GUIDEnano: A tool for risk assessment of nano-enabled products considering the whole life cycle

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under grant agreement nº604387.

Main Goal

Develop innovative methodologies to **evaluate** and **manage** **human and environmental health risks of NM-enabled products, considering the whole product life cycle**

Interactive digital Guidance Tool

Ensure good practises & safety

Main intended users

Communication Tool

The rationale

Scientific data gaps

No specific regulatory guidance

→ **How should we proceed?**

One decade of intensive research on nanosafety

Continuously increasing NM-enabled products to the market

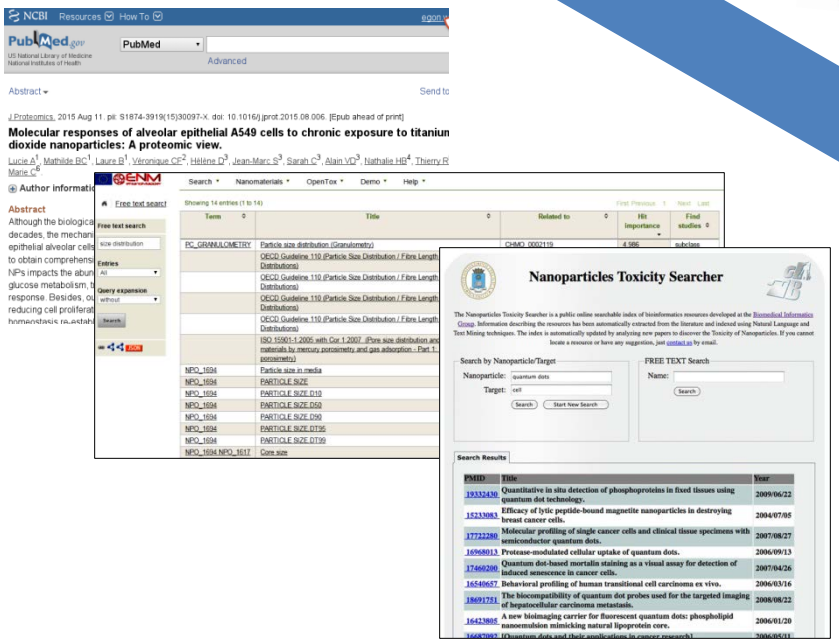
Societal concerns (but society cannot easily discriminate in which cases there should be concern and which not)

↓

Industry needs that this knowledge is transferred in an organized manner, in a way that it can become informative for their own cases

The rationale

Consortium experts



Web-based Tool

GUIDEnano version 3.0

This tool will guide the nano-enabled product developers (industry) into the design and application of the most appropriate risk assessment & mitigation strategy for a specific product.

Learn more »

How does it compare to existing Tools?

Name	RA			Type	Output
	Worker	Consumer	Environment		
ANSES Tool	X			Tool	CB
Sttofenmanager Nano	X			Tool	CB
CB NanoTool	X			Tool	CB
Swiss Prec. Matrix	X	X	X	Tool	CB
Groso's Method	X			DSS	CB
US NANOTOOL	X			DSS	CB
STM Nano	X			Model	CB
SSD			X	Model	Q
NanoSafer 2	X			Model	CB/SQ
NanoRiskCat	X	X	X	Model	CB
NRST	X	X	X	DSS	CB
FINE			X	Model	Q
REACHnano ToolKit	X	X	X	Tool	CB/Q
LICARA NanoScan	X	X	X	Tool	CB
MARINA	X	X	X	Strategy	CB/Q
ConsExpo nano		X		Tool	Q
SimpleBox4nano	X	X	X	Model	Q
DF4nanoGrouping	X	X	X	Strategy	CB

- Most of the methods focus on occupational human health
- Less than half of the methods include the environment
- Most of them are control banding methods
- A number of methods assess nano-enabled products

How does it compare to existing Tools?

GUIDEnano

Comprehensive:

- Includes all phases of the risk assessment
- Focuses on environmental and human RA

Allows assessments with different levels of data availability

- When limited data is available, worse case defaults are used
- When further information is available, this is used to refine parameters in the risk assessment process

Risk Assessment estimate is quantitative

Flexible structure built to allow extensions and updates following scientific/ regulatory progress

GUIDE nano
version 3.0
This tool will guide the nano-enabled product developers (industry) into the design and application of the most appropriate risk assessment & mitigation strategy for a specific product.
Learn more »

Conceptual framework

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report

Materials

Similarity

Activities

Compartments / Fate

Exposure

Lung

Hazard

Risk assessment and management

GUIDEnano About Contact Log in

GUIDEnano version 3.0

This tool will guide th… …ndustry) into the design and applicatio… …ment & mitigation strategy for a specific…

Learn more »

Getting started

To use this tool and get started you will need an account.

Ask for an account »

If you already have an account please:

Login »

Development

This tool is developed using ThinkWorks Intelligent Objects engine.

ThinkWorks »

GUIDEnano About Contact

Log in.

Group

ThinkWorks

User name

Ralph

Password

••••••

Remember me?

Log in

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…gramme

GUIDEnano case
- Activities
- (Nano)materials
- Compartments
- Exposure
- Toxicity studies
- Risk assessment

GUIDEnano case

With the GUIDEnano tool you can define a nano enabled product life cycle and assess the identified risks of the released nanomaterial forms for both human health and environmental fate.

Via the menu at the top you can define:

- the activities related to the product before, during and after it's life;
- the relevant nano enabled articles, (nano)materials, substances, mixtures, chemicals and their properties;
- the environmental compartments and zones where (nano)materials are released into;
- the exposure scenarios for both human and eco species;
- hazard assessment for each relevant hazard endpoint for both environment and humans;

Finally, a risk assessment overview of human health and environmental fate is presented showing the risk outcome for each individual exposure scenario.

Identity | Author(s) | Report info

Name of this case: TiO2 enabled tiles

General description and goal:

Assess the environmental risk using Ceramic tiles coated with photo catalytic TiO2 NP on 5000 facades in a city.

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Project funded from the European Union´s Seventh Framework Programme
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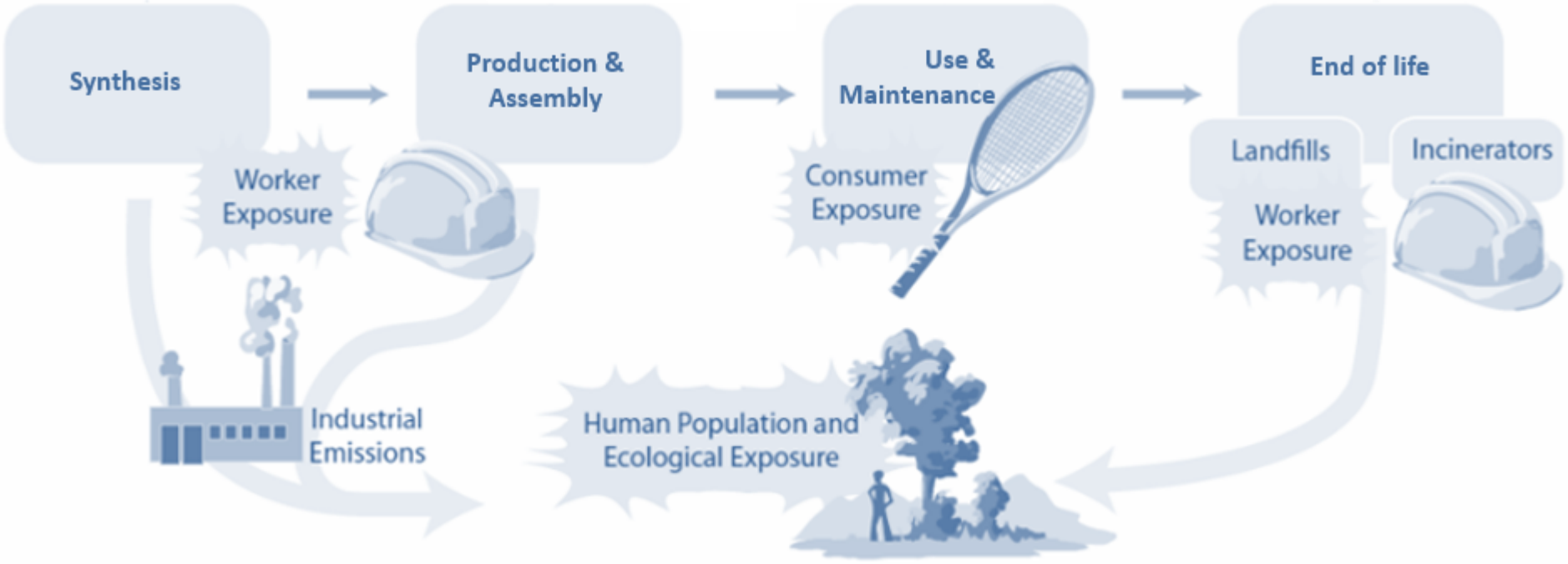
Life Cycle Activities

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report



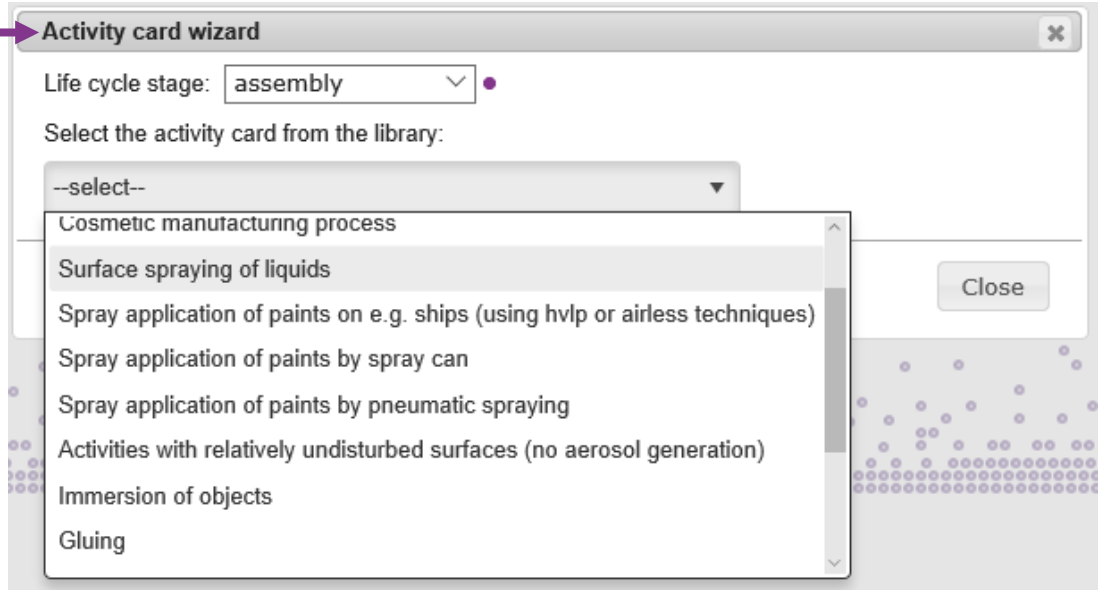
Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report

Activities

Activities

		activity name	setting/scale	life cycle phase	locations
		Synthesis of TiO2 NP's	small industry	synthesis	1
		Production of TiO2 NP formulation	small industry	production	1
		Coating the ceramic tiles with spray gun	small industry	assembly	1
		Curing the ceramic tiles with coating	large industry	assembly	1
		Citywide use + Weathering	other domestic	use/maintenance	5000
		Removal and disposing of old tiles	small industry	end of life	1
+					

Activity card wizard

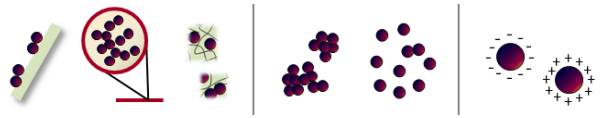


Building in Release Knowledge

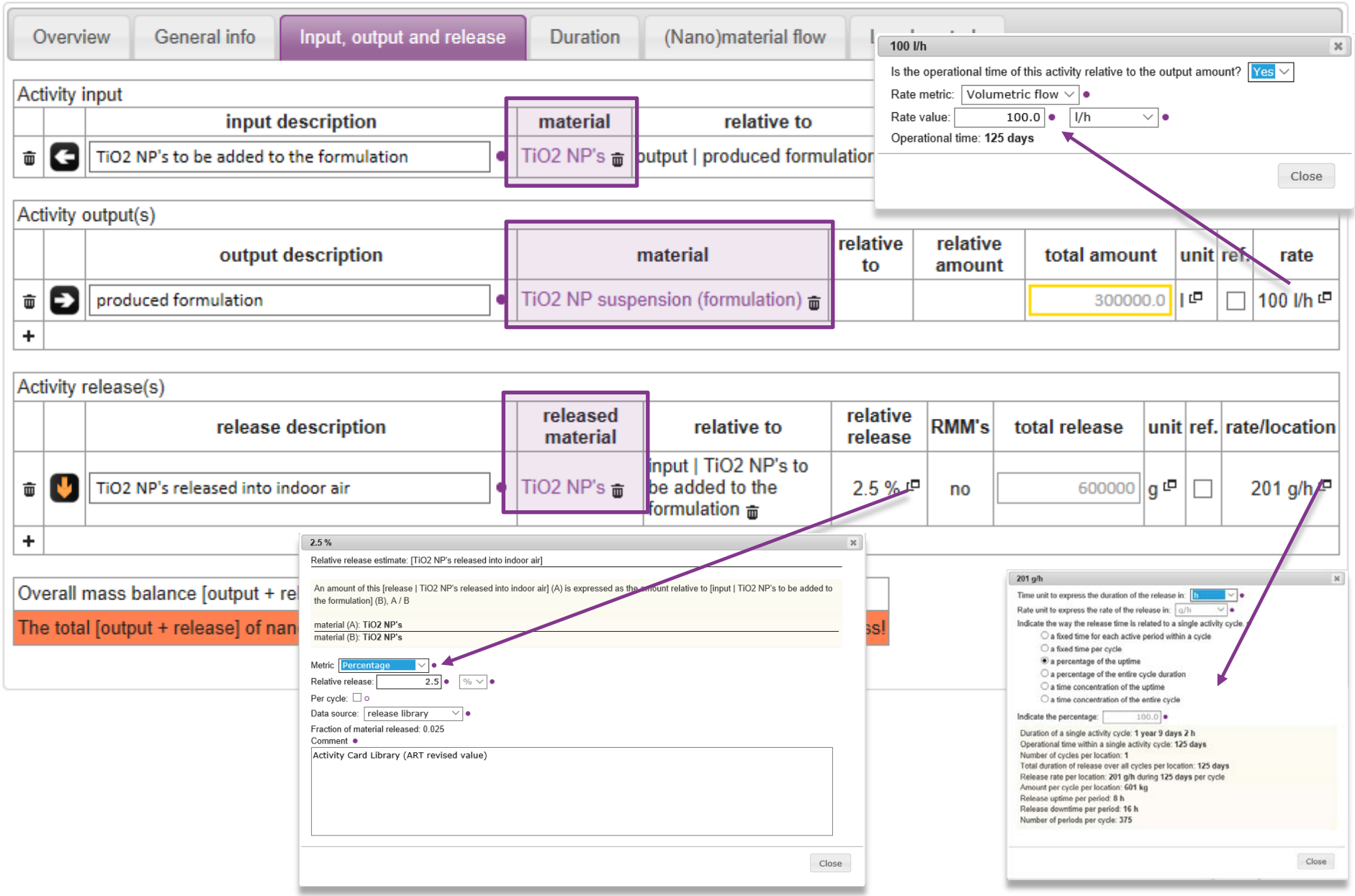
Collect relevant data in literature + *Information by project partners* + *ECHA Guidance (worst case)* + *Experimental work*

- *Release factor*
- *Exposure relevant form*
- *Receptor compartment*

Amount per product/time period



Activity: Production of TiO2 NP formulation



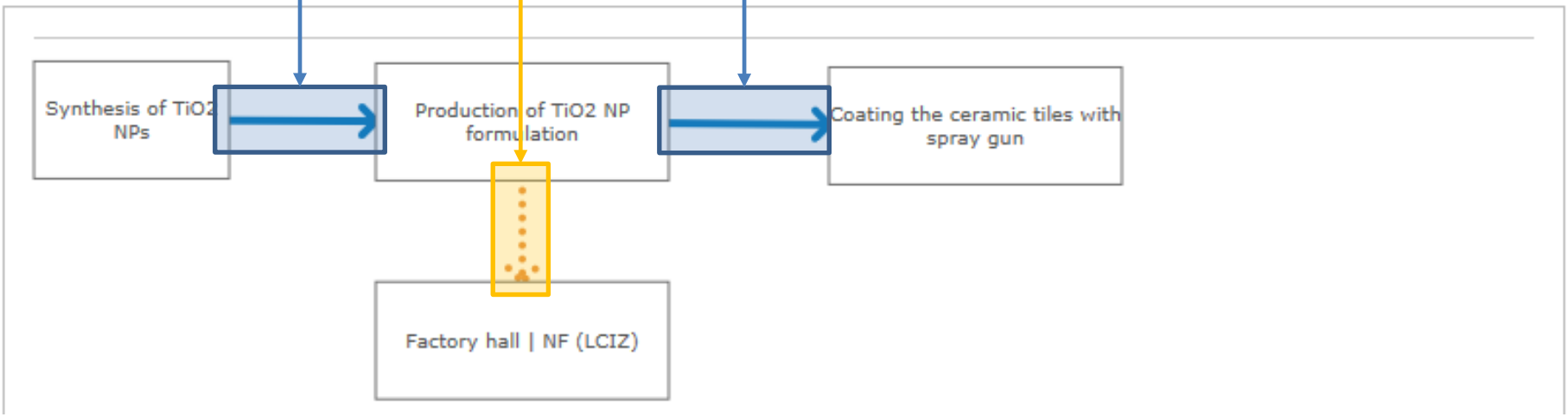
Activity: Production of TiO2 NP formulation

Overview | General info | Input, output and release | Duration | (Nano)material flow | Local controls

	input	from preceeding activity	transport time	unit
←	TiO2 NP's to be added to the formulation	Synthesis of TiO2 NP's | synthesized TiO2 NP's	0.0	h

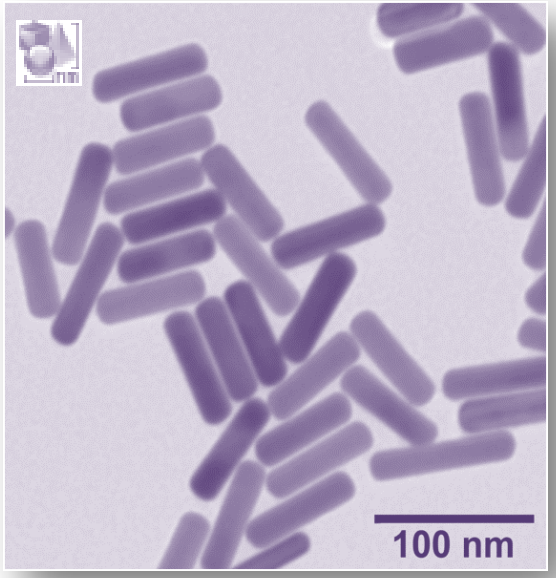
	output(s)	to succeeding activity	transport time	unit
→	produced formulation	Coating the ceramic tiles with spray gun | coating to be applied	0.0	h

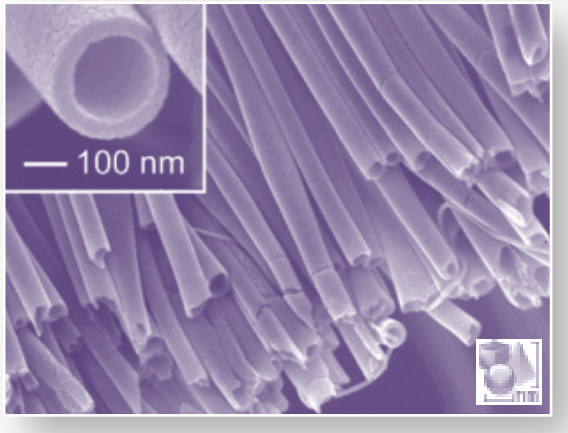
release(s)	into compartment | zone	or directly in contact with
release | TiO2 NP's released into indoor air	Factory hall | NF (LCIZ)	Workers in factory | dermal contact of TiO2 powder during mixing
release | TiO2 NP's dermal contact release		+ --select--

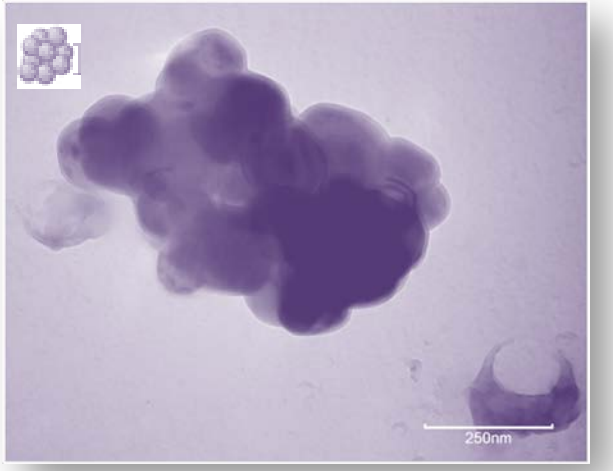


(Nano)materials

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report







Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment

(Nano)materials

Below you can add '+' the different (nano)materials, substances and mixtures relevant before, during and after the life of the nano enabled product. Think of synthesized nanoparticles, manufactured materials with nano features, released nanomaterials into the environment. But also the (nano)materials, chemicals and substances used for toxicity tests and read accross.

Scenario relevant (nano)materials:

		name	description	category	nano constituents	chem.	hazard statements
🗑	art	TiO2 coated tiles 50x50 (virgin)	Tiles to be applied outside 50x50 cm and 20 kg/m2	*article*	TiO2 NP's		constituent(s) with hazard label(s) exist!
🗑	nano	TiO2 NP's	Titanium Dioxide (anatase) nano particles used to c	*nanoparticle*	TiO2 NP's	TiO2 (s)	H351 (also constituent(s) with hazard label(s) exist!)
🗑		TiO2 NP suspension (formulation)	Suspension applied onto the tiles	*suspension*	TiO2 NP's		constituent(s) with hazard label(s) exist!
🗑		Ceramic (untreated)	New ceramic material (uncoated)	*composite*			
🗑		Ceramic TiO2 NP sprayed with formulation	Ceramic with sprayed formulation (uncured)	*composite*	TiO2 NP's		constituent(s) with hazard label(s) exist!
🗑		Ceramic TiO2 NP coated and cured (virgin)	New TiO2 NP coated ceramic material	*composite*	TiO2 NP's		constituent(s) with hazard label(s) exist!
🗑	art	Weathered/ used tiles 50x50	Old tiles to be disposed of after use phase	*article*	TiO2 NP's		constituent(s) with hazard label(s) exist!
🗑		Weathered ceramic (old)	Aged ceramic material (less NP's)	*composite*	TiO2 NP's		constituent(s) with hazard label(s) exist!
🗑	nano	TiO2 NP's used in tox study	NP used in toxicity study	*nanoparticle*	TiO2 NP's used in tox study	TiO2 (s)	
+	select--						

select--
article
substance/mixture
nano-object
nanostructured aggregate
nanostructured agglomerate

(Nano)material classes

(ISO 80004 compliant)

- Nano-object
- Nano-aggregate | agglomerate

NOAA

- Substance
  - Pure substance
  - Mixture | Structure

Composite, Layers
Suspension, Emulsion
Mixture, Gel, Gas
Etc.

+

nano enabled

Nanocomposite,
Nanosuspension,
Nano-emulsion
Nano-aerosol
Etc.

- Article
- *Eco medium (zone or ecotox specific)*
- *Chemical | Element (leave constituents)*

Structuring the (nano)material

- Article, *TiO_2 photocatalytic tile 50x50 cm*
  - Nanocomposite, *TiO_2 NP coated ceramic material* [role = contained]
    - Composite, *Ceramic* [role = solid matrix]
      - Slim porcelane [role=layered]
      - Engobe [role=layered]
      - Etc..
    - Nano particle, TiO_2 NP [role = surface bound]
      - TiO_2 chemical [role = core]
      - Phosphorus [role = impurity]

Size and shape

TiO2 NP's

Physico-chemical characteristics | Constituents(2) | Presence(7)

Nanomaterial category: nanoparticle

- Identification
- Shape and size
- Physical properties
- Surface properties
- Function(s)
- Mass conversion
- Chemical info
- Reactivity info
- Classification & Labelling
- Toxicity studies
- Quality: (78.0%)

Shape

Morphology / shape: spherical

Mean size

Mean nanoscaled particle diameter (D1 ~ D2 ~ D3) in nm: 55

Aspect ratio: 1.0

Size method/distribution

Size distribution data available? Yes

Method used: Aerodynamic Particle Sizer (APS) Size type: aerodynamic size

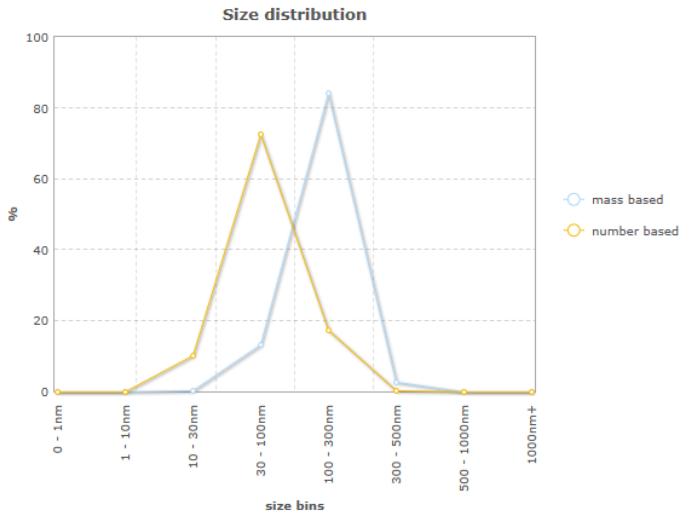
Size distribution

Metric: Number based Distribution: Log Normal Geometric mean: 60.0 Geometric standard deviation: 1.72

Primary size distribution

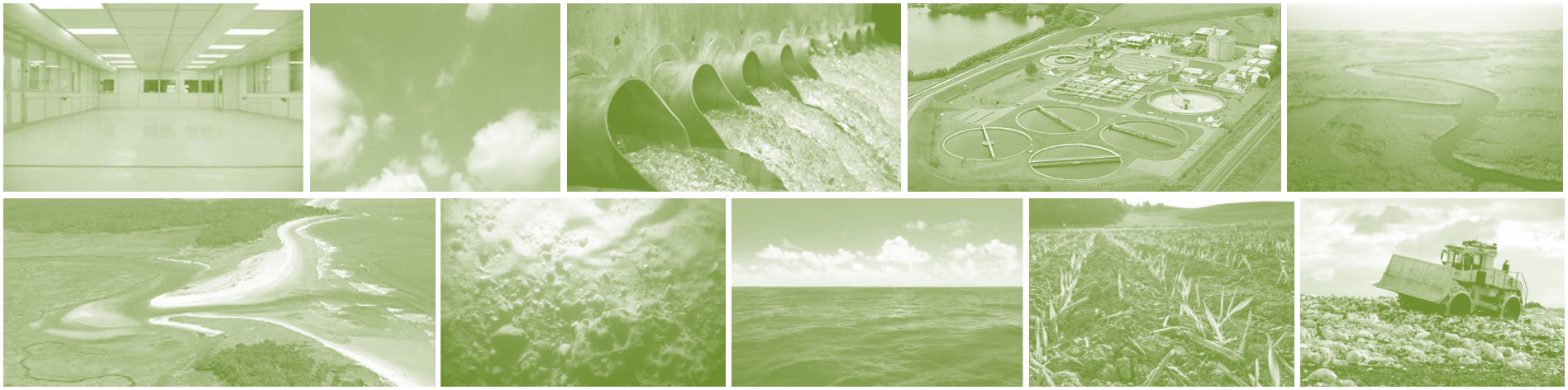
diameter	%	m2/g	mass%	number%
0 - 1nm	0.0	2006	0%	0%
1 - 10nm	0.0	200.4	0%	0%
10 - 30nm	10.0	66.03	0.04898%	10.01%
30 - 100nm	72.6	19.87	13.04%	72.67%
100 - 300nm	17.2	6.603	84.25%	17.22%
300 - 500nm	0.1	3.757	2.659%	0.1001%
500 - 1000nm	0.0	1.928	0%	0%
1000nm+	0.0	0.002003	0%	0%

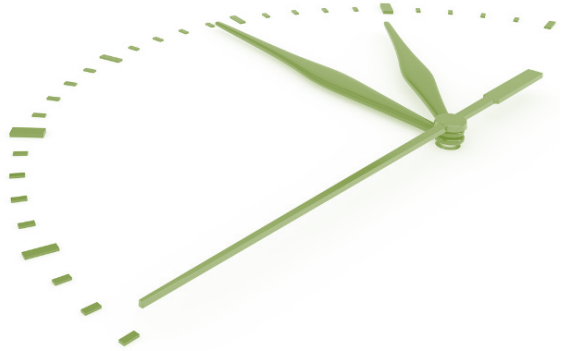
Particle density: **3.77 g/cm3**
Particles per gram: **1.8E14 particles/g** [TiO2 NP's]
Average mass per particle: **5.642E-15 g/particle** [TiO2 NP's]
Surface area per gram: **8.287 m2/g** [TiO2 NP's]
Average volume based size: **102.5 nm**
Percentage of particles in nanoscale: **82.6 %**



Environmental fate

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report





World model

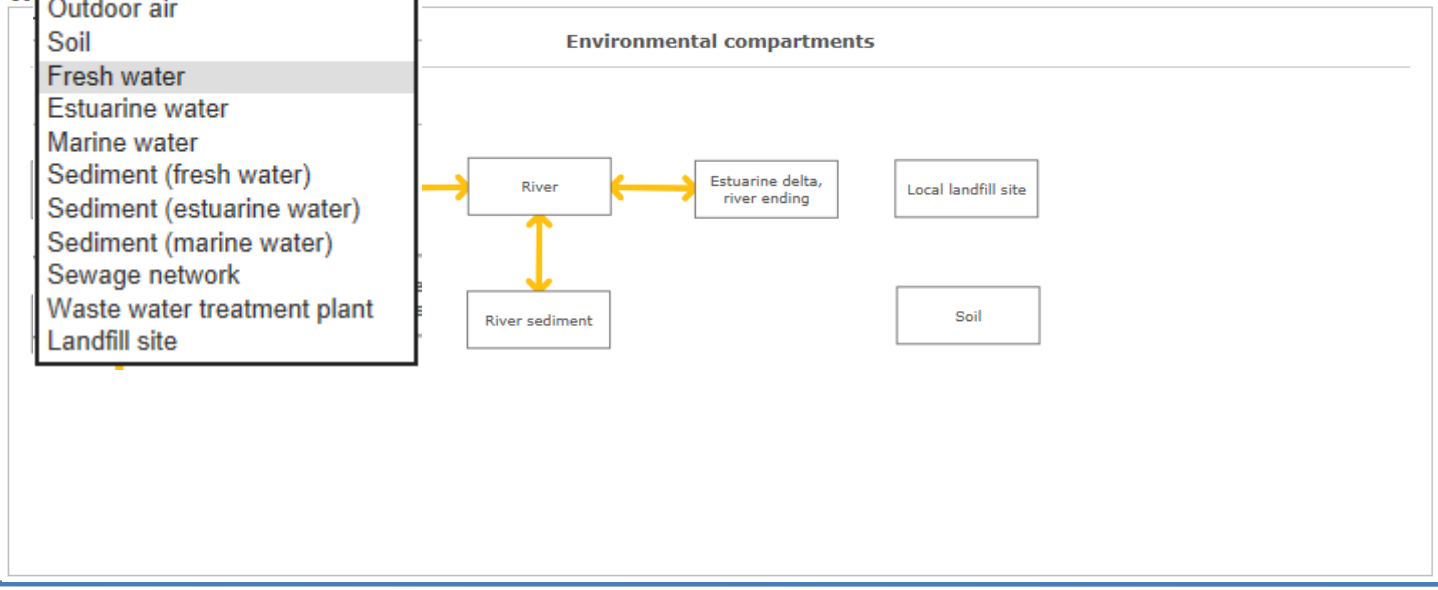
Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment

Compartments

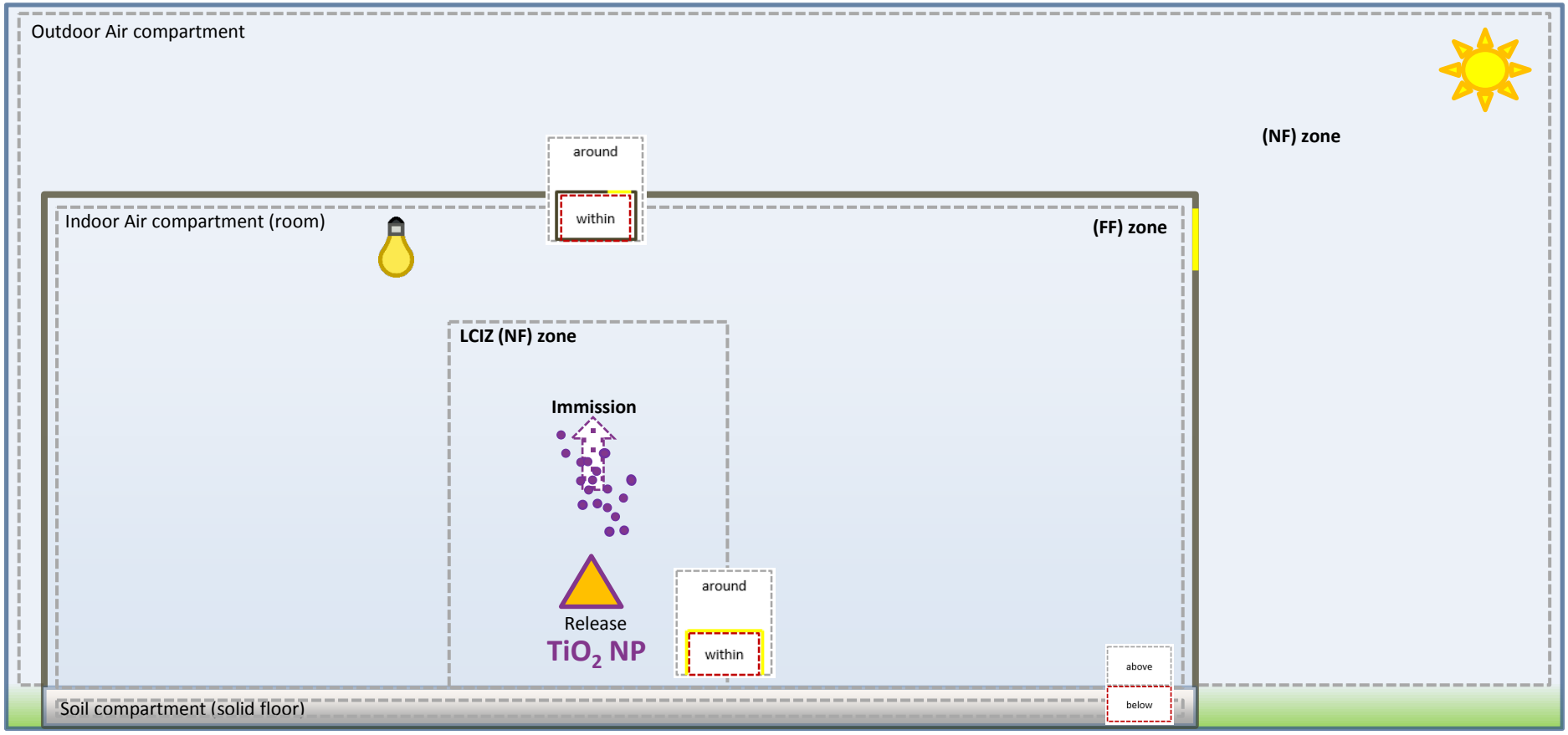
Environmental compartments

	type	name
🗑	Indoor air	Factory hall
🗑	Outdoor air	Air outside factory
🗑	Sewage network	Sewage network system
🗑	Fresh water	River
🗑	Sediment (fresh water)	River sediment
🗑	Estuarine water	Estuarine delta, river ending
🗑	Landfill site	Local landfill site
🗑	Soil	Soil
+		

select--
Indoor air
Outdoor air
Soil
Fresh water
Estuarine water
Marine water
Sediment (fresh water)
Sediment (estuarine water)
Sediment (marine water)
Sewage network
Waste water treatment plant
Landfill site

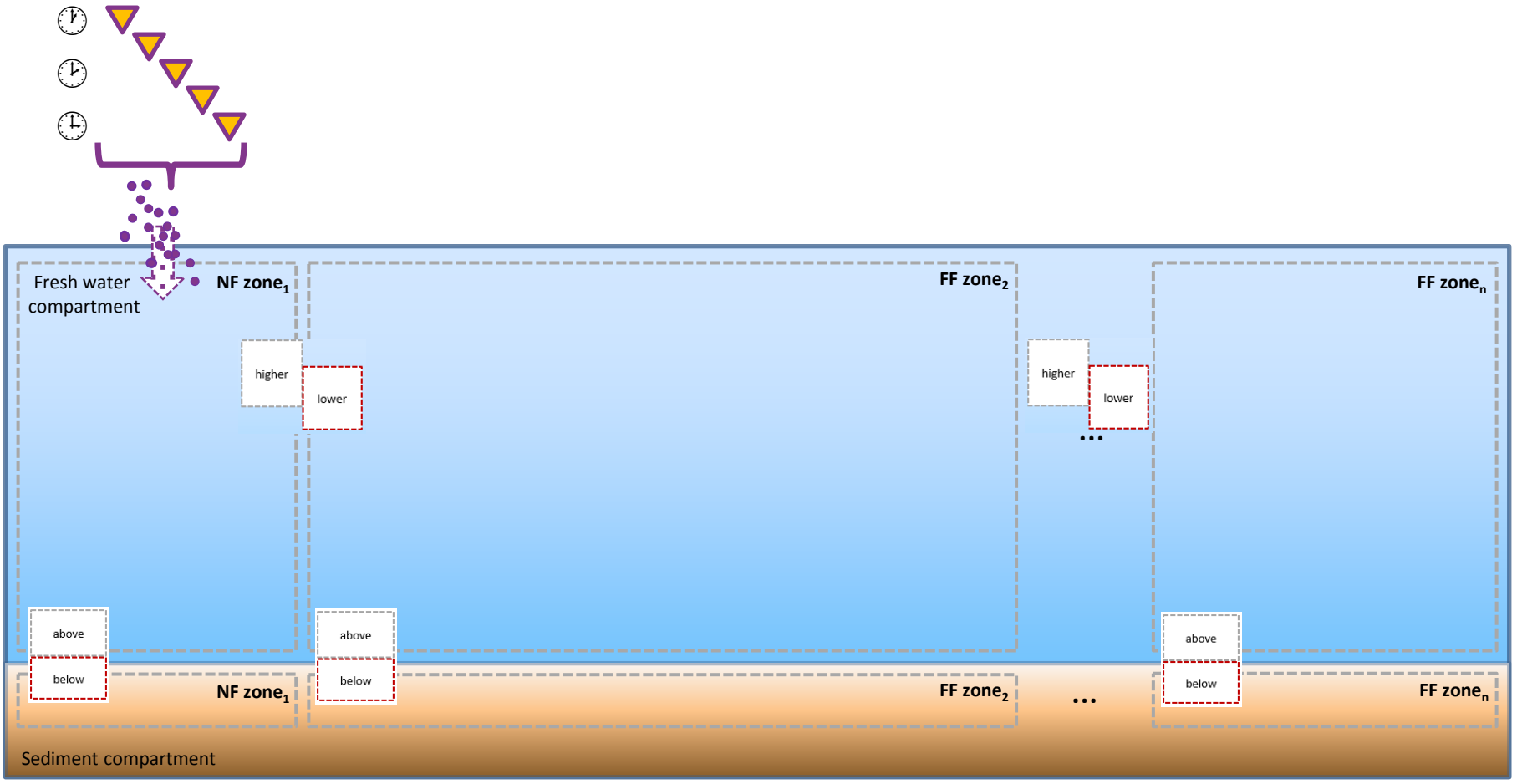


Factory hall & outdoor
(release of TiO_2 NP)

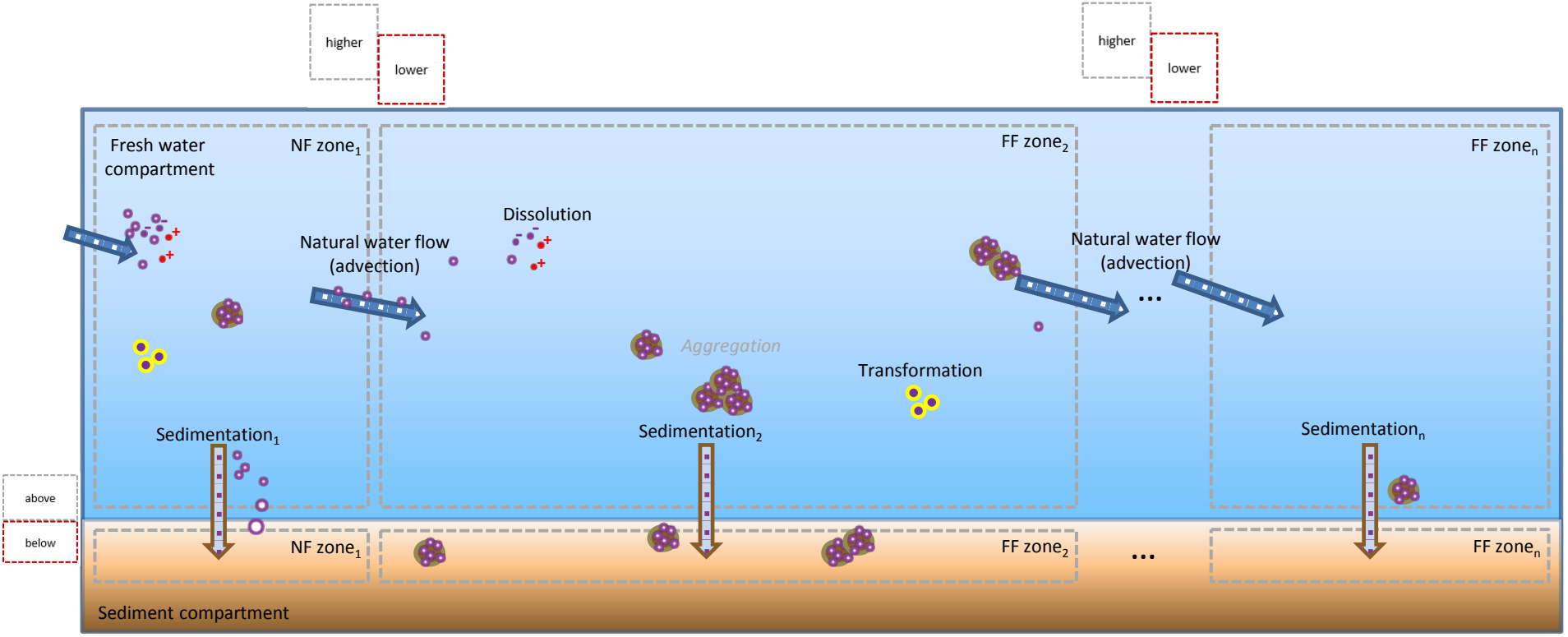


River & Sediment

(Static release of TiO_2 NP's)



Kinetic Fate in River & Sediment



Chemical reactions

Constituents of aquatic medium |

	category	name/identifier	phase	role of constituent	conc.	unit
	chemical	water	liquid	liquid medium	0.000481995996	mol/l
	chemical	oxigen	liquid	dispersed		mol/l
	chemical	H+	ions	dissolved	1E-7	mol/l
	chemical	phosphate	ions	dissolved		mol/l
	chemical	calcium	ions	dissolved	4.25E-5	mol/l
	chemical	magnesium	ions	dissolved	4.89E-5	mol/l
	chemical	sodium	ions	dissolved	1.35E-5	mol/l
	chemical	potassium	ions	dissolved	1.16E-5	mol/l
	chemical	nitrate	ions	dissolved	0.000108	mol/l
	chemical	cloride	ions	dissolved	1.5E-5	mol/l
	chemical	sulfate	ions	dissolved	1.0001742463B4	mol/l
	chemical	bicarbonate	ions	dissolved	4.51E-5	mol/l
	chemica	IronSulfate	solid	dispersed	300.0	µg/l
+	select--					

Zone: A fresh water zone

- Properties
- Composition
- Contact zones
- Immission(s)
- Processes
- Chemical speciation
- Kinetics
- Exposure Agent(s)
- Exposed

importing process | imported species | source zone

process	input species	output species	destination zone
Immission		species: 1 silver NP, start: 0	local
Ag(s) + 1/2 O2(aq) + 2H+ -> 2Ag+ + H2O(aq)	species: 1 silver NP | Silver, start: 0, rate: 0 g/s; 2 O2(aq), 0, 0 g/s; 3 H+, 0, 0 g/s	species: 1 Ag+, start: 0; 2 H2O(aq), 0; Degraded[silver NP], 0	local
2 Ag+ + FeS(s) -> Ag2S(s) + Fe2+	species: 1 Ag+, start: 0, rate: 0 g/s; 2 FeS(s), 0, 0 g/s	species: 1 Ag2S(s), start: 0; 2 Fe+2, 0	local
Ag2S(s) + 2O2 -> 2Ag+ + SO4-2	species: 1 Ag2S(s), start: 0, rate: 0 g/s; 2 O2(aq), 0, 0 g/s	species: 1 Ag+, start: 0; 2 SO4-2, 0	local

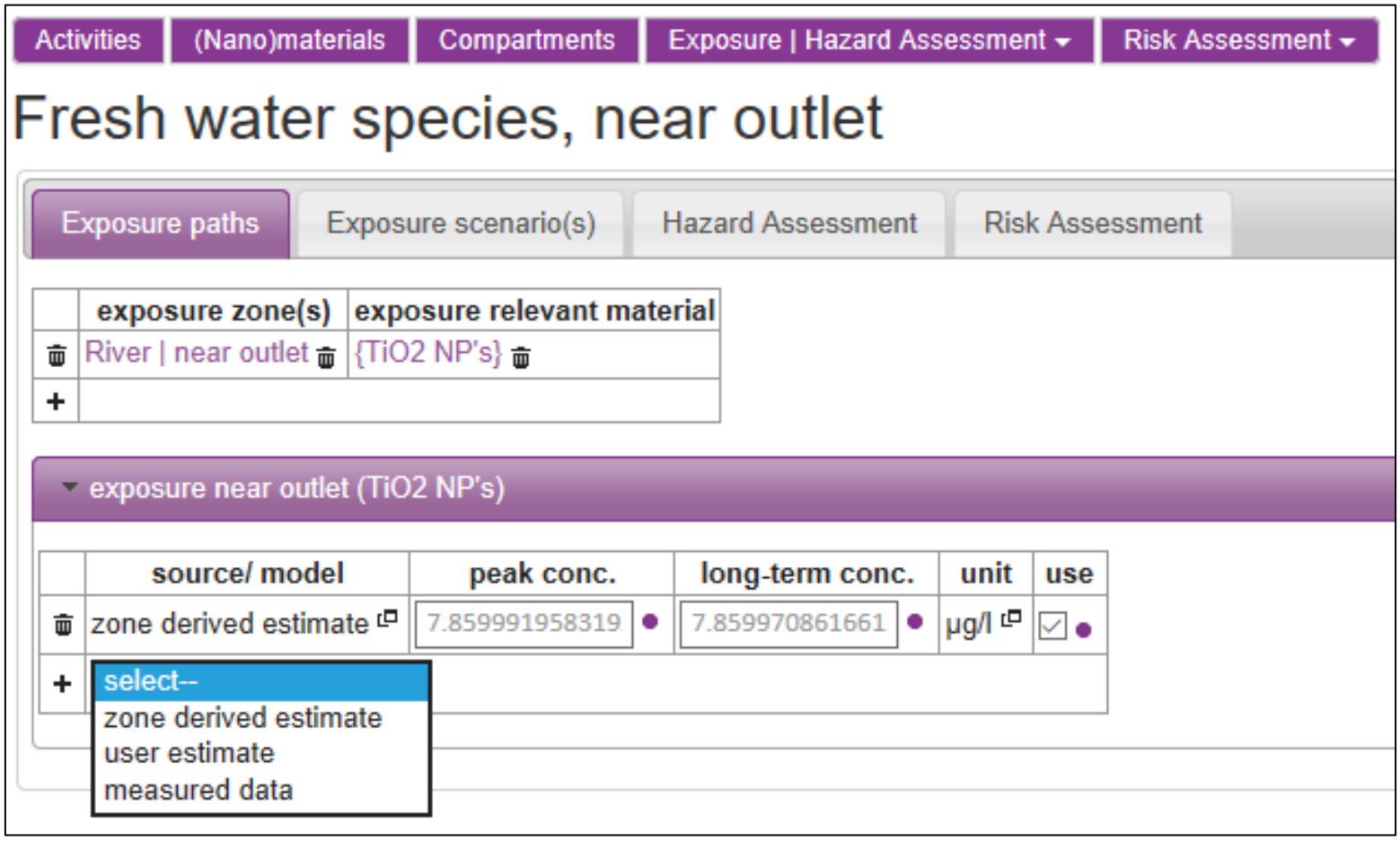
Exposure Module

Estimate ultimate **exposure resulting from the release of NM during an activity**

- ❑ Estimate directly derived from the fate models
- ❑ The Tool will be coupled to the **GUIDEnano exposure scenario** library (based on MARINA Library)
- ❑ The Tool **contains internal exposure models and** also guides the user into appropriate **external exposure assessment models** for each type of activity
- ❑ User estimate
- ❑ Measured data

For human exposure only

Exposure Estimations



Hazard assessment

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report

GOAL

- ✓ Predict Hazard reference values for human and environmental health

  DNEL-like and PNEC-like values

- ✓ Predict need for hazard classification for major hazard endpoints

  Irritant, mutagenic, sensitizer…

Hazard Assessment Strategy

First - Extract from GUIDEnano databases existing reference values /hazard classification for similar materials

Second - Propose worst case default values based on generic grouping

Third - Derive tailored reference values /hazard classification based on available toxicity studies

A) Evaluate each study in terms of :

- **SIMILARITY** of the TEST MATERIAL vs. the EXPOSURE RELEVANT MATERIAL
- **RELEVANCE** of the TEST for the HAZARD endpoint to be assessed
- **QUALITY**: Is it "Trustable"?

B) Derive a Hazard value for the Environmental Compartment / Human Endpoint of interest

Hazard Assessment

Workers in factory

General | Available Protective Controls | Exposure paths | Exposure scenario(s) | Hazard Assessment | Risk Assessment

- repeated dose toxicity (inhalation)
- repeated dose toxicity (dermal)
- carcinogenicity (inhalation)
- carcinogenicity (dermal)
- mutagenicity
- reproductive toxicity (inhalation)
- reproductive toxicity (dermal)
- acute toxicity (inhalation)
- acute toxicity (dermal)
- absorption/ accumulation/ elimination
- respiratory sensitization
- skin sensitization
- skin irritation/corrosion
- developmental toxicity (inhalation)

Workers in factory | repeated dose toxicity (inhalation)

Exposure relevant material: **TiO2 NP's**

STEP 1

Are there regulatory binding or provisional OELs/DNELs for the **exposure relevant** material? (long term exposure) No

STEP 2

Are toxicity studies with the **exposure relevant or similar** material available? Yes

Select existing or new toxicity studies with the **exposure relevant or similar** material

	guide line	name study	studied material
🗑	STIS | STIS - short term inhalation studies (subacute)		TiO2 NP's used in tox study
+	--select--		

Available studies	Score		Override	Accepted	Study Effect Level(s)	DNEL(s)	Uncertainty
STIS	similarity	0.78	0.9	Yes	subacute NOAEL 1.3 mg/m3	long-term DNEL 0.0005889 mg/m3	22.22x
	quality	1.0	-				
	relevance	0.3	0.3				

STEP 3b, Default values based on generic grouping

Lowest DNEL is used

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment

Workers in factory

General | Available Protective Controls | Exposure paths | Exposure scenario(s) | Hazard Assessment | Risk Assessment

- repeated dose toxicity (inhalation)
- repeated dose toxicity (dermal)
- carcinogenicity (inhalation)
- carcinogenicity (dermal)
- mutagenicity
- reproductive toxicity (inhalation)
- reproductive toxicity (dermal)
- acute toxicity (inhalation)
- acute toxicity (dermal)
- absorption/ accumulation/ elimination
- respiratory sensitization
- skin sensitization
- skin irritation/corrosion
- developmental toxicity (inhalation)
- developmental toxicity (dermal)

Workers in factory | repeated dose toxicity (inhalation)

Exposure relevant material: **TiO2 NP's**

STEP 1

Are there regulatory binding or provisional OELs/DNELs for the **exposure relevant** material? (long term exposure) No

STEP 2

Are toxicity studies with the **exposure relevant or similar** material available? Yes

Select existing or new toxicity studies with the **exposure relevant or similar** material

	guide line	name study	studied material
🗑	STIS | STIS - short term inhalation studies (subacute)	STIS xyz	TiO2 NP's used in tox study
🗑	OECD 413 | Subchronic Inhalation Toxicity: 90-day Study		TiO2 NP's used in tox study
+	--select--		

Available studies	Score		Override	Accepted	Study Effect Level(s)	DNEL(s)	Uncertainty
STIS	similarity	0.78	0.9	Yes	subacute NOAEL 1.3 mg/m3	long-term DNEL 0.0005889 mg/m3	22.22x
	quality	1.0	-				
	relevance	0.3	0.3				
OECD 413	similarity	0.78	0.78	No			
	quality	0.0	0.0				
	relevance	0.5	0.5				

STEP 4

Final safety limit value for this endpoint:

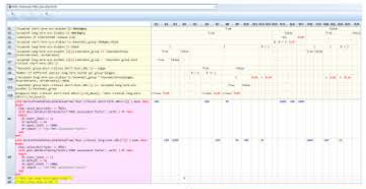
Type	Final safety limit value	Uncertainty
DNEL	long-term DNEL 0.0005889 mg/m3	22.22x

Study based PNEC derivation

Available studies	Score		Override	Accepted	Study Effect Level(s)	Lower Boundary Effect Level(s)	Uncertainty
OECD 203	similarity	0.0	0.9	Yes	short-term LC50 124500 µg/l	LC50 112050 µg/l	1.11x
	quality	1.0	-				
	relevance	1.0	-				
OPPTS 850.1300	similarity	0.0	0.9	Yes	long-term NOEC 3000 µg/l	NOEC 2700 µg/l	1.11x
	quality	1.0	-				
	relevance	1.0	-				
OECD 215	similarity	0.0	0.9	Yes	long-term NOEC 500 µg/l	NOEC 450 µg/l	1.11x
	quality	1.0	-				
	relevance	1.0	-				

STEP 3a

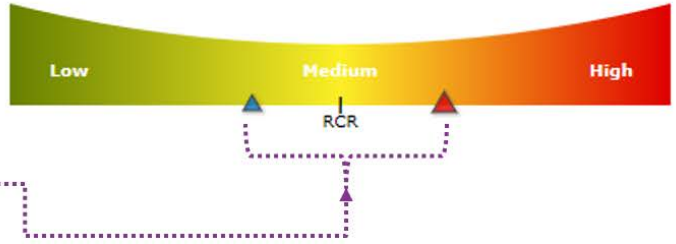
Most critical short-term lower boundary effect level: LC50 112050 µg/l
Taxonomic groups: vertebrates
Most critical long-term lower boundary effect level: NOEC 450 µg/l
Taxonomic groups: invertebrates, vertebrates



Factors overview

Lower Boundary Effect Level	Type	Factor	What does it address	Options for uncertainty reduction
NOEC 450 µg/l				
'similarity override'	uncertainty	1.111x	uncertainty due to dissimilarity between exposure relevant and the studied material	*uncertainty = 1 / override similarity score for now*
'PNEC assessment factor'	uncertainty	50.0x	the PNEC assessment factor	
Derived PNEC		PNEC 9 µg/l	9.0	

Close



STEP 4

Final safety limit value for this endpoint:		
Type	**Final safety limit value**	**Uncertainty**
PNEC	PNEC 9 µg/l	55.56x

Risk assessment

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report

Overall overviews

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment

Human health

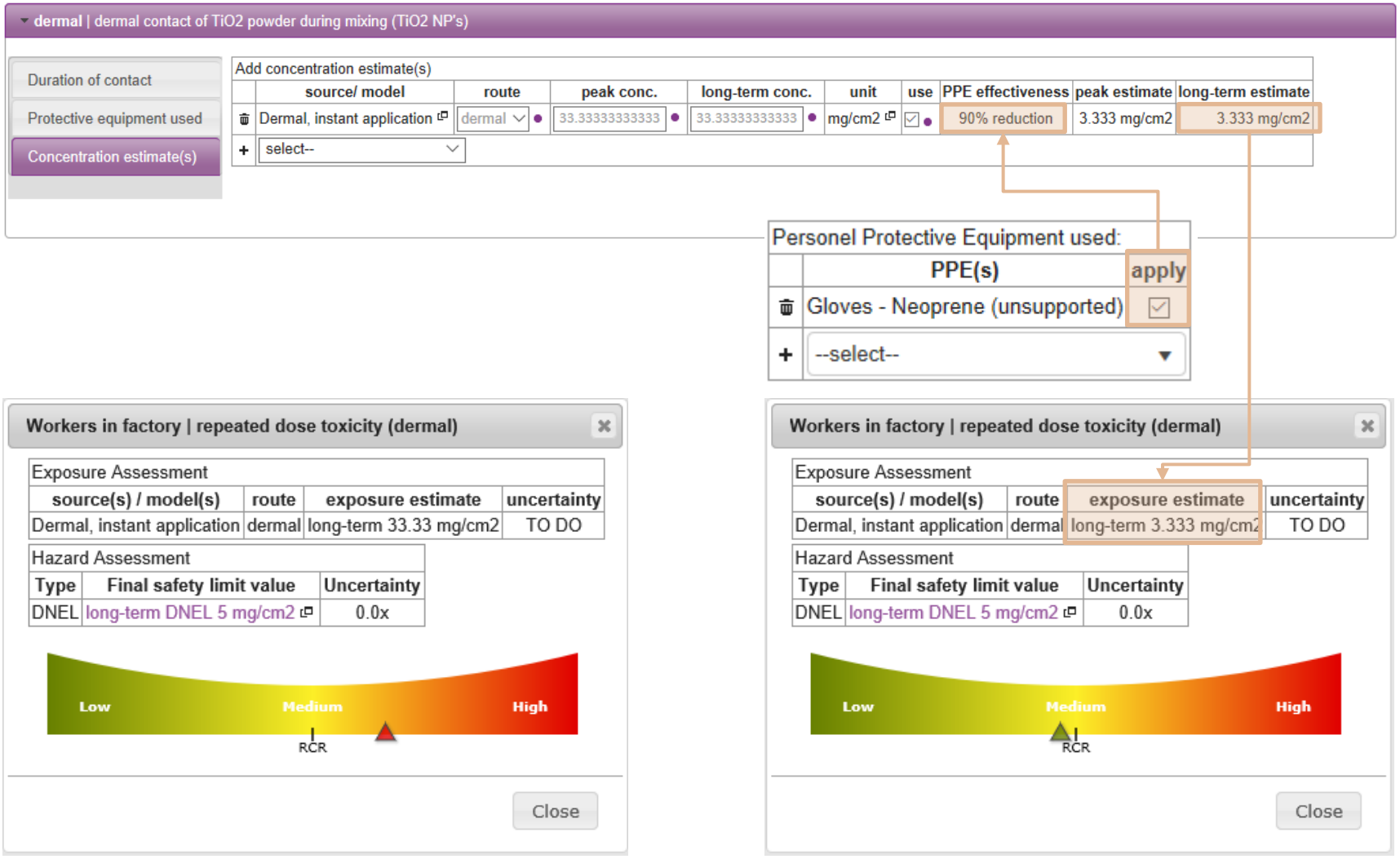
Human exposure	Endpoints human hazard assessment																					
population | exposure	repeated dose toxicity			carcinogenicity			mutagenicity	reproductive toxicity			acute toxicity			absorption/ accumulation/ elimination	sensitization			irritation/ corrosion	developmental toxicity		
	inhalation	oral	dermal	inhalation	oral	dermal		inhalation	oral	dermal	inhalation	oral	dermal		respiratory	oral	skin	skin	inhalation	oral	dermal
Workers in factory																					
- Worker exposure (formulation mixing)		-			-				-			-				-				-	
Living nearby the factory																					
- People living nearby the factory (< 500m)		-	-		-	-			-	-		-	-			-	-	-		-	-

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment

Environmental fate

Environmental fate	Hazard endpoints environmental hazard assessment	
specie | exposure		
Fresh water species, near outlet	PNEC fresh water	PNEC secondary poisoning
- The fresh water species exposed to the TiO2 particles living nearby the outlet of the sewage network.		
Fresh water sediment species, near outlet	PNEC fresh water sediment	
-		
Fresh water species, downstream	PNEC fresh water	PNEC secondary poisoning
-		
Fresh water sediment species, downstream	PNEC fresh water sediment	
-		
Marine water species	PNEC marine water	PNEC secondary poisoning
-		
Soil specie	PNEC soil	PNEC secondary poisoning
Soil specie	PNEC soil	PNEC secondary poisoning

RMM effects

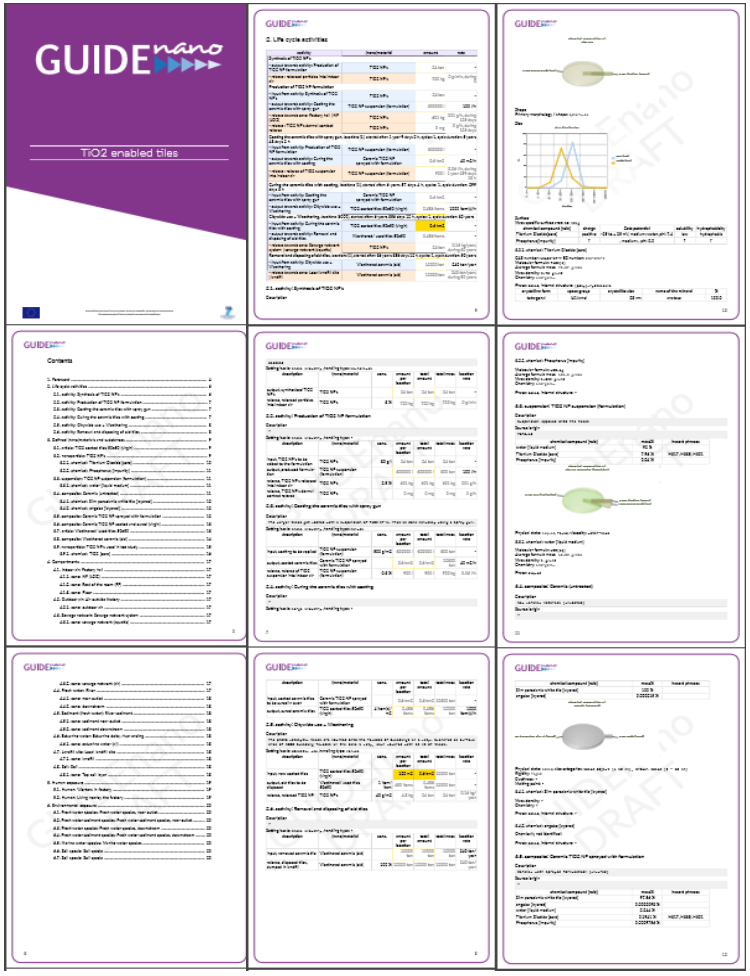


Scenario without gloves

Scenario with gloves

Output report

Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment | Report



BIG THANKS to GUIDEnano Consortium

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