et al. 2015
	P100			99.98 - 99,99%	≥ 99.97 %	

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2. Effectiveness of common RMMs against ENMs

Protective Clothes

PPEs	Type	ENM	Size (nm)	Efficiency (ENMs)	Certified efficiency	Reference
Protective clothes	Cotton fabric	Graphite	35 - 40	F.F.E: 73,00%	≥70 %	Golanski L, et al. 2009
	HD Polyethylene textile			F.F.E: 99,40%	≥ 99.7 %	
	Cotton fabric	TiO2	9 - 90	F.F.E: 73%	≥70 %	Golanski L, et al. 2010,
	HD Polyethylene textile	Pt	9 - 19	F.F.E: 99,40%	≥ 99.7 %	
	Woven and fibrous fabrics	NaCl	100- 500	F.F.E: 50 - 80%	≥ 97 %	Huang S.H, et al. 2007
	Nonwoven fabrics (A,B,C)	NaCl	14 - 400	F.F.E: A, B, C >99%	≥ 99.7 %	Ben Salah, et al 2016
	Woven fabrics (D, E)			F.F.E: 91.5%	≥ 97 %	

Protective Clothes

PPEs	Type	ENM	Size (nm)	Efficiency (ENMs)	Certified efficiency	Reference
Protective gloves	Nitrile	TiO_2 NPs	5nm	Penetration observed	Only for liquids	Vinches et al. 2011
	Nitrile / Neoprene /Latex/ Vinyl	Graphite	40 nm	No penetration		Golanski et al. 2009a
	Latex / Nitrile	Silver	90 nm	Penetration observed		Park et al. 2011
	Nitrile and latex glove	Nanoclay Al2O3		No penetration		Ahn et al.

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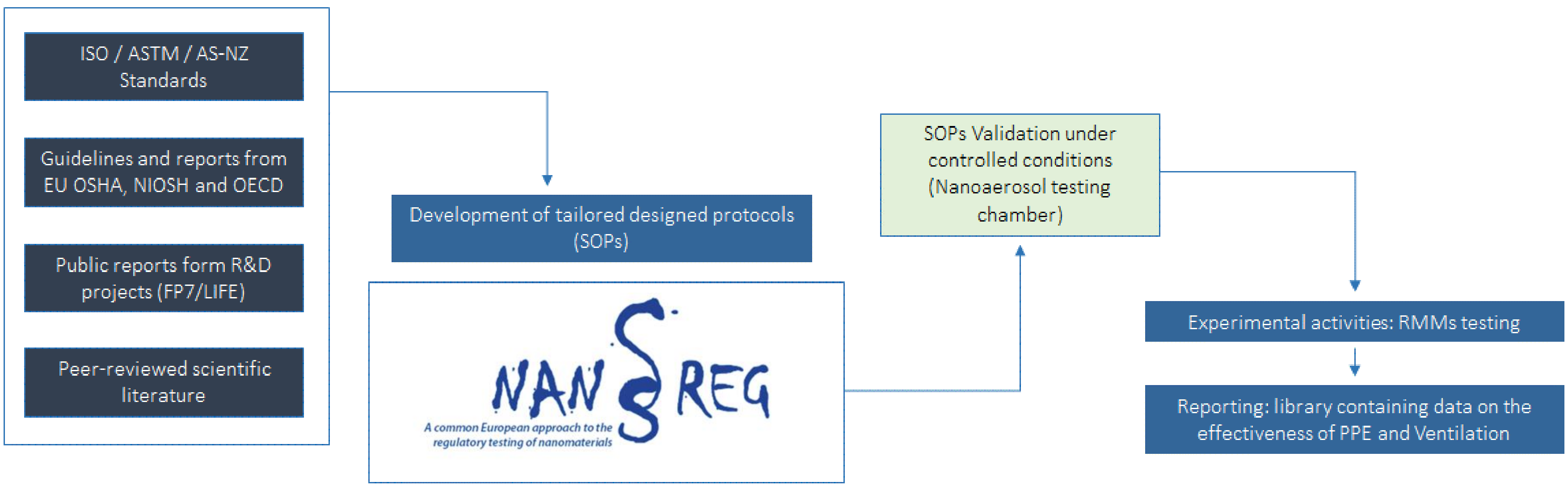
3. Standardization: SOPs for common RMMs testing against ENMs

Definition of testing approaches (SOPs)

- Considering these conflicting results, as well as the current lack of harmonized approaches, In the nanoREG project, we proposed a work plan based on the definition of reproducible and robust standard operating procedures (SOPs) based on principles and procedures stablished in existing standards, as well as experi-mental approaches retrieved form peer reviewed publications.



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3. Standardization: SOPs for common RMMs testing against ENMs

Definition of testing approaches (SOPs)

- A total of 8 SOPs were developed, including 3 for respiratory protection (masks, filters), 3 for protective clothing (coats, gloves), 2 for engineering controls (LEVs).

1. Determination of inward leakage of nanoparticles
2. Determination of total inward leakage of nanoparticles
3. Determination of particle filter penetration by nanoparticles
4. Determination of inward leakage of aerosols of nanoparticles into suits
5. Determination of resistance to penetration by spraying a liquid solution of nanoparticles
6. Determination of permeation to nanoparticles in gloves
7. Determination of the capture efficiency of local exhaust ventilation
8. Determination of fume hood effectiveness

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3. Standardization: SOPs for common RMMs testing against ENMs

Definition of testing approaches (SOPs)

- The testing and validation experiments were conducted in our exposure chamber prototype, developed within the EU funded project NanoRisk and placed at the ITENE facilities.

The developed SOPs were validated prior to the beginning of the experimental activities under controlled conditions to support a quantitative evaluation of the potential differences in the performance factors values resulting from test conducted by different technicians.

The experimental set-ups were developed, adapted and refined to comply with the requirements of the SOPs stablished. Moreover, protocols were revisited and when necessary, adapted to the limitations of the experimental tests.

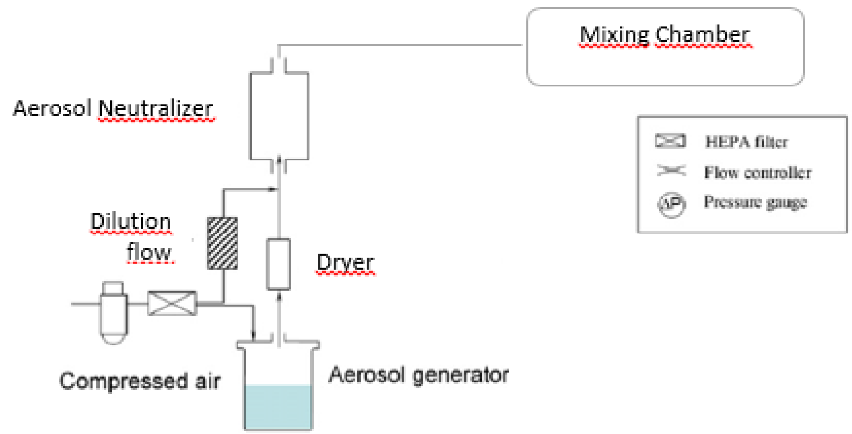
NANOREG
A common European approach to the regulatory testing of nanomaterials

Definition of testing approaches (SOPs)

- Aerosol generation: NaCl and metal oxides nanoparticles

The experimental protocols defined in selected harmonized standards require the use of non-toxic gases or particles to perform the studies. The use of sodium chloride (NaCl) is the preferred solution according with peer reviewed publications and harmonized standards, being selected as testing substance.

The generation of NaCl particles was achieved by means of a submicrometer aerosol generation system composed of constant output atomizer (TSI 3076), a diffusion dryer (TSI 3062) and an aerosol Neutralizer (TSI 3012). Compressed air first passes through a Filtered Air Supply, where the air is cleaned and dried. This conditioned air is used to power a Constant Output Atomizer (TSI 3076).



16. New SOPs for RMMs testing - NanoREG

zation: SOPs for common RMMs testing against ENMs

erating procedures (SOPs)

Cover page, including document history and version control

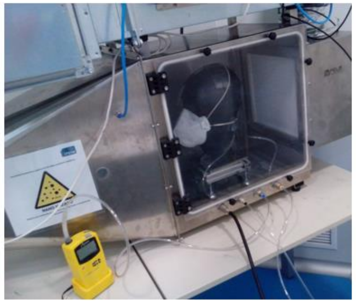
1. **Scope and objectives of the SOP**
   Chapter 1 defines the types of risk management measures covered by the SOP, reference standards, and main goal of the operating procedure.
2. **Definitions**
   Chapter 2 contains definitions of technical terms used within the operating procedure.
3. **Performance factor and principle of the method**
   Chapter 3 clearly defines the performance factor to be characterized under the scope of the procedure, as well as the working principle of the operating procedure.
4. **Requirements**
   Chapter 4 defines basic considerations of the procedure, including minimum number of samples and replicates, testing concentration, sample conditioning, and issues concerning health and safety. The structure of the chapter can be split as follows:
   4.1. Number of Samples
   4.2. Testing Concentration
   4.3. Conditioning
   4.4. Replicates and control
   4.5. Safety and health
5. **Measurement Equipment**
   Chapter 5 provides information on the specifications of the equipment to be used to characterize the performance of the RMM under the scope of the procedure.
6. **Pre-requisites**
   Chapter 6 includes a list of elements to be considered before starting the test, including sampling storage, visual examinations or pre-testing, among others.
7. **Operating procedure**
   Chapter 7 details the steps to be conducted to evaluate the performance of the risk management measures to be studied under the scope of the operating procedure. The experimental set-up and testing protocol are detailed in figures to support the reproduction of the procedure.
8. **Calculation procedure**
   Chapter 8 provides instructions to analyse the data and calculate the values of the performance factors defined under the scope of the procedure.
9. **Validation criteria**
   Chapter 9 provides information on the quality criteria to be considered to validate the results of the test completed.
10. **Data treatment and reporting**
    Chapter 10 provides instructions to report the results of the test, including recommended forms, units and contextual information to be provided.
11. **References**
    Chapter 11 provides a list of related harmonised standards and peer reviewed publications.

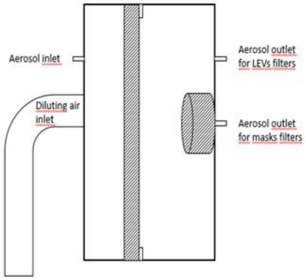
Parameter	Units	Plexiglass box	Nanoaerosol testing chamber
Concentration of Sodium Chloride solution	%	0.5	0.5
Initial temperature - Chamber	ºC	25.6	25.6
Initial relative humidity - Chamber	%	45.2	45.2
Final temperature - Chamber	ºC	27	27
Final relative humidity - Chamber	%	50.5	50.5
Sample flow	L/min	0.6	0.6
Maximum concentration	Nº pt/cm3	2.78E5	2.78E5
Minimum concentration	Nº pt/cm3	3.0×10^4 part/cm^3	3.0×10^4 part/cm^3
Particle diameter	nm	42 nm	48 nm
Particle size distribution	nm	40 - 44	40 - 55

NanoSafe 16. New SOPs for RMMs testing - NanoREG

3. Standardization: SOPs for common RMMs testing against ENMs

Standard Operating procedures (SOPs)

RMM	PF	Description	Set up pictures
Respiratory Protective Equipment (RPE)	Inward Leakage (IL) / Total inward leakage (TIL)	Scope: characterization of the efficiency of respiratory protective equipment (RPE), including the experimental evaluation of Total inward leakage (TIL) and inward leakage (IL). TIL, is defined as the penetration of particles into the respiratory protection device (RPD), including face seal, valves and gaskets, and penetration through the filter. IL refers the penetration of particles into RPD excluding filters. Objective: ensure that RPD are capable of providing a minimum level of protection against airborne nanoparticles. Reference substance: NaCl particles (50 – 80 nm) Set up (1) – Test with a Sheffield head NaCl particles are conducted to the testing furnace, where a Sheffield head carrying a respirator is placed. The Sheffield head is a manikin head with internal pipes, which let to collect the air from the inside of the mask Set up (2) – Test with human subjects Subjects are placed on a treadmill and while walking, they are asked to do a list exercises defined in current ISO standards. In both set ups, the concentration of NaCl particles is measured inside and outside the RPD tested by means of direct reading devices (CPC, OPS, P-Track, SMPS). Performance factor: RPD efficiency and particle penetration (P) expressed as percentage. $Penetration\ \boldsymbol{P}(\%) = 1{,}25 * \frac{C_2}{C_1} * 100$ Efficiency $\boldsymbol{E}(\%) = 100 - P(\%)$ Where, C1: test concentration C2: average concentration measured inside the facepiece 1,25 is a correction factor due to the retention of sodium chloride in the lungs	  



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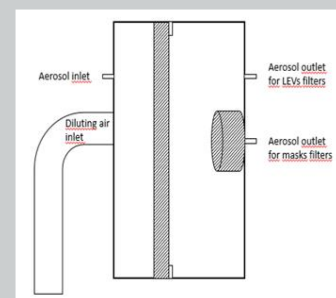
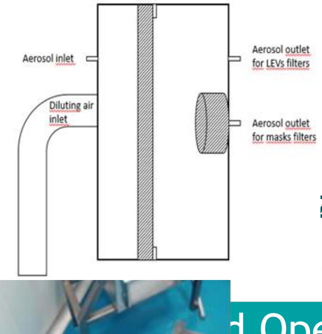
zation: SOPs for common RMMs testing against ENMs

Standard Operating procedures (SOPs)

RMM	PF	Description	Set up pictures
Respiratory Protective Equipment (RPE)	Filter penetration	Scope: characterization of the penetration of ENMs through particulate filters during exposure to an aerosol flow. Objective: ensure that particulate filters are capable of providing a minimum level of protection against ENMs. Reference substance: NaCl particles (50 – 80 nm) Set up: the evaluation of the filter penetration is conducted using a metal box in which an aerosol containing NaCl nanoparticles is inserted and diluted with clean and dry air. The metal box is equipped with a filter holder especially structured to contain either the LEV filter or a masks respiratory filter. The levels of ENMs are measured upstream and downstream of the filter being tested by means of direct reading devices (CPC, OPS, P-Track, SMPS). Performance factor: particle penetration (P) $P(\%) = \frac{C_2}{C_1} * 100$ Efficiency $\boldsymbol{E}(\%) = 100 - P(\%)$ Where, C_1 NaCl concentration before the filter; C_2 average concentration measured after the filter.	 



16. New SOPs for RMMs testing - NanoREG

zation: SOPs for common RMMs testing against ENMs

d Operating procedures (SOPs)

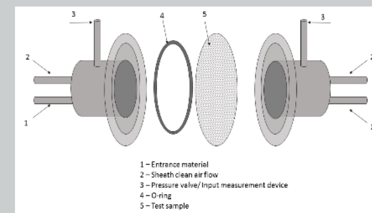
RMM	PF	Description	Set up pictures
Protective clothes	Particle penetration	Scope: characterization of the penetration of ENMs through chemical protective clothing (CPC) during exposure to an aerosol flow. Objective: ensure that CPC are capable of providing a minimum level of protection against airborne nanoparticles. Reference substance: NaCl particles (50 – 80 nm) Set up: tests can be performed using a mannequin (static) or volunteers (dynamic). Three points of the suit are selected to measure the concentration inside, which is then compared with the concentration outside the suit A sheath flow of clean dry air is supplied inside the suit at the same flowrate as the measuring devices are suctioning in order to no create depression or a false result. The sleeve ends of the suit, as well as seams, closures, zips, etc. are sealed to avoid penetration through opened parts and only test the suit material. Test conditions (human subjects): - 3 min standing - 3 min walking - 3 min squatting. - 3 measurement probes: chest, waist and knee - Six suits tested Performance factor: Nominal Protection factor (NPF) and Total average inward leakage (TIL_A). Total average inward leakage is reported as a ratio of the test particle concentration inside the suit and the test chamber (For all six suits, all the exercises and all 3 probes). $TIL_A = \frac{Concentration\ of\ test\ particles\ (inside\ suit)}{Concentration\ of\ test\ particles\ in\ the\ chamber}$ Nominal protection factor = 100/(TILA) Reference standard: UNE-EN ISO 13982-2 2005	 

3 – Pressure valve/Input measurement device
4 – O-ring
5 – Test sample

16. New SOPs for RMMs testing - NanoREG

zation: SOPs for common RMMs testing againts ENMs

erating procedures (SOPs)

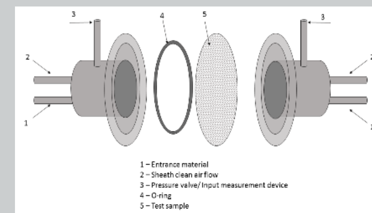
RMM	PF	Description	Set up pictures
Chemical protective gloves	Particle Penetration	Scope: characterization of the penetration of airborne nanoparticles through glove material Objective: ensure that chemical protective gloves are capable of providing a minimum level of protection against airborne nanoparticles. Reference substance: NaCl particles (50 – 80 nm) Set up: a specimen is cut from the glove and clamped into a test cell as a barrier membrane. The "exterior" side of the specimen is exposed to airborne NaCl nanoparticles, and concentrations are measured at both sides of the glove and compared. Performance factor: particle penetration (P_n (%)) The percentage of penetration is calculated from the measurements at each side of the glove, considering C_{out} the concentration right before the glove and C_{in} after the glove sample. $P_n(\%) = \frac{C_{in}}{C_{out}} * 100$ Reference standard:	
Protective gloves	Permeation	Scope: characterization of the penetration of nanoparticles diluted in a water based solution through the glove material by permeation mechanisms. Objective: ensure that chemical protective gloves are capable of providing a minimum level of protection against nanoparticles dispersed in water or solvents. Reference substance: NaCl particles (50 – 80 nm) Set up: to test permeation to liquid dispersions of nanoparticles, a Teflon cell is required. In this case, a circular sample of the glove is placed in rest between the liquid dispersion and a filter sampler that will be analyzed after 8 hours of being in contact. Performance factor: particle permeation Reference standard:	

3 – Pressure valve/Input measurement device
4 – O-ring
5 – Test sample

16. New SOPs for RMMs testing - NanoREG

zation: SOPs for common RMMs testing against ENMs

erating procedures (SOPs)

RMM	PF	Description	Set up pictures
Chemical protective gloves	Particle Penetration	Scope: characterization of the penetration of airborne nanoparticles through glove material Objective: ensure that chemical protective gloves are capable of providing a minimum level of protection against airborne nanoparticles. Reference substance: NaCl particles (50 – 80 nm) Set up: a specimen is cut from the glove and clamped into a test cell as a barrier membrane. The “exterior” side of the specimen is exposed to airborne NaCl nanoparticles, and concentrations are measured at both sides of the glove and compared. Performance factor: particle penetration (P_n (%)) The percentage of penetration is calculated from the measurements at each side of the glove, considering C_{out} the concentration right before the glove and C_{in} after the glove sample. $$P_n(\%) = \frac{C_{in}}{C_{out}} * 100$$ Reference standard:	
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4

CONCLUSIONS

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4. CONCLUSIONS

- A set of 8 SOPs covering personal protective and technical measures were developed and validated
- This SOPs provide a robust experimental set up to evaluate the effectiveness of common PPE and technical measures when dealing with ENMs in the workplace.
- SOPs are expected to be available by March 2017 as part of the SOPs included in the NanoREG Toolbox.
- Results from testing activities show that a key parameter to ensure the effectiveness of respiratory protective equipment is the face seal. It is highly recommended to use RPE offering innovation in face seal, ranging from new silicone based materials to inflatable seals.
- The use of double glove is recommended. Wear latex or nitrile gloves when handling nanoparticle powders and nanoparticles in water suspension. The use butyl rubber gloves in highly recommended when dealing with ENMs dispersed in solvents.
- The use of non-woven materials made of non-woven high density polyethylene textile offers excellent barrier protection for sub-micron particles.

ISES 2016. RMMs TO CONTROL THE EXPOSURE TO ENMs

Acknowledgements

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A common European approach to the regulatory testing of nanomaterials
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