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Webinar Precautionary Matrix for Nanomaterials


Guidelines on the Precautionary Matrix for Synthetic Nanomaterials

Sabine Frey & Christoph Studer
Federal Office of Public Health

caLIBRAte, March 8, 2018

Agenda

- Welcome
- **Andrea Porcari**, introduction to caLIBRAte and the webinar
- **Christoph Studer**, The Precautionary Matrix
- **Sabine Frey**, Precautionary Matrix demo, based on a case study
- General discussion
- Concluding remarks

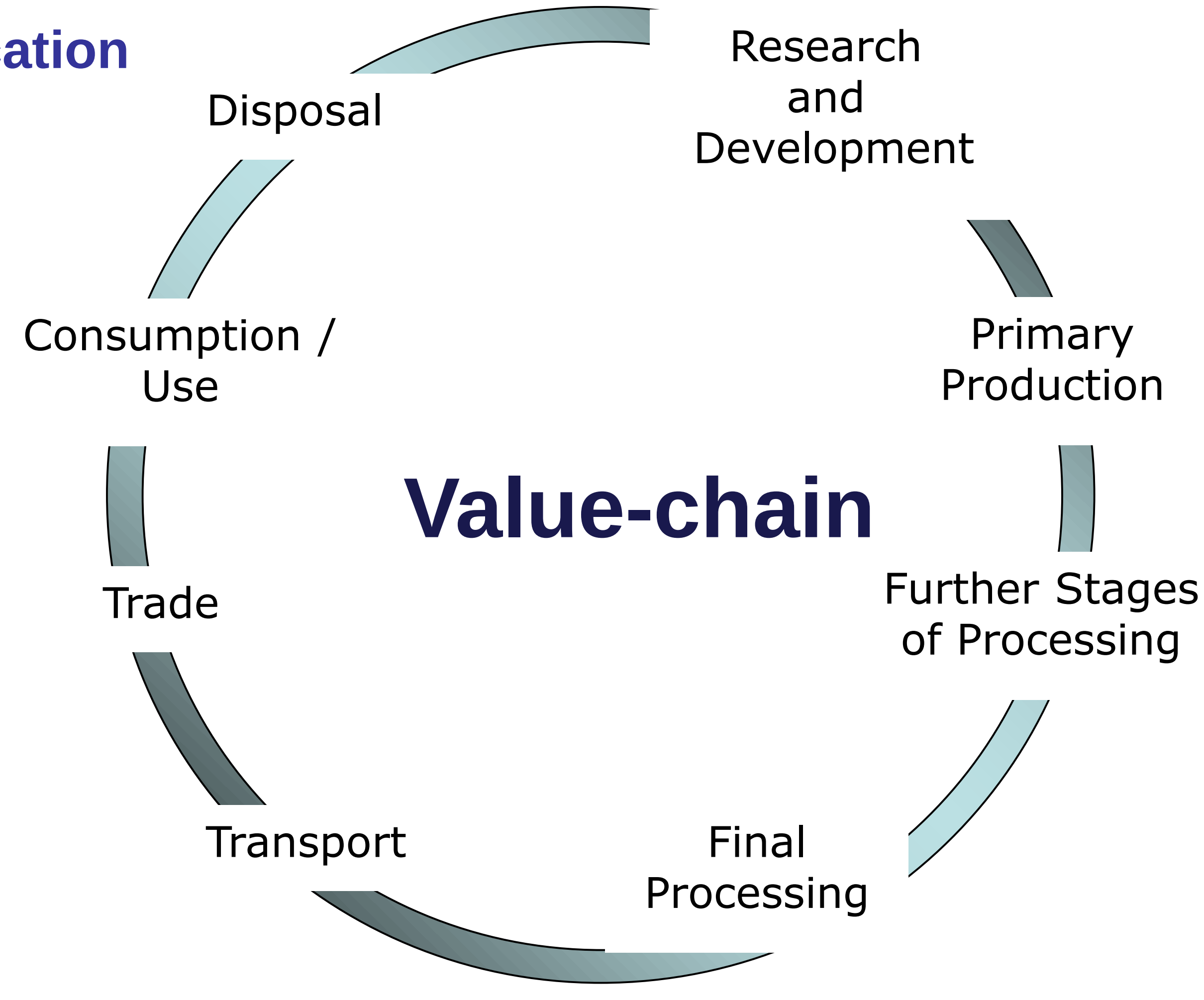
Moderator: **Claire Skentelbery**

The Precaurionary Matrix:

- Is a controle banding tool based on a limited number of parameters
- Can be applied early in the safe-by-design process
- Is generally applicable
- Gives an indication of where a need for precautionary measures exisit
- Helps to detect knowledge gaps and risk potentials for workers, consumers and the environment

The Precautionary Matrix does not replace risk assessment

Field of application



Set-up of the Precautionary Matrix:

Context (N,I)

- Nano-relevance; yes / no (N)
- Current state of knowledge (I)

Potential Effects (W)

Reactivity and Stability

P = N(W·E+I)

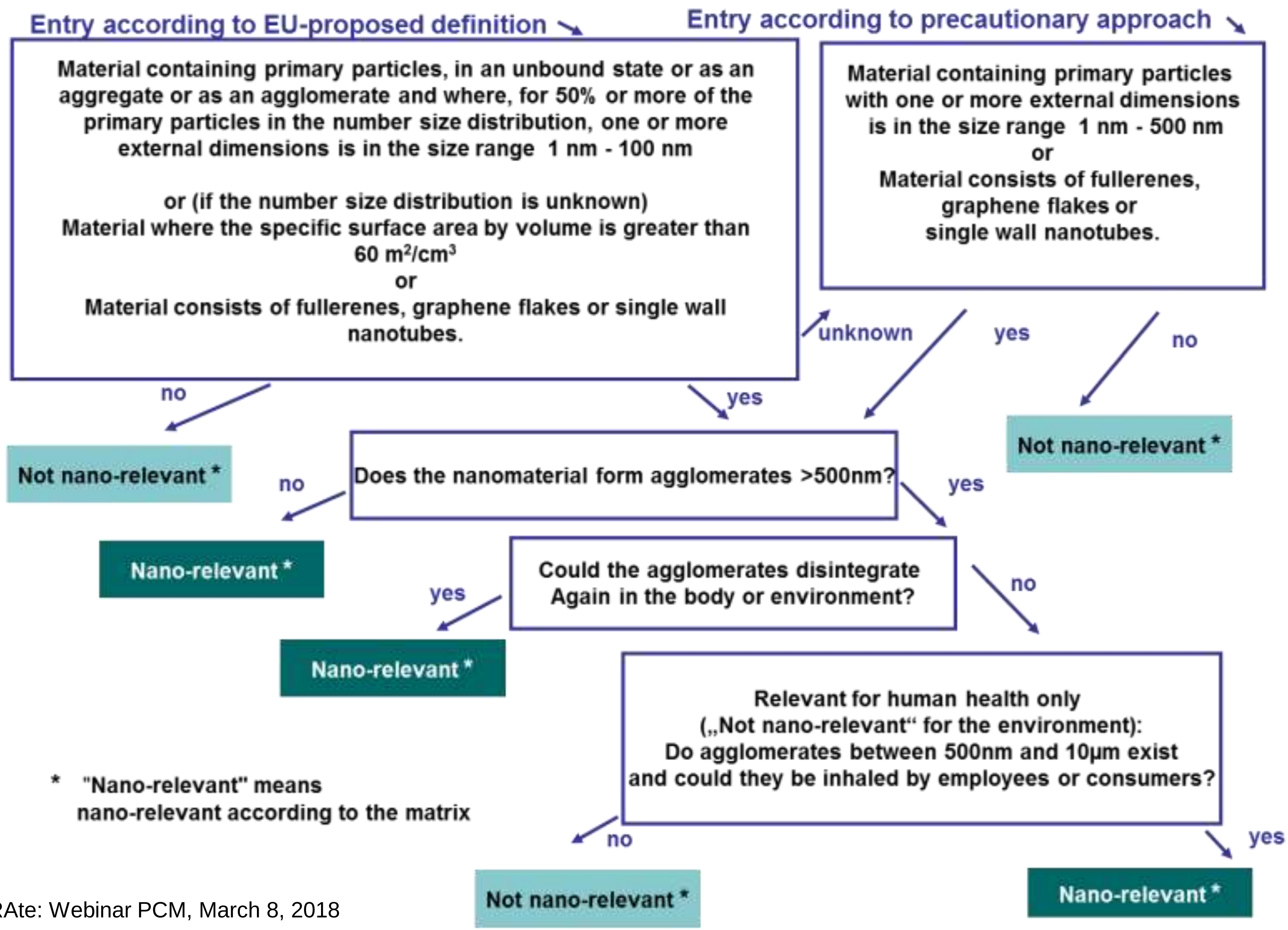
Potential for Human Exposure(E)

Potential Emission into the Environment (E)

P = Need for precautionary action

⇒ Result is a number, the higher the number the higher the need for a closer look

Nano-relevance



Potential effect and exposure of human beings / input into the environment

<table>
<tr><th>Potential effect (W)</th><th colspan="2">Potential exposure of human beings / input into the environment (E)</th></tr>
<tr><td rowspan="2">Reactivity: redox activity, catalytic activity, oxidative stress, induction of proinflammatory cytokines
Stability of the nanomaterial in different media (Halflife)</td><td colspan="2">Physical Matrix in which the nanomaterial is embedded</td></tr>
<tr><td>Total amount handled / used by workers or consumers per day
Frequency of potential exposure</td><td>Emissions into the environment from production
Annual amount of nanomaterials marketed in consumer products</td></tr>
</table>

Examples: reactivities of some nanomaterials

Nanomaterial Reactivity (data refer to uncoated and non-functionalised nanomaterials)	Redox activity (pH7) Estimated, based on the standard redox potential or the position of the conduction band[19]			ROS-formation behaviour or induction of inflammation reactions			(Photo)catalytic activity (at environmental temperatures)		
	low (1)	medium (5)	high (9)	low (1)	medium (5)	high (9)	low (1)	medium (5)	high (9)
Ag[0]		X			X[c]			X	
Ag_2O		X						X	
CeO_2	X				X[a]		X		
CuO		X					X		
Fe[0]		X			X[*]			X[*]	
FeO		X			X[*]			X[*]	
Fe_3O_4	X				X[*]			X[*]	
Fe_2O_3		X			X[b]		X		
SiO_2 (amorph)	X			X[b]			X		
TiO_2 (anatase)		X			X[a,b,c]				X
TiO_2 (rutile)		X			X[c]			X	
ZnO	X					X[c]		X	

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Reactivities of nanomaterials

Draft revised version (March 2018)

low

medium

high

Nano-material (uncoated and unfunction-alized)	Calculated or Acellular Reactivity			Cellular Reactivity			
	Redox-activity (Band Gap)	Fotocatalytic activity	Biological oxidative damage, BOD	Induction of IL-8, IL-1b or TNFa	ROS induction	GSH depleation	Protein carbony-lation
Ag (0)			c (Ø: 35-60nm)	d, NM300 (Ø:8-47nm)	d, NM300	d, NM300	
CeO_2	a (Ø: 18.3nm)		c (Ø: 7-25nm)	f, h (Ø: 9.7nm)			
Co_3O_4	a (Ø: 10.0nm)		c (Ø: 20nm)	f (Ø: 18.4nm)			
CuO	a (Ø: 12.8nm)		c (Ø: 18-34nm)	f (Ø: 23.1nm)			
Fe_2O_3	a (Ø: 12.3nm)		c (Ø: 30nm)	h (Ø: 15nm)			
Fe_3O_4	a (Ø: 12.0nm)		c (Ø: 25nm)				
Mn_2O_3	a (Ø: 51.5nm)		c (Ø: 45nm)				
SiO_2 (amorph)	a (Ø: 13.5nm)		c (Ø: 15nm)	h, i (Ø: 14nm)	g, i, NM200, NM203 (Ø: ~15nm)		g (Ø: 15nm)
TiO_2 (anatase)	a (Ø: 12.4nm)	b (Ø: 10-100nm)	c (Ø: 10-25nm)	h, i, P25 Ø: 20-80nm)	i, P25	d, NM101 (Ø: 4-100nm)	g, NM105 (Ø: 21nm)
TiO_2 (rutil)		b (Ø: 100nm)	c (Ø: 5000nm)	f (Ø: 30nm)	d (Ø: 80-400nm)	d (Ø: 80-400nm)	
$BaSO_4$				h, NM 220 (Ø: 25nm)			g, NM 220 (Ø: 32nm)
MWCNT			c (Ø: 8nm, L: 20µm)	d, NM400 (Ø: ~14nm, L: ~850nm)	d, NM400	d, NM400	g, NM400
MWCNT			c (Ø: 15nm, L: 1-40µm)	d, NM402 (Ø: ~12nm, L: ~1370nm)	d, NM402	d, NM402	g, NM402

Predictive power of the calculated, acellular and the cellular assays for lung toxicity

Draft revised version (March 2018)

	Correct prediction	False positiv prediction	False negativ prediction	Evaluated datasets
Calculated and acellular (in vitro) reactivities ⇨ acute lung toxicity (in vivo)	8	1	4	13
Calculated and acellular (in vitro) reactivities ⇨ Subchronic inhalation toxicity (in vivo)	3	0	4	7
Cellular reactivities (in vitro) ⇨ acute lung toxicity (in vivo)	9	2	1	12
Cellular reactivities (in vitro) ⇨ Subchronic inhalation toxicity (in vivo)	8	0	0	8
Calculated and acellular (in vitro) **or** Cellular reactivities (in vitro) ⇨ acute lung toxicity (in vivo)	10	2	0	12
Calculated and acellular (in vitro) **or** Cellular reactivities (in vitro) ⇨ Subchronic inhalation toxicity (in vivo)	8	0	0	8

Classification

Number of points	Classification	
0 - 20	A	The nanospecific risks can be classified as low. No further clarification is necessary.
> 20	B	Possible nanospecific risks cannot be excluded. Further clarification of the risks is needed or measures for risk reduction have to be taken as regards manufacture, use and disposal, with a view to a precautionary approach.

Available documents:

- Guidance on the Precautionary Matrix for Synthetic Nanomaterials
- FAQs and Responses on the Precautionary Matrix for Synthetic Nanomaterials

Checklist for users

1. Draw up an inventory of materials/products/applications
2. Check the nano-relevance of each material
3. Find and separate steps in the value chain to be evaluated
4. Decide for which steps a matrix has to be completed
5. Comlete the matrixes as far as possible
6. Obtain lacking information using the relevant questions from the matrix
7. Finish the matrix and localise the relevant precautionary need
8. Clarify any need for action (commence further clarifications, protection measures and measures to provide information)

Recommendation

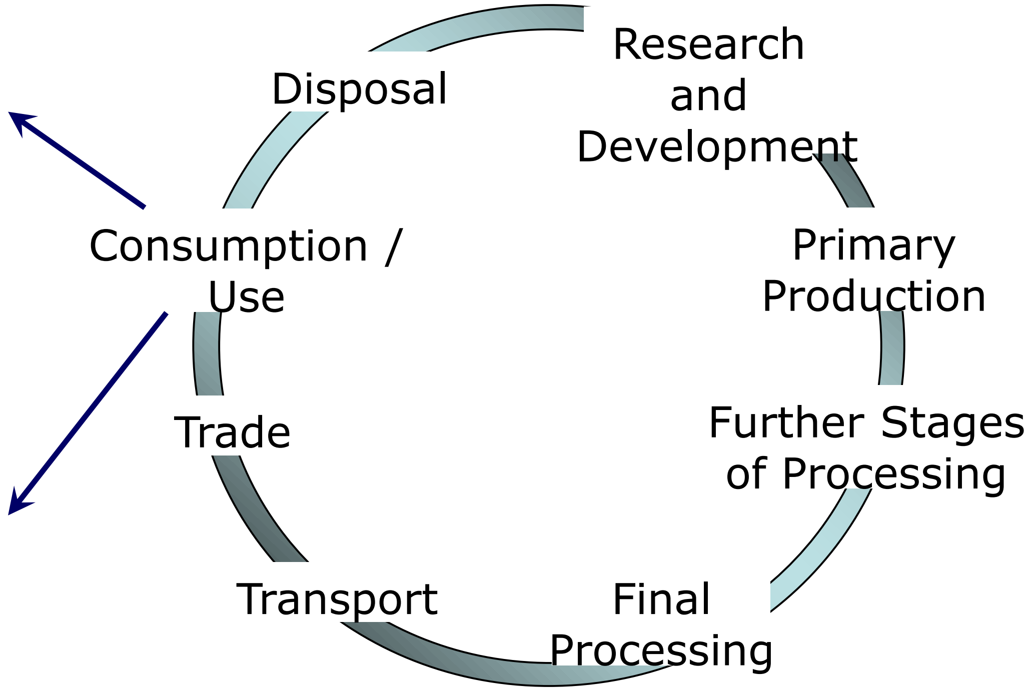
It is recommended to completed and evaluated the precautionary matrix in two iterative steps:

1. A first rapid evaluation demonstrates knowledge gaps and uncertainties and leads to a preliminary precautionary matrix.

2. An additional data-gathering step and clarifications regarding knowledge gaps will lead to the final evaluation.

Case Study

Scratsh-resistant varnish for parquet flooring containing nano SiO_2



Collecting information

General informaiton

- Product name: Nano Anti-Scratch
- Product contains amorphous SiO_2 (primary particle size 10-20 nm)

- Value-cain processes to be evaluated:
  a) Varnishing the floor with Nano Anti-Scratch
  b) Consumer living in a room with a varnished floor

Information for process a) Varnishing the floor with Nano Anti-Scratch

Informaiton on the product and its application

- Varnish is a aquious formulation
- Product contains 5% amorphous nano SiO_2
- Required amount of varnish: 5 kg/ 10 m^2
- Worker can treat 50 m^2 /day

Informaiton on amorphous SiO_2

- Particle size 10-20 nm; no coating, no surface treatment
- Potential effect of amourphous nano SiO2:

Redox-activity: low
ROS induction: low
Induction of proinflammatory cytokines: medium
Stability (halflife in the body): unknown

} Data from literature

Precautionary Matrix: Web application

↓

https://www.bag.admin.ch/bag/en/home/themen/mensch-gesundheit/chemikalien/nanotechnologie/sicherer-umgang-mit-nanomaterialien.html

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Precautionary matrix for synthetic nanomaterials

save / load data | print preview | entry page

1. General information 2. Relevance 3. Uncertainties 4. Effect 5. Exposition 6. Evaluation

General information

General information

Precautionary matrix completed by / responsible contact person

The wooden floor company; Contact person: John Rain

Brief description of the considered nanospecific field (type of nanomaterials, which surrounding, in which application)

Varnishing the floor with the product "Nano Anti Scratch" by professional worker

Brief description of the considered (process) step (production, packaging, transport, further stages of processing, disposal, use...), brief description

Size of varnished floor: 50m2; Amount of varnish required: 25 kg; Amount of amorpous SiO2 nanolarticles (diameter 10-20 nm) in required varnish: 1.25 kg (5%); Wast.: Waste disposed in specialiced facilitie

Choose scenario

Scenario: Calculation of the precautionary need…

- [x] for employees
- [ ] for consumers
- [x] for a specific disposal step (see footer 35 in the guidelines)

Attention: when inputs are changed, the worksheet "Exposure" will be reset

Are coated / functionalised nanomaterials involved?

- ○ if yes, see statements in the guidelines , section 4.5
- ◉ no

› Insert note

next

1. General information | **2. Relevance** | 3. Uncertainties
4. Effect | 5. Exposition | 6. Evaluation

Nano-relevance

The precautionary matrix includes two approaches for the clarification of nano-relevance. The first approach is based on the EU proposed definition 2011/696/EU. The second precautionary approach includes primary particles with external dimensions from 1 to 500 nm, as nano-specific effects on biological systems can also be caused by particle sizes of 100-500 nm.

- Entry according to EU-proposed definition (2011/696/EU)
- Entry according to precautionary approach (external dimensions of primary particle from 1 to 500 nm)

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guidelines section 4.3	A	V	U
N Nano-relevance according to the precautionary matrix	1	1	1
N-EU **EU recommendation on the definition of nanomaterial** Material containing primary particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the primary particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm or (if the number size distribution is unknown) Material where the specific surface area by volume is greater than $60 m^2/cm^3$ or Material consists of fullerenes, graphene flakes or single wall nanotubes. ◉ true (→go to N1a) ○ untrue (→go to N-EUa) ○ unknown (→go to N1)	1	1	1

N-EUa Do you want to include primary particles from 1 to 500 nm in your evaluation?

○ no (→ evaluation terminated)

◉ yes (→go to N1)

> Remark: According to the EU-proposed definition, primary particles larger than 100 nm are not nano-relevant.

N1 Order of size of the primary particles in the materials (free, bound, aggregated or agglomerated) ○ over 500 nm (→ evaluation terminated) ◉ 1-500 nm (→go to N1a) Note: primary particles larger than 500nm are not nano-relevant. If applicable, evaluation can be concluded.	1	1	1
N1a Do the primary particles form agglomerates >500 nm? ◉ no ○ yes (→go to N2AV and N2U)	1	1	1

Insert note

N1a: Agglomeration status unknown. Worst case assumption: No agglomeration

next

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1. General information | 2. Relevance | **3. Uncertainties** | 4. Effect | 5. Exposition | 6. Evaluation

Information on the life cycle

guidelines section 4.4	A	V	U
I Information on the life cycle	6	6	6
I1 Is the origin of the (nanoscale) starting materials known? ○ yes ◉ partly ○ no	3	3	3
I2 Is sufficient information available to complete the precautionary matrix for nanoscale starting materials? ○ yes ◉ partly ○ no	3	3	3
I3 Are the subsequent users of the considered nanomaterials known? ◉ yes ○ partly ○ no	0	0	0

I4 How accurately is the material system known, or can disturbing factors (e.g. impurities) be estimated?

- (●) accurately
- ( ) not accurately
- ( ) unknown

0	0	0

› Insert note

next

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1. General information | 2. Relevance | 3. Uncertainties

4. Effect | 5. Exposition | 6. Evaluation

Potential effect

guidelines section 4.5	A	V	U
W Potential effect	45	45	45
W1 Reactivity	5	5	5
W1 Redox activity of the nanomaterial ◉ low ○ medium ○ high ○ not known	1	1	1
W1 Catalytic activity of the nanomaterial ◉ low ○ medium ○ high ○ not known	1	1	1

W1 Oxygen radical formation potential of the nanomaterial ◉ low ○ medium ○ high ○ not known	1	1	1
W1 Induction potential for inflammatory reactions of the nanomaterial ○ low ◉ medium ○ high ○ not known	5	5	5

W2 Stability

W2AV Stability (half-life) of the primary particles present in the nanomaterial in the body ○ hours ○ days-weeks ○ months ◉ not known	9	9	
W2U Stability (half-life) of the primary particles present in the nanomaterial under environmental conditions ○ hours ○ days-weeks ○ months ◉ not known			9

› Insert note

next

1. General information 2. Relevance 3. Uncertainties
4. Effect **5. Exposition** 6. Evaluation

Potential exposure

guidelines section 04.06.01	$E1_{A,V}$	$E1_U$
E1 Carrier material	0.1	1
○ Air, Aerosols <10 µm ○ Air, Aerosols >10 µm ◉ Liquid media ○ Solid matrix, not stable under relevant process conditions or conditions of use ○ Solid matrix, stable under relevant process conditions or conditions of use, nanomaterial mobile ○ Solid matrix, stable under relevant process conditions or conditions of use, nanomaterial not mobile	0.1	1

› Insert note

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guidelines section 04.06.02	A	A^{wc}	V
E2 Maximum possible exposure of humans	0.9	0.9	0
E2.1 Amount of nanomaterials which a worker handles per day ○ up to 1.2 mg ○ 1.2 - 12 mg ◉ over 12 mg ○ not known	9		
E2.2 Amount of nanomaterials with which a worker comes into contact in the "worst case" ○ up to 12 mg ○ 12 - 120 mg ◉ over 120 mg ○ not known		9	
E2.3 Frequency with which a worker handles the nanomaterial ◉ monthly ○ weekly ○ daily ○ not known	1		

› Insert note

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guidelines section 04.06.03	U^P	U^G	$U^{G.spz}$	U^{PSE}
E3 Maximum possible input into the environment	1	0	0	9
E3.1 Amount of nanomaterials reaching the environment from wastewater, exhaust gases, solid waste per year ◉ up to 5 kg ○ 5 - 500 kg ○ over 500 kg ○ not known	1			
E3.3 Amount of disposed nanomaterials per year ○ up to 5 kg ○ 5 - 500 kg ◉ over 500 kg ○ not known				9

Insert note

E3.1 All waste is collected at the building site and disposed off in a specialized facility; E3.3: Wast from treated wood during deconstruction

next

Evaluation precautionary needs

The precautionary matrix calculates a total score for workers, consumers and the environment. A precautionary need is given for **scores over 20** (see statements in the guidelines , section 5.3)

Please note: The precautionary matrix does not produce a definitive evaluation in terms of a risk assessment!

for workers		
Precautionary need for employees	V_A	47
Precautionary need for employees (Worst Case)	V_A^{WC}	87
for environment		
Precautionary need environment production	V_U^P	51
Precautionary need environment (disposal step production waste)	V_U^{PSE}	411
Precautionary need environment (disposal step utility product)	V_U^{GSE}	411

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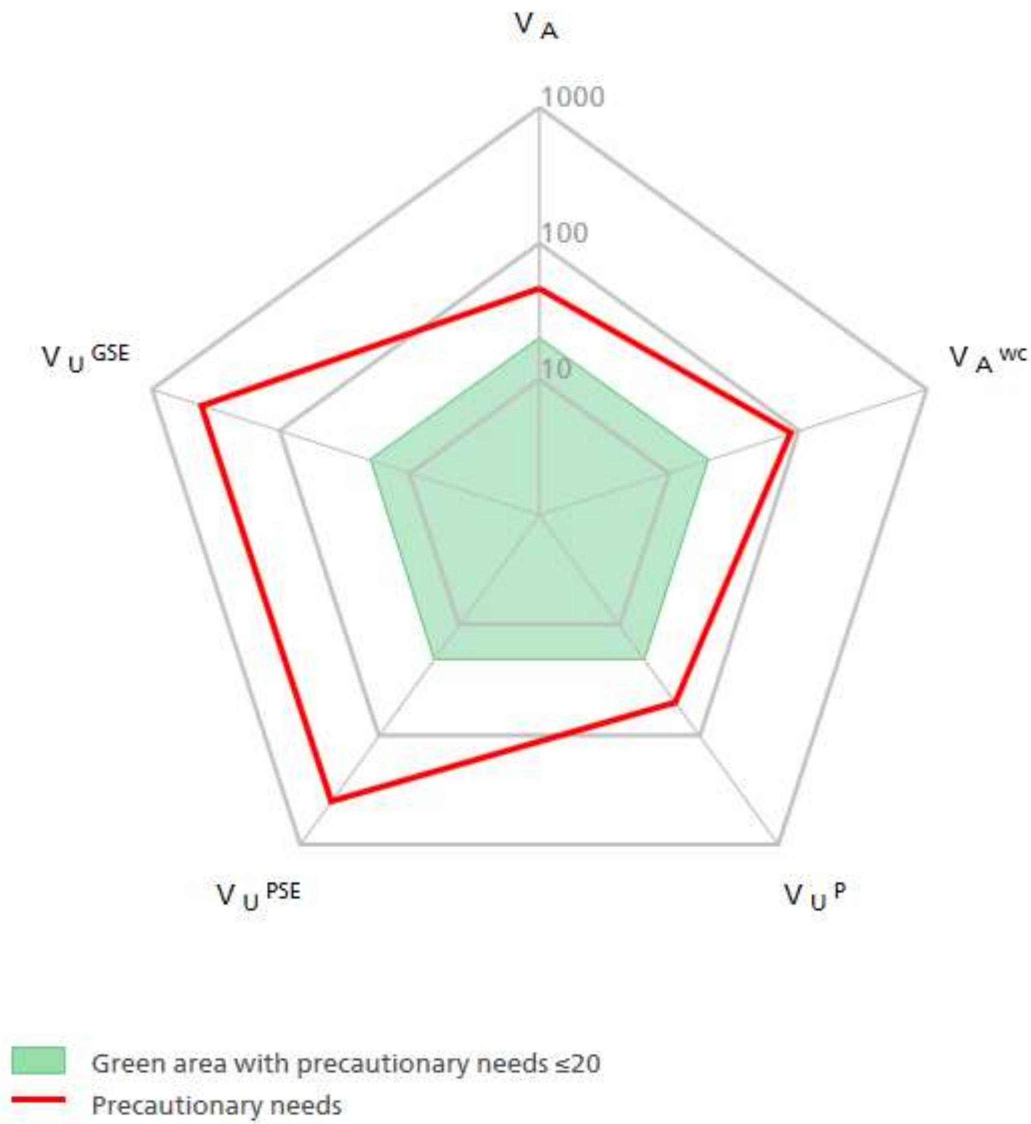

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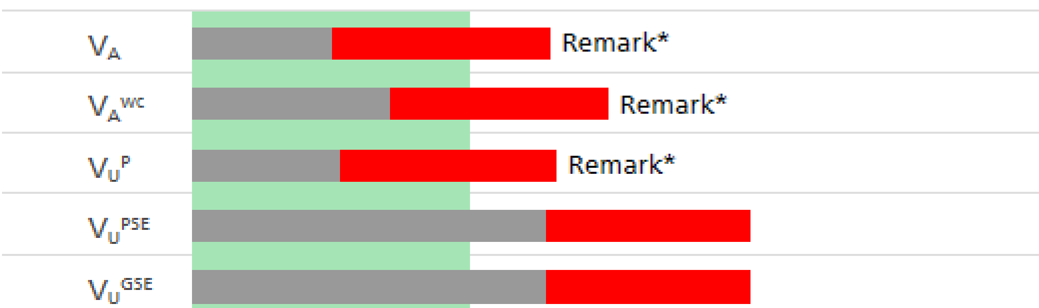
Calculated data

	$V = N \times (W \times E + I)$	N	W	E	I
V_A	46.5	1	45	0.9	6
V_A^{wc}	87	1	45	1.8	6
V_U^P	51	1	45	1	6
V_U^{PSE}	411	1	45	9	6
V_U^{GSE}	411	1	45	9	6

"Unknown" fraction

This diagram shows the unknown part of the result (red bar). If the unknown part is consequential, a few clarifications can lead to a significantly more favourable result.



* Further clarification can possibly allow these values to fall into the green zone.

Preliminary conclusion for the process «Varnishing the floor with Nano Anti-Scratch»

There is a precautionary need and therefore measures are necessary

- Unknowns could be responsible for the precautionary need for employees

  ⬇

  Second data gathering round, risk assessment and/or personal protection of employees necessary

- Regarding environmental safety additional data will not reduce the the precautionary needs in all cases

  ⬇

  Collect wast and make sure, that it is disposed off in a safe manner or conduct risk assessment for the environment

W2 Stability

W2AV Stability (half-life) of the primary particles present in the nanomaterial in the body ○ hours ◉ days-weeks ○ months ○ not known	5	5	
W2U Stability (half-life) of the primary particles present in the nanomaterial under environmental conditions ○ hours ◉ days-weeks ○ months ○ not known			5

› Insert note

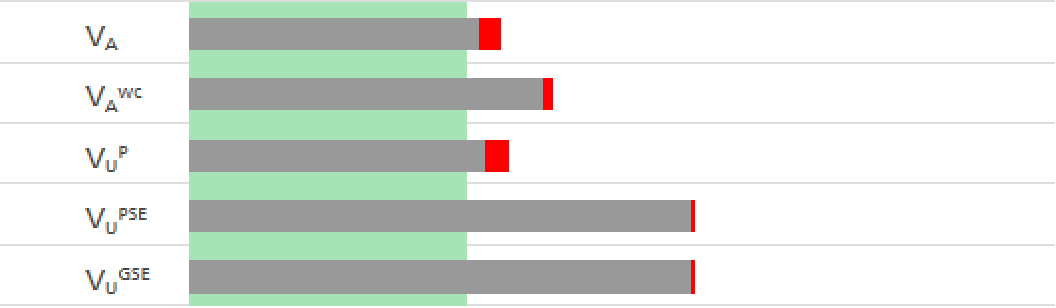
[next]

Calculated data

	$V = N \times (W \times E + I)$	N	W	E	I
V_A	28.5	1	25	0.9	6
V_A^{wc}	51	1	25	1.8	6
V_U^P	31	1	25	1	6
V_U^{PSE}	231	1	25	9	6
V_U^{GSE}	231	1	25	9	6

"Unknown" fraction

This diagram shows the unknown part of the result (red bar). If the unknown part is consequential, a few clarifications can lead to a significantly more favourable result.



Final conclusion for theprocess «Varnishing the floor with Nano Anti-Scratch»

There is a precautionary need and therefore measures are necessary

- Unknowns are only partly responsible for the precautionary need for employees

  ⬇

  Risk assessment and/or personal protection of employees is necessary
-

- Regarding environmental safety additional data will not reduce the the precautionary needs in all cases

  ⬇

  Collect wast and make sure, that it is disposed off in a safe manner or conduct risk assessment for the environment

Information for process b) Consumer living in a room with a varnished floor

Informaiton in relation to consumer exporure

- Varnish forms a solid coating on the floor
- Room size: 50 m^2
- Amorphous nano SiO_2 content in the floor coating of the room: 1.25 kg

1. General information | 2. Relevance | 3. Uncertainties
4. Effect | 5. Exposition | 6. Evaluation

General information

General information

Precautionary matrix completed by / responsible contact person

> The wooden floor company; Contact person: John Rain

Brief description of the considered nanospecific field (type of nanomaterials, which surrounding, in which application)

> Consumer living in a room with a varnished (name of product: Nano Anti Scratch) floor

Brief description of the considered (process) step (production, packaging, transport, further stages of processing, disposal, use...), brief description

> Varnish forms a solid coating on the floor; Room size: 50m2; Amount of amorpous SiO2 nanolarticles (diameter 10-20 nm) in coating: 1.25 kg

Choose scenario

Scenario: Calculation of the precautionary need…

- [ ] for employees
- [x] for consumers
- [ ] for a specific disposal step (see footer 35 in the guidelines)

Attention: when inputs are changed, the worksheet "Exposure" will be reset

1. General information 2. Relevance 3. Uncertainties

4. Effect **5. Exposition** 6. Evaluation

Potential exposure

guidelines section 04.06.01	$E1_{A,V}$	$E1_U$
E1 Carrier material	0.0001	0.0001
○ Air, Aerosols <10 µm ○ Air, Aerosols >10 µm ○ Liquid media ○ Solid matrix, not stable under relevant process conditions or conditions of use ○ Solid matrix, stable under relevant process conditions or conditions of use, nanomaterial mobile ◉ Solid matrix, stable under relevant process conditions or conditions of use, nanomaterial not mobile	0.0001	0.0001

› Insert note

guidelines section 04.06.02	A	A^wc	V
E2 Maximum possible exposure of humans	0	0	0.0081
E2.4 Amount of nanomaterials which a consumer handles daily through the utility product ○ up to 1.2 mg ○ 1.2 - 12 mg ◉ over 12 mg ○ not known			9
E2.5 Frequency with which a consumer uses the utility product ○ monthly ○ weekly ◉ daily ○ not known			9

› Insert note

guidelines section 04.06.03	U^P	U^G	$U^{G.spz}$	U^{PSE}
E3 Maximum possible input into the environment	0	9	0.0009	0
E3.2 Amount of nanomaterials in utility products per year ○ up to 5 kg ○ 5 - 500 kg ○ over 500 kg ◉ not known		9	9	

Insert note

E3.2: It is unknown how wast from treated wood will be desposed of after deconstruction of the floor

Evaluation precautionary needs

The precautionary matrix calculates a total score for workers, consumers and the environment. A precautionary need is given for **scores over 20** (see statements in the guidelines , section 5.3)

Please note: The precautionary matrix does not produce a definitive evaluation in terms of a risk assessment!

for consumers		
Precautionary need for consumers	V_V	11
for environment		
Precautionary need environment (during use with specific waste disposal)	$V_U^{G.spz}$	11
Precautionary need environment (during use without specific waste disposal)	V_U^G	416

Final conclusion for the process «Consumer living in a room with a varnished floor»

There is no need for precautionary measures to protect consumers

There is a need for precautionary measures regarding environmental safety (wast disposal)

Additional data will not reduce the the precautionary needs in all cases

⬇

Collect wast and make sure, that it is disposed off in a safe manner or conduct risk assessment for the environment

Q&A of the participants