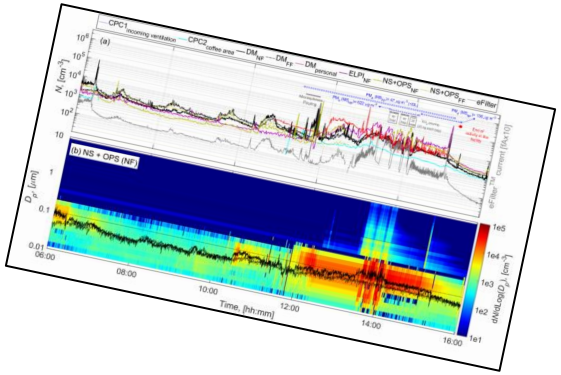
National Research Centre for the Working Environment

nanoSAFE

Value-chain case-studies with high quality conceptual information for model testing

caLIBRAte
nano risk governance



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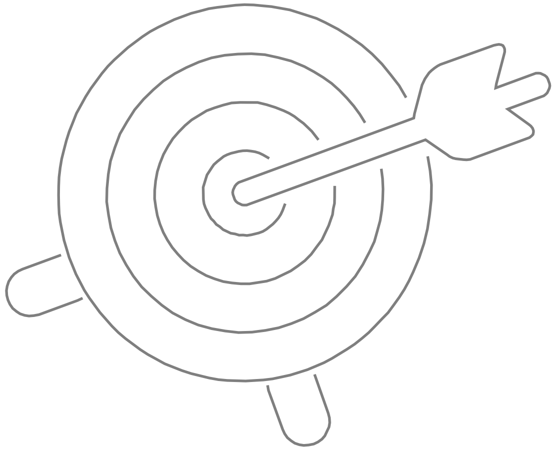
Tuesday, 6 November 2018

OUTLINE



- **Current challenges in nano risk governance**
- **Models and tools for risk assessment**
  - CaLIBRAte models and tools
  - Input parameters required
- **Performance testing**
  - Identification of data sources
  - Evaluation of data availability to cover requirements by the different models
  - Inventory of case studies
  - Evaluation of data quality
- **Example of a case study**
  - Measured vs. modeled exposures
- **Conclusions and research needs**

CURRENT CHALLENGES IN NANO RISK GOVERNANCE

Fast moving market of nanomaterials

Risk assessment approach is inadequate for enabling safe use of NM. Lacking robust sources of quantitative data

So far, the existing **nano-specific control banding tools and quantitative models** were **not thoroughly tested, calibrated and validated**!

caLIBRAte nano risk governance

Next generation (system-of-systems) risk governance portal for assessment and management of human and environmental risks of NM

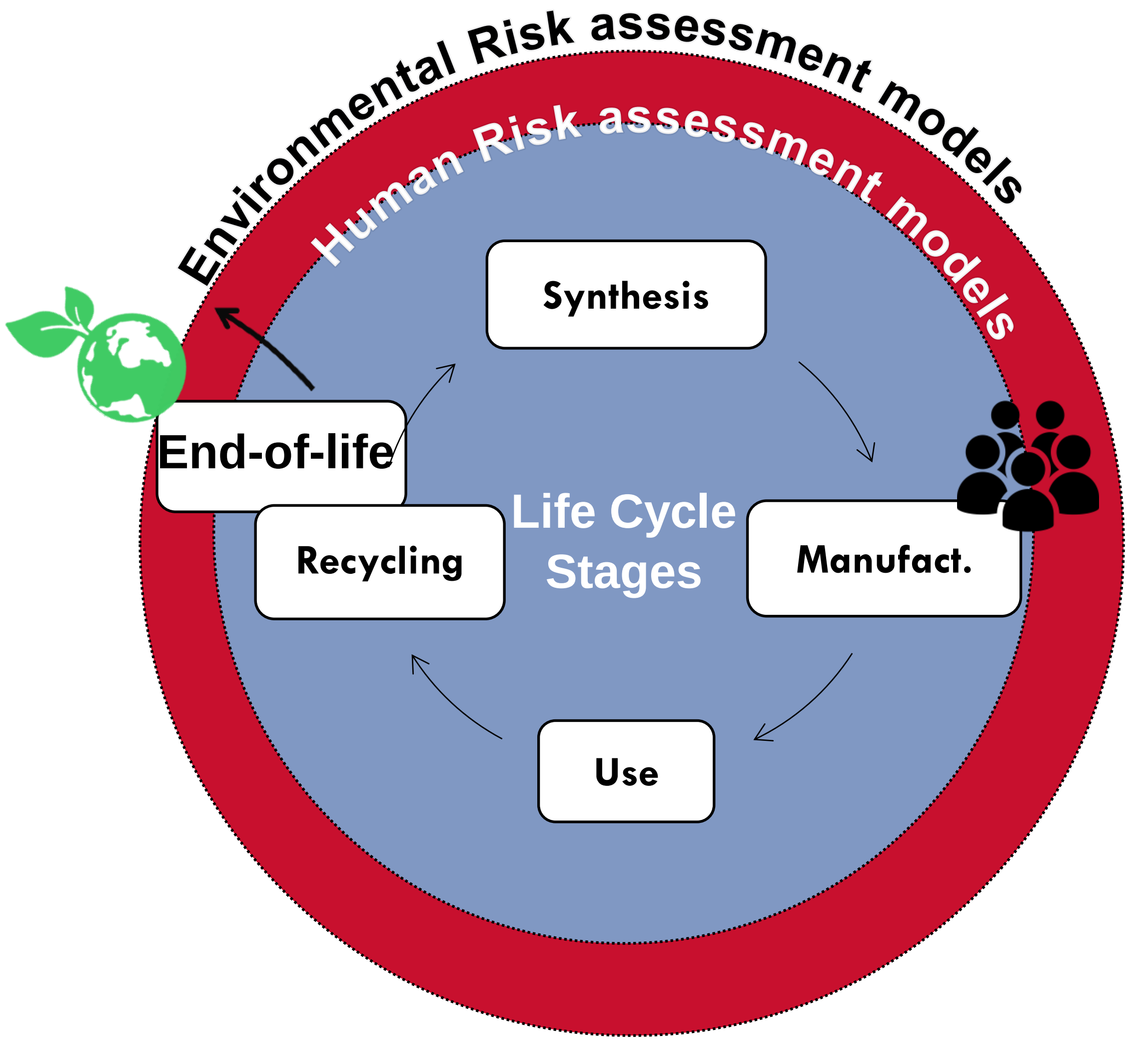
- Design safer nano-enabled products
- Facilitate decision-making on risk uncertainties
- Support compliance with regulatory frameworks
- Provide homogenous rules for safe management of NMs

See poster number A91810KJ!!

SELECTION OF MODELS AND TOOLS FOR RISK ASSESSMENT

No.	Model name	Application area	Owner	Model type
1	ANSES tool	Work	ANSES	CB
2	ISO TS 12901 CB tool	Work	ISO	CB
3	US Nanotool	Work	LLNL (USA)	CB
4	StM Nano	Work	Cosanta (NL)	CB / RM
5	NanoSafer CB	Work	NRCWE	CB / RM
6	ConsExpo Nano	Cons	RIVM	QEA
7	BAUA SprayExpo	Work	BaUA (DE)	QEA
8	RiskofDerm	Work	TNO	QEA
9	IEAT	Work	IOM	QEA
10	Swiss PM	Env/Cons/Work	FOPH (CH)	Risk Cat
11	LICARA NanoScan	Env/Cons/Work	EMPA/TNO	Risk Benefit
12	SUNDS	Env/Cons/Work	UNIVE / GD	RA / RM
13	GuideNano	Env/Cons/Work	LEITAT	RA / RM
14	nano-QSAR	Human/Env.	Tomas Puzyn	QHA
15	SimpleBox4Nano	Env	RIVM	QEA
16	Mendnano	Env	UCAL (USA)	QEA
17	NanoDuFlow	Env	WA (NL)	QEA
18	RedNano	Env	UCAL (USA)	QEA
19	n-SSWD	Env	UNIVE	QEcotox

Abbreviations: Env - environmental, Cons - consumer, CB – Contol Banding, RA – Risk Assessment, RM –Risk Management, QEA – Quantitative Exposure Assessment, QHA – Quantitative Hazard assessment, Risk Cat – Risk Categorization



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Tier 0: Risk categorization (qualitative)

Tier 1: Control-banding (qualitative or semi-quantitative)

Tier 2: Basic predictive control banding / risk assessment (one or two box models)

Tier 3: Quantitative risk assessment

REQUIRED INPUT PARAMETERS

HRA tools and models

1. **<u>Material/particle properties (200):</u>** morphology/shape, average size, density, dustiness,…

2. **<u>Environment/room properties (59):</u>** room geometry, emission controls, ventilation rate,…

3. **<u>Process properties (240):</u>** Descriptors for emissions/concentrations (e.g. task duration and frequency, emission rate,…).

4. **<u>Limit values/Toxicity (84):</u>** Descriptors for the material hazardousness/toxicity (e.g. proposed OELs, DNEL, shape, and solubility).

5. **<u>Other parameters (143):</u>** All the variables that were not classified under the other groups. Examples of such variables include variables required for linking to other (sub)models, some natural constants, and variables for operating the numerical solvers of the models.

PERFORMANCE TESTING

Modelings *vs.* Measurements

Model INPUT
Real Data

Model OUTPUT
Predicted Data

Tested by comparing the modelling results with the observations (real data)

REQUIREMENT

High quality measurement data with comprehensive contextual information

- Exposure databases (NECID, GUIDEnano library)
- Data generated in EU Projects
- Literature

\+

Dustiness library
Continuous Drop & Rotating Drum
Dustiness index
Dustiness kinetics

PROC-USE[1]
Release data library
Spray
Mechanical wear
Mechanical reduction
Leaching

ECEL[2]
Emission control efficiency library
Engineered control equipment

[1] PROC-USE: Process and Product Use; Data based on Mackevicka and Hansen (2016) and Koivisto *et al.* (2017)

[2] ECEL: Emission Control Efficiency Library for nanomaterials (Fransman *et al*. 2008)

EVALUATION OF DATA AVAILABILITY

Exposure databases

Category	Human exposure: occupational and consumer exposure parameter	NECID	MARINA
Test substance	Physical-chemical characteristics (see Annex 3)	✓	✓
	Type of product (~100% nano or intermediate/final product; incl. weight fraction of nano in product)	✗	✓
	Physical form of nanomaterial/product (liquid, powder, solid matrix)	✓	✓
	In case of powders: dustiness category (e.g. very high, high, medium, low).	✓	✓
	Moisture for powders	✓	✗
	Occupational exposure limits (also respirable dust)	✗	✗
	In case of liquid: viscosity (e.g. low, medium, high)	✓	✗
	Product category and preferable product type	✗	✗
Test subject	Exposed body area (cm^2)	✗	✗
	Measurement location (breathing zone, source, distance from source/ person)	✓	✓
	Amount of nanomaterial/nanoproduct used.	✓	✓
	Route of exposure	✓	✓
	Location (inside/outside and size of room in m^3)	✓	✓
Activity / Process / Methods	Description of exposure scenario (type, room dimensions, ventilation rate)	✓	✓
	Activity/application method (spraying, brushing, pouring, etc.) or description of use product (amount of product used)	✓	✓
	Release/emission rate (mass/time)	✗	✗
	Activity handling energy factor	✓	✓
	Frequency, duration of exposure and exposure pattern	✓	✓
	Cleaning and maintenance of the room	✓	✓
	Used exposure controls (Local & General Exhaust Ventilation Monitoring ; LEV/GEV, personal protection equipment; PPEs etc.) and preferably type of LEV/GEV, PPE used and efficiency (air changes per hour).	✓	✓
	Background concentration	✓	✓
	Activity level in room (Describes the environment in which the activity, exposure or release of nanoparticles occurs, e.g. distance from the source)	✓	✓
	Detailed description of experimental measurements and procedures	✓	✓
	Climate conditions (temperature and relative humidity)	✓	✓
	Description of secondary sources (diesel engines, cigarette smoke, welding, busy road, etc.	✓	✓

- GUIDEnano library and NECID cover most of the parameters dealing with occupational exposure requested by the HRA models.

release/emission rates and OEL are not included.

- Some datasets are available

- Other databases have been identified to cover single parameters (release/emission rates, dustiness).

COLLECTION OF HUMAN EXPOSURE SCENARIOS

Examples for TiO_2

Phase	Source domain	Specific activity	Source
Synthesis (1)	Handling and transfer of bulk manufactured NM powders	TiO_2 particle collection during flame spray synthesis	(Koivisto et al., 2012) (NANOHEALTH)
Synthesis (2)	Handling and transfer of bulk manufactured NM powders	Jet -milling and packing processes of pigment and nano-TiO_2	(Koivisto et al., 2012) (TEKES and FinNano Program)
Synthesis (3)	Handling and transfer of bulk manufactured NM powders	Recovery and handling of TiO_2 NFs during product finalization	(Bressot et al., 2018) SANOWORK
Synthesis (4)	Synthesis and Handling and transfer of bulk manufactured NM powders	Sol-gel synthesis and handling of nano-TiO_2 in an industrial research laboratory (in a fume hood)	(Fonseca et al., 2018) SUN and HINAMOX
Synthesis (5)	Synthesis	Manufacture of TiO_2 Nanoparticles. Synthesis by flame pyrolysis	GUIDEnano library (ES377)
Synthesis (6)	Handling and transfer of bulk manufactured NM powders	Packing of TiO_2	GUIDEnano library (ES352)

COLLECTION OF HUMAN EXPOSURE SCENARIOS

Life cycle chain of TiO_2 and SiO_2

Human Exposure

	Synthesis	Manufacturing	Professional Use	End-of-life
SiO_2	•Handling and transfer of NM powder (X14) •Dispersion of intermediates/application of ready-to-use products (liq. and pow.) (X4) **18 ES**	• Handling and transfer of NM powder (X1) •Dispersion of intermediates/application of ready-to-use products (liq.) (x1) •Hot processes (X2) •Compressing of powders or granules (x1) • Fracturing and abrasion of •solid objects (x6) **11 ES**	•Fracturing and abrasion of solid objects (x4) •Spraying /Rolling activities (x10) **10 ES**	**GAP**
TiO_2	•Flame pyrolysis •Application of liquids in high speed processes •Wet chemistry •Laser ablation •Movement and agitation of powders or granules (X8) •Handling and transfer of powder **13 ES**	• Surface and spraying applications of liquids (X5) • Deposition / thermal treatments (x2) • Cleaning and maintenance (x2) •Activities with relatively undisturbed surfaces (no aerosol, x2) • Fracturing. and abrasion of solid Objects (x2) **13 ES**	**GAP**	**GAP**

COLLECTION OF HUMAN EXPOSURE SCENARIOS

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SiO_2	•Handling and transfer of NM powder (X14) •Dispersion of intermediates/application of ready-to-use products (liq. and pow.) (X4) 18 ES	• Handling and transfer of NM powder (X1) •Dispersion of intermediates/application of ready-to-use products (liq.) (x1) •Hot processes (X2) •Compressing of powders or granules (x1) • Fracturing and abrasion of •solid objects (x6) 11 ES	•Fracturing and abrasion of solid objects (x4) •Spraying /Rolling activities (x10) 10 ES	GAP
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- Largest number of exposure studies available: SiO_2>TiO_2>Ag>Cu-based
- Some clear general gaps: end-of-life stages
- Typical missing parameters in exposure scenarios: emission rates, dustiness, ventilation, physico-chemical properties etc. Therefore should be taken from other sources or recalculated

DATA INVENTORY FOR PERFORMANCE TESTING

- Data quality evaluated for 67 occupational exposure scenarios

47 studies were classified with rank > 0.7 [0 to 1]

	Weighing factor	Experiment code (**Exp_A1**) and NM, activity (**CuO, Pouring under fume hood**)	Experiment code (**Exp_A2**) and NM, activity (**TiO2, Spilling under fume hood**)
Overall quality		**1**	**0,90**
Relevance parameters		**Present in the study? (yes=1 no=0)**	**Present in the study? (y[illegible]**
Is any of the NMs (TiO2, SiO2, Ag, CuO, MWCNT) investigated in the study?	0	1	1
Is the activity belonging to any of these source domains (Release of primary particles during actual sinthesis; Handling of bulk aggregated/agglomerated nanopowders; Spraying or dispersion of ready-to-use nanoproduct)?	0	1	[illegible]
Reliability (=Quality) parameters		**Present in the study? (ye[illegible]**	**[illegible]=0)**
Study design			
Background measurements (mass preferably; If mass concentrations are not available a factor of 0.5 should be used)	4	1	[illegible]
Offline measurements	[illegible]	[illegible]	1
Personal sampling (mass preferably; If mass concentrations are not available a factor of 0.5 should be used)	[illegible]	[illegible]	0,5
NF and FF measurements in study? (mass preferably; If mass concentrations are not available a factor [illegible] be used)	[illegible]	[illegible]	0,5
Substance information			
NM identity (SDS of the specific material available)	5	1	1
Primary particle size/particle size distribution	3	1	1
Weight fraction (of NM in the product)	3	1	1
Morphology/Shape of the NM	3	1	1
Activity information			
Description of the activity[illegible]	5	1	1
Indoor/outdoor[illegible]	3	1	1
Produ[illegible]	3	1	1
[illegible]	3	1	1
[illegible]	5	1	1
[illegible] model testing WP6 will consider that no PPEs have been used		not considered in the formula	not considered in the formula
C[illegible] parameters		**Present in the study? (yes=1 no=0)**	**Present in the study? (yes=1 no=0)**
Du[illegible]ess of NM	5	1	1
Emission rate	3	1	1
Daily cleaning and monthly inspection	1	1	1
Room Size (m3)	3	1	1
Ventilation system (natural, mechanical, …)	3	1	1
Air exchange per hour (#/h)	1	1	1

EXAMPLE OF A CASE STUDY

Measured vs. modeled exposures

Pouring 700 g of CuO in a laboratory fume hood

J Nanopart Res (2018) 20:48
https://doi.org/10.1007/s11051-018-4136-3

CrossMark

RESEARCH PAPER

Particle release and control of worker exposure during laboratory-scale synthesis, handling and simulated spills of manufactured nanomaterials in fume hoods

Ana S. Fonseca · Eelco Kuijpers · Kirsten I. Kling · Marcus Levin · Antti J. Koivisto · Signe H. Nielsen · W. Fransman · Yijri Fedutik · Keld A. Jensen · Ismo K. Koponen

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National Research Centre for the Working Environment

Fonseca *et al*. (2018) J Nanopart Res., 20:48

MEASURED EXPOSURES

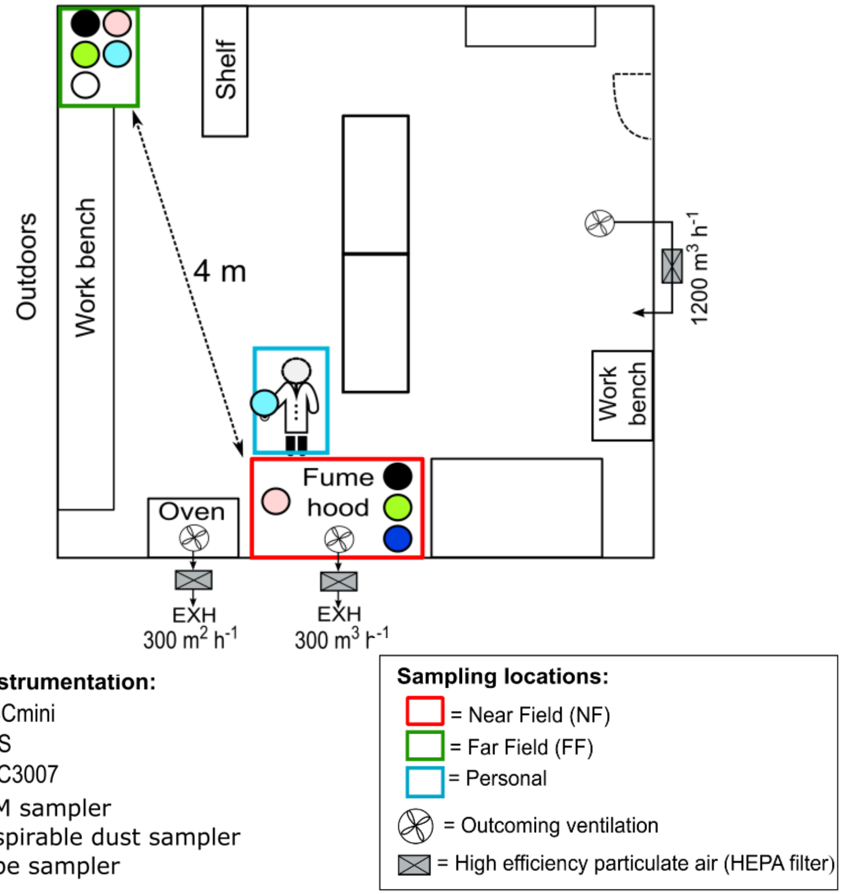
Pouring 700g CuO under a fume hood

- CuO (CAS No.1317-38-0)
- Primary size 40±10 nm

Material and safety data entered	Exposure situation data entered
Manufacturer: PlasmaChem GmbH	**Process type:** Powder handling
CAS: 1317-38-0	**Energy level:** H2 (0.25) : Low energy - (eg. < 5 cm drop height; handling of contaminated or leaking bags)
Relevance: Yes	**Amount used in cycle:** 0.7 kg
Coated: No	**Cyclus duration:** 1 min
Known shape: Yes	**Number of cycles per day:** 1 times
Morphology: Spherical / Isometric	**Pause between cycles:** 0 min
Shortest dimension: 40 nm	**Mass handled per task in cycle:** 0.7 kg
Size is known: No	**Time required per task in cycle:** 1 min
Average size: No	**Length room:** 7.25 meters
Size range known: No	**Width room:** 5.24 meters
Surface area: 15 m2/g	**Height room:** 3.52 meters
Relative density: 6.5 g/cm3	**Room air exchange** n/hour times per hour
Solubility: Insoluble (< 1 g/L)	**Activity level room:** Moderate
Respirable dustiness: 1.04 mg/kg	

Local control (fume hood) factor = 0.01

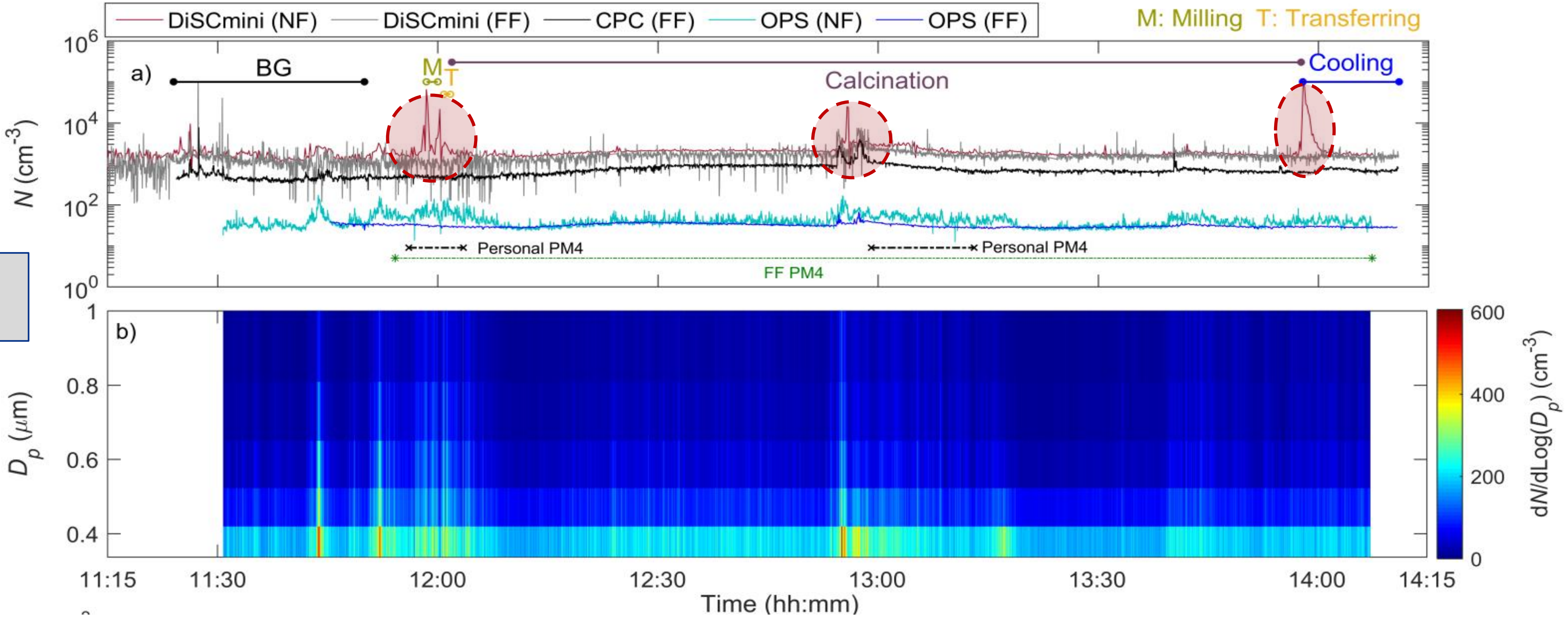
- NF (in the fume-hood)
- FF (4 m away from fume-hood)



MEASURED EXPOSURES

Pouring 700g CuO under a fume hood

- NF (in the fume-hood)
- FF (4 m away from fume-hood)



CuO average exposure level = 9.2 μg m^{-3}

Ratio NF/FF= 2.8

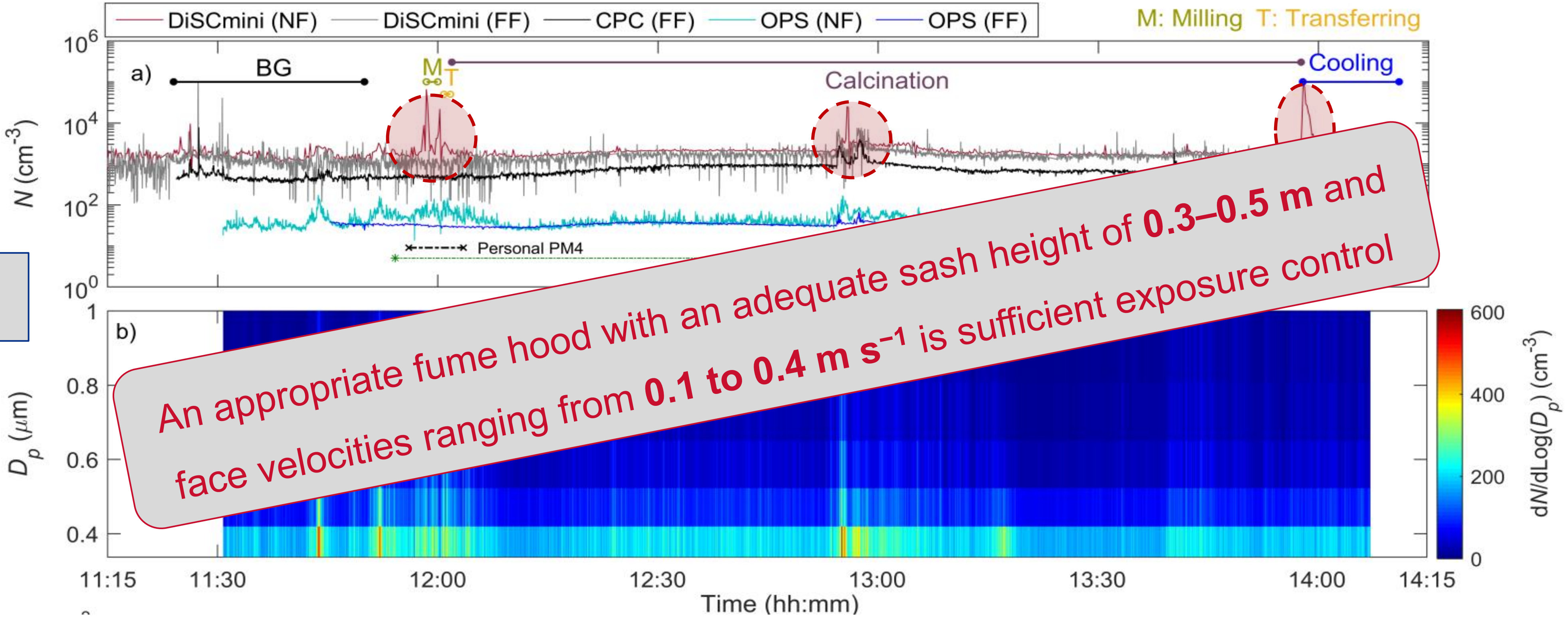
NP exposure may occur if the fume-hood is not working properly!

MEASURED EXPOSURES

Pouring 700g CuO under a fume hood

- NF (in the fume-hood)
- FF (4 m away from fume-hood)

CuO average exposure level = 9.2 μg m^{-3}



An appropriate fume hood with an adequate sash height of **0.3–0.5 m** and face velocities ranging from **0.1 to 0.4 m s^{-1}** is sufficient exposure control

Ratio NF/FF= 2.8

NP exposure may occur if the fume-hood is not working properly!

MODELED EXPOSURES

Pouring 700g CuO under a fume hood

ASSESSMENT BY TIER 2

NanoSafer v 1.1

Result of assessment

Estimated hazard level 0.2
The hazard level is estimated based on
High aspect ratio material: No
A high volume specific surface area of 97.50 m2/cm3
OEL of analogue bulk material: 1 mg/m3
Solubility: Insoluble (< 1 g/L)
Presence of surface coating: No
Known hazards of analogue bulk material

Estimated time-resolved exposure index

Near-field Acute	Near-field Daily	Far-field Acute	Far-field Daily
0.0025 EB1: Very low exposure potential	0.0000 EB1: Very low exposure potential	0.0002 EB1: Very low exposure potential	0.0000 EB1: Very low exposure potential

NF=1.5 µg m^{-3} < $M_{NF\ real\ work\ environment}$ (9.2 µg m^{-3})

Exposure \ Toxicity	0.76-1.00	0.51-0.75	0.25-0.50	0.00-0.25
>1.00	RL5	RL5	RL5	RL5
0.51-1.00	RL5	RL5	RL4	RL4
0.26-0.50	RL5	RL4	RL4	RL3
0.11-0.25	RL4	RL4	RL3	RL2
< 0.11	RL4	RL3	RL2	RL1

RL1: Very low toxicity and low exposure potential

$$OEL_{nano} = OEL \cdot \frac{30 \cdot \frac{1}{\delta}}{SSA_{nano}}$$

$$EXP_{Acute} = \frac{C_{Acute}}{2 \cdot OEL_{nano}}$$

$$EXP_{8-hour} = \frac{C_{8-hour}}{OEL_{nano}}$$

Specific density of the nanomaterial (g/cm³)

Specific surface area of the nanomaterial [SSA]; m²/g

MODELED EXPOSURES

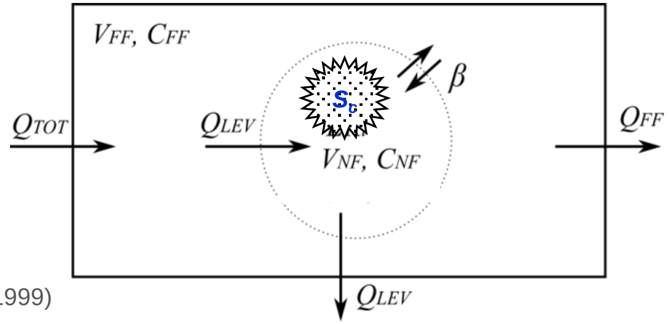
Pouring 700g CuO under a fume hood

ASSESSMENT BY TIER 2

Mass-balance 2-box model (NF/FF)

Modelling parameters:

Q_{TOT}	1200 $m^3\ h^{-1}$	Known
Q_{LEV}	300 $m^3\ h^{-1}$	Known
Q_{FF}	900 $m^3\ h^{-1}$	Known
λ	9 h^{-1}	Known (Q_{TOT} / V_{FF})
V_{FF}	133.6 m^3	Known
dM/dt	700 g min^{-1}	Known
V_{NF}	8 m^3	Assumed, same as Cherrie (1999)
β	10 $m^3\ min^{-1}$	Assumed



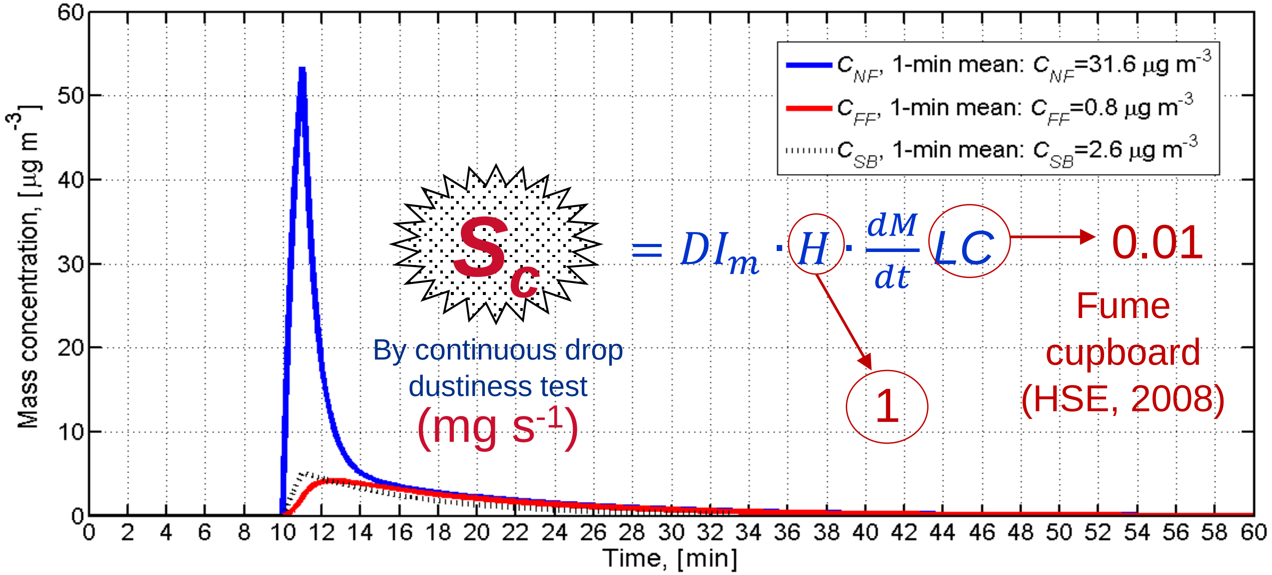
$$1{:}\ V_{FF}\frac{dC_{FF}(t)}{dt} = \beta C_{NF}(t) - (\beta + Q)C_{FF}(t)$$

$$2{:}\ V_{NF}\frac{dC_{NF}(t)}{dt} = S_C(t) + \beta C_{FF}(t) - \beta C_{NF}(t)$$

Particle removal by ventilation

Emission source strength

Compartment concentration



$$S_C = DI_m \cdot H \cdot \frac{dM}{dt} LC$$

S_C: By continuous drop dustiness test (mg s^{-1})

H → 1

LC → 0.01 Fume cupboard (HSE, 2008)

Pouring process under fume hood	DI_m ±σ [mg kg^{-1}]	S_c [mg min^{-1}]	M_{NF} real work environment [μg m^{-3}]	2-box Model: $M_{,NF}$ modeled [μg m^{-3}]	2-box Model: $M_{,FF}$ modeled [μg m^{-3}]
700 g CuO/ min	104	72.8	**9.2**	**31.6**	0.8

WELL PREDICTED!!

$$M_{NF\ modeled} > M_{NF\ real\ work\ environment}$$

Ganser & Hewett (2017) J Occup. Environ. Hyg., 14:1, 58-71

Zhang *et al*. (2009) Ann. Occup. Hyg., 53, 409–424

CONCLUSIONS

- ✓ We have models and tools for human risk assessment
- ✓ Validation and demonstration in real exposure scenarios is needed
- ✓ **STATUS:** All parameters requested by models have been described and sources of data identified.
  - **Largest number of exposure studies available:** SiO_2>TiO_2>Ag>Cu-based
  - **Only recent studies** take into account most of the parameters requested by HRA models
  - **Typical missing parameters:** emission rates, dustiness, ventilation, physico-chemical properties
  - **Some clear gaps of knowledge**: end-of-life stages
- ✓ Particle levels are fairly well predicted under aerosol modeling (Nanosafer and "*standard*" two-box model)

RESEARCH NEEDS:

- **High quality measurement data for model testing is needed!!**
- **Harmonized data libraries**

ACKNOWLEDGEMENTS

Home About Consortium News Newsletter Library Contact Project activities

Welcome

We are an interdisciplinary group of researchers, risk assessors, test facilities, and industry developing tools that manufacturers, authorities and companies can use to manage workplace risks during innovation, production and use of manufactured nanomaterials. Together, we are the caLIBRAte project.

Our Project

Currently, none of the existing REACH compliance models are suited or validated for risk assessment of manufactured nanomaterials and many existing exposure limits are not suitable for nanomaterials. CaLIBRAte will change this by developing a "systems-of-systems" based on a suite of tested and calibrated nano-specific risk prioritization and control banding tools. Our work will leverage more than a decade of nanosafety research and resources to develop models for next generation nano-risk governance framework.

Our Objectives

The key objective of the caLIBRAte project is to funnel the state-of-the-art in nanosafety research and merge it with state-of-the-art risk governance and communication sciences to establish a versatile risk governance framework for assessment and management of human and environmental risks of MN and MN-enabled products. The ultimate goal is that the quality and trust in the nano-specific models in the caLIBRAte risk governance framework will exceed current level of most existing REACH tools.

caLIBRAte
nano risk governance

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National Research Centre for the Working Environment

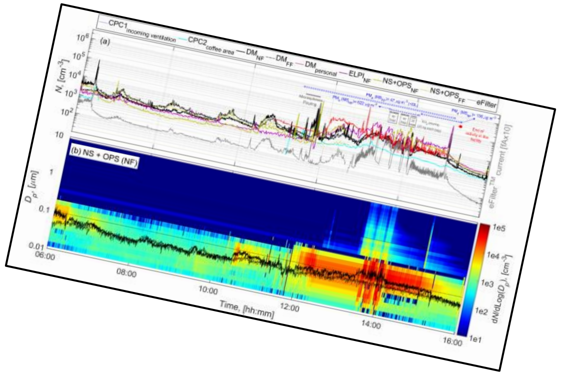
Webpage: www.nanocalibrate.eu

National Research Centre
for the Working Environment

nano SAFE

THANK YOU VERY MUCH FOR YOUR ATTENTION!

caLIBRAte
nano risk governance



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