GUIDEnano Tool.v3
Risk Model Testing
The rationale

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)

One decade of intensive research on nanosafety

We need to be able to make use of CURRENT KNOWLEDGE to provide approximated RISK EVALUATIONS
The rationale

Consortium experts

Web-based Tool
V3 was launched at the end of GUIDEnano project.
This version is accessible, but not completed (restricted to certain processes, NMs and toxicity endpoints).
Ongoing projects will extend some of the modules (e.g. NanoCommons, GRACIOUS), but looking for funding to finalize the Tool.

https://tool.guidenano.eu/
For access, please contact Lion Traas (l.traas@thinkworks.nl)
Example case

Antimicrobial

- Will it be **safe for the worker** during the coating process?
- Will it be **safe for the people that wears** it?
- Will it be **safe for the environment** if Ag NPs get released during washing?
Conceptual framework

Activities

Compartments / Fate

Exposure

Hazard

Materials

Similarity

Risk assessment and management
CASE STUDY: TiO$_2$ used for coating of photocatalytic tiles

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.

Name of this case: TiO$_2$ enabled tiles

General description and goal:
Assess the environmental risk using Ceramic tiles coated with photo catalytic TiO$_2$ NP on 5000 facades in a city.
### Activities

<table>
<thead>
<tr>
<th>Activity name</th>
<th>Setting/scale</th>
<th>Life cycle phase</th>
<th>Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthesis of TiO2 NP’s</td>
<td>small industry</td>
<td>synthesis</td>
<td>1</td>
</tr>
<tr>
<td>Production of TiO2 NP formulation</td>
<td>small industry</td>
<td>production</td>
<td>1</td>
</tr>
<tr>
<td>Coating the ceramic tiles with spray gun</td>
<td>small industry</td>
<td>assembly</td>
<td>1</td>
</tr>
<tr>
<td>Curing the ceramic tiles with coating</td>
<td>large industry</td>
<td>assembly</td>
<td>1</td>
</tr>
<tr>
<td>Citywide use + Weathering</td>
<td>other domestic</td>
<td>use/maintenance</td>
<td>5000</td>
</tr>
<tr>
<td>Removal and disposing of old tiles</td>
<td>small industry</td>
<td>end of life</td>
<td>1</td>
</tr>
</tbody>
</table>

**Activity card wizard**

Life cycle stage: **assembly**

Select the activity card from the library:

- --select--
- Cosmetic manufacturing process
- Surface spraying of liquids
- Spray application of paints on e.g. ships (using hvlp or airless techniques)
- Spray application of paints by spray can
- Spray application of paints by pneumatic spraying
- Activities with relatively undisturbed surfaces (no aerosol generation)
- Immersion of objects
- Gluing
Activity: Production of TiO2 NP formulation

<table>
<thead>
<tr>
<th>Activity input</th>
<th>input description</th>
<th>material</th>
<th>relative to</th>
<th>relative amount</th>
<th>total amount</th>
<th>unit</th>
<th>ref.</th>
<th>rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO2 NP's to be added to the formulation</td>
<td>TiO2 NP's</td>
<td>output</td>
<td>produced formulation</td>
<td>80 g/L</td>
<td>24.0 ton</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Activity output(s)</th>
<th>output description</th>
<th>material</th>
<th>relative to</th>
<th>relative amount</th>
<th>total amount</th>
<th>unit</th>
<th>ref.</th>
<th>rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>produced formulation</td>
<td>TiO2 NP suspension (formulation)</td>
<td></td>
<td></td>
<td>300000.0</td>
<td></td>
<td>100 l/h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Activity release(s)</th>
<th>release description</th>
<th>released material</th>
<th>relative to</th>
<th>relative release</th>
<th>RMM's</th>
<th>total release</th>
<th>unit</th>
<th>ref.</th>
<th>rate/location</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO2 NP's released into indoor air</td>
<td>TiO2 NP's</td>
<td>Input</td>
<td>TiO2 NP's to be added to the formulation</td>
<td>2.5 %</td>
<td>no</td>
<td>600000 g</td>
<td></td>
<td>201 g/h</td>
<td></td>
</tr>
</tbody>
</table>
Activity: Coating the ceramic tiles with spray gun

### Activity input
- **input description**: coating to be applied
- **material**: TiO2 NP suspension (formulation)
- **relative to**: coated ceramic tiles
- **relative amount**: 500 g/m²
- **total amount**: 300000.0
- **unit**: [ ]
- **ref. rate**: [ ]

### Activity output(s)
- **output description**: coated ceramic tiles
- **material**: Ceramic TiO2 NP sprayed with formulation
- **relative to**: [ ]
- **relative amount**: [ ]
- **total amount**: 600000.0
- **unit**: m²
- **ref. rate**: 40 m²/h

### Activity release(s)
- **release description**: release of TiO2 suspension into indoor air
- **released material**: TiO2 NP suspension (formulation)
- **relative to**: coating to be applied
- **relative release**: 3 %
- **RMM’s**: 900
- **total release**: [ ]
- **unit**: [ ]
- **ref. rate/location**: 0.06 l/h

---

**Overall mass balance [output + release] / inout**: 42

**The total [output + release] of nanomaterial(s)**: [ ]

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**Local control wizard**

Select the local control from the library.

- Containment - no extraction - Medium
- Containment - no extraction - High
- LEV - Capturing hoods - Fixed capturing hoods
- LEV - Capturing hoods - Movable capturing hoods
- LEV - Capturing hoods - On-tool extraction
- LEV - Capturing hoods - Other receiving hoods
- LEV - Capturing hoods - Canopy hoods
- LEV - Capturing hoods - Other receiving hoods
- LEV - Enclosing hoods - Fume cupboard

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*caLIBRAte, user testing sessions. February, 22nd 2018*
# Activity: Production of TiO2 NP formulation

## Overview

<table>
<thead>
<tr>
<th>Input</th>
<th>From preceding activity</th>
<th>Transport time</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO2 NP’s to be added to the formulation</td>
<td>Synthesis of TiO2 NP’s</td>
<td>0.0 h</td>
<td>h</td>
</tr>
</tbody>
</table>

## Output(s)

<table>
<thead>
<tr>
<th>Output(s)</th>
<th>To succeeding activity</th>
<th>Transport time</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Produced formulation</td>
<td>Coating the ceramic tiles with spray gun</td>
<td>0.0 h</td>
<td>h</td>
</tr>
</tbody>
</table>

## Release(s)

<table>
<thead>
<tr>
<th>Release(s)</th>
<th>Into compartment</th>
<th>Or directly in contact with</th>
</tr>
</thead>
<tbody>
<tr>
<td>TiO2 NP’s released into indoor air</td>
<td>Factory hall</td>
<td>Workers in factory</td>
</tr>
</tbody>
</table>

## Diagram

1. Synthesis of TiO2 NPs
2. Production of TiO2 NP formulation
3. Coating the ceramic tiles with spray gun
4. Factory hall | NF (LCIZ)
(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 across.

<table>
<thead>
<tr>
<th>name</th>
<th>description</th>
<th>category</th>
<th>nano constituents</th>
<th>chem.</th>
<th>hazard statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIO2 coated tiles 50x50 (virgin)</td>
<td>Tiles to be applied outside 50x50 cm and 20 kg/m²</td>
<td>article</td>
<td>TIO2 NP’s</td>
<td></td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
<tr>
<td>TIO2 NP’s</td>
<td>Titanium Dioxide (anatase) nano particles used to c</td>
<td>nanoparticle</td>
<td>TIO2 NP’s</td>
<td></td>
<td>H351 (also constituent(s) with hazard label(s) exist!)</td>
</tr>
<tr>
<td>TIO2 NP suspension (formulation)</td>
<td>Suspension applied onto the tiles</td>
<td>suspension</td>
<td>TIO2 NP’s</td>
<td></td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
<tr>
<td>Ceramic (untreated)</td>
<td>New ceramic material (uncoated)</td>
<td>composite</td>
<td></td>
<td></td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
<tr>
<td>Ceramic TIO2 NP sprayed with formulation</td>
<td>Ceramic with sprayed formulation (uncured)</td>
<td>composite</td>
<td>TIO2 NP’s</td>
<td></td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
<tr>
<td>Ceramic TIO2 NP coated and cured (virgin)</td>
<td>New TIO2 NP coated ceramic material</td>
<td>composite</td>
<td>TIO2 NP’s</td>
<td></td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
<tr>
<td>Weathered/ used tiles 50x50</td>
<td>Old tiles to be disposed of after use phase</td>
<td>article</td>
<td>TIO2 NP’s</td>
<td></td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
<tr>
<td>Weathered ceramic (old)</td>
<td>Aged ceramic material (less NP’s)</td>
<td>composite</td>
<td>TIO2 NP’s</td>
<td></td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
<tr>
<td>TIO2 NP’s used in tox study</td>
<td>NP used in toxicity study</td>
<td>nanoparticle</td>
<td>TIO2 NP’s used in tox study</td>
<td>TIO2 (s)</td>
<td>constituent(s) with hazard label(s) exist!</td>
</tr>
</tbody>
</table>

select--
article
substance/mixture
nano-object
nanostructured aggregate
nanostructured agglomerate
TiO2 NP's

**Shape**
- Morphology / shape: spherical

**Mean size**
- Mean nanoscaled particle diameter (D1 ~ D2 ~ D3) ln 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

<table>
<thead>
<tr>
<th>diameter</th>
<th>%</th>
<th>m2/g</th>
<th>mass%</th>
<th>number%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 1nm</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>1 - 10nm</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>10 - 30nm</td>
<td>10.0</td>
<td>66.03</td>
<td>0.4698%</td>
<td>10.01%</td>
</tr>
<tr>
<td>30 - 100nm</td>
<td>72.6</td>
<td>19.87</td>
<td>13.04%</td>
<td>72.67%</td>
</tr>
<tr>
<td>100 - 300nm</td>
<td>17.2</td>
<td>6.603</td>
<td>64.25%</td>
<td>17.22%</td>
</tr>
<tr>
<td>300 - 500nm</td>
<td>0.1</td>
<td>3.757</td>
<td>2.653%</td>
<td>0.1001%</td>
</tr>
<tr>
<td>500 - 1000nm</td>
<td>0.0</td>
<td>1.928</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>1000nm+</td>
<td>0.0</td>
<td>0.002903</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

Particle density: 3.77 g/cm³
Particles per gram: 1.8E+14 particles/g [TiO2 NP's]
Average mass per particle: 5.642E-15 g/particle [TiO2 NP's]
Surface area per gram: 6.287 m²/g [TiO2 NP's]
Average volume based size: 102.5 nm
Percentage of particles in nanoscale: 82.6%
**TiO2 NP's**

**Physico-chemical characteristics**

- **Mass density:** 3.770215 g/cm³

**Constituents of nano-object | TiO2 NP's**

<table>
<thead>
<tr>
<th>category</th>
<th>name/identifier</th>
<th>phase</th>
<th>role of constituent</th>
<th>conc.</th>
<th>unit</th>
<th>mass perc.</th>
<th>hazard statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>chemical</td>
<td>Titanium Dioxide</td>
<td>solid</td>
<td>core</td>
<td>99.5%</td>
<td>%</td>
<td>~ 99.5%</td>
<td>H317, H335, H301</td>
</tr>
<tr>
<td>chemical</td>
<td>Phosphorus</td>
<td>solid</td>
<td>impurity</td>
<td>0.5%</td>
<td>%</td>
<td>~ 0.5%</td>
<td>H228, H412</td>
</tr>
</tbody>
</table>

**Identification**

- **Chemically identified by:** CAS/EC number
- **CAS number:** 7723-14-0
- **EC number:** 231-768-7
- **Chemical name:** Phosphorus
- **Molecular formula:** P(s)
- **Average formula mass in [g/mol]:** 30.9738
- **Density:** 1.823 g/cm³
- **Chemistry:** inorganic
**Internal properties**

**Identification**
- **Chemically identified by:** CAS/EC number
  - CAS number: 13463-67-7
  - EC number: 235-675-5
- **Chemical name:** Titanium Dioxide
- **Molecular formula:** TiO_2(s)
- **Average formula mass in [g/mol]:** 79.8658
- **Density:** 3.78 g/cm³
- **Chemistry:** inorganic

**Physical properties**
- **Phase:** solid
- **Rigidity:** rigid
- **Internal structure:** (poly)crystalline

<table>
<thead>
<tr>
<th>Crystalline form</th>
<th>Space group</th>
<th>Crystallite size [nm]</th>
<th>Name of the mineral</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>tetragonal</td>
<td>141/amd</td>
<td>28.0</td>
<td>anatase</td>
<td>100.0</td>
</tr>
</tbody>
</table>

- **Melting point in °C:** 1830.0
- **Boiling point in °C:** 2972.0

**Hazard statements**
- H317: May cause an allergic skin reaction.
- H335: May cause respiratory irritation.
- H301: Toxic if swallowed.

Substances (imported and merged from, EPI Phys database, IUCLID 6) Contains approx. 145,000 substances with CAS number / EC number.
**TiO2 NP's**

**Physico-chemical characteristics**

**General**

The nanoparticle [TiO2 NP’s] has been completely identified: Yes
- core | Titanium Dioxide: Yes
- impurity | Phosphorus: Yes

Information on the source/origin of the substance is given: Yes
The purity of the substance is given: Yes
Impurities are stated: Yes

**Nano specific**

The size is given: Yes
The shape is given: Yes
The surface area is given: Yes
The surface charge is given: Yes
The surface reactivity is given: Yes
Environmental fate

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## Compartments

<table>
<thead>
<tr>
<th>Environmental compartments</th>
<th>name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indoor air</td>
<td>Factory hall</td>
</tr>
<tr>
<td>Outdoor air</td>
<td>Air outside factory</td>
</tr>
<tr>
<td>Sewage network</td>
<td>Sewage network system</td>
</tr>
<tr>
<td>Fresh water</td>
<td>River</td>
</tr>
<tr>
<td>Sediment (fresh water)</td>
<td>River sediment</td>
</tr>
<tr>
<td>Estuarine water</td>
<td>Estuarine delta, river ending</td>
</tr>
<tr>
<td>Landfill site</td>
<td>Local landfill site</td>
</tr>
<tr>
<td>Soil</td>
<td>Soil</td>
</tr>
</tbody>
</table>

**Case | Activities | (Nano)materials | Compartments | Exposure | Hazard Assessment | Risk Assessment**
Factory hall & outdoor
(release of TiO$_2$ NP’s)

Outdoor Air compartment

Indoor Air compartment (room)

LCIZ (NF) zone

Immission

Release TiO$_2$ NP’s

Soil compartment (solid floor)

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**Compartment properties**

**Zone related properties**

Factory hall

**General**

**Zones**

Name: Factory hall
Description: Room where tiles are sprayed.

- **Width of the room:** 20.0 m
- **Length of the room:** 40.0 m
- **Surface area of the room:** 800.0 m²
- **Height of the room:** 6.0 m
- **Total volume of the room:** 4800.0 m³
- **Deposition surface in [m²]:** 2320.0

<table>
<thead>
<tr>
<th>zone description</th>
<th>number</th>
<th>medium</th>
<th>size</th>
<th>unit</th>
<th>total dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td>NF (LO2)</td>
<td>1</td>
<td>air</td>
<td>8.0</td>
<td>m³</td>
<td>8 m³</td>
</tr>
<tr>
<td>Rest of the room (FF)</td>
<td>1</td>
<td>air</td>
<td>4792.0</td>
<td>m³</td>
<td>4792 m³</td>
</tr>
<tr>
<td>Floor</td>
<td>1</td>
<td>solid</td>
<td>800.0</td>
<td>m²</td>
<td>800 m²</td>
</tr>
</tbody>
</table>

---

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Relevant processes in Air
Indoor Air compartment (room)

Outdoor Air compartment

Soil compartment (solid floor)

LCIZ (NF) zone

1.4x10^7#/cm^3 8h average (NF)

4.5x10^6#/cm^3 8h average (FF)

TiO2 NPs

TiO2 NPs, 10 - 30nm (mobile)

TiO2 NPs, 30 - 100nm (mobile)

TiO2 NPs, 100 - 300nm (mobile)

TiO2 NPs, 300 - 500nm (mobile)
Kinetic Fate in River & Sediment
Exposed human populations

- Outdoor Air compartment
- Indoor Air compartment (room)
- Soil compartment (solid floor)
- LCIZ (NF) zone
- Immission
- Release
- Worker
- Bystander
- NF (LCIZ), min. 120
- Rest of the room (FF), min. 360
**Workers in factory**

**Population name:** Workers in factory

**Description:**
Worker population in the factory hall, responsible for production of the suspension.

**Population category:** worker(s)

<table>
<thead>
<tr>
<th>Body weight [kg]</th>
<th>67.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total working years</td>
<td>40.0</td>
</tr>
<tr>
<td>Workweeks a year</td>
<td>42.0</td>
</tr>
<tr>
<td>Workdays a year</td>
<td>210.0</td>
</tr>
<tr>
<td>Workdays a week</td>
<td>5.0</td>
</tr>
<tr>
<td>Working hours a day</td>
<td>8.0</td>
</tr>
</tbody>
</table>
Workers in factory

### Available Protective Controls

<table>
<thead>
<tr>
<th>Available Personal Protective Equipment</th>
<th>Effectiveness Inhalation</th>
<th>Effectiveness Dermal (Solid)</th>
<th>Effectiveness Dermal (Liquid)</th>
<th>Effectiveness Oral</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtering half mask (elastomeric face piece) - P2</td>
<td>0.8</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gloves - Neoprene (unsupported)</td>
<td>0.0</td>
<td>0.9</td>
<td>0.85</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PPE selection wizard**

Select the PPE from the library.

- Filtering half mask (elastomeric face piece) - P1*
- Filtering half mask (elastomeric face piece) - P2
- Filtering half mask (elastomeric face piece) - P3
- Filtering half mask (elastomeric face piece) - GasX
- Filtering full face mask (unpowered) - P1*
- Filtering full face mask (unpowered) - P2
- Filtering full face mask (unpowered) - P3
- Filtering full face mask (unpowered) - GasX
## Exposure paths

### Workers in factory

<table>
<thead>
<tr>
<th>Indirect through zone(s)</th>
<th>Direct contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factory hall</td>
<td>Factory hall</td>
</tr>
</tbody>
</table>

#### Indirect

- **exposure zone(s)**
  - Factory hall | NF (LCIZ)
  - Factory hall | Rest of the room (FF)

- **route(s)**
  - Inhalation
  - Dermal
  - Oral

- **exposure relevant material**
  - TiO2 NPs

#### Inhalation | exposure NF (LCIZ) (TiO2 NPs)

<table>
<thead>
<tr>
<th>Concentration estimate(s)</th>
<th>Zone derived estimate(s)</th>
<th>ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source/model</td>
<td>route</td>
<td>peak conc.</td>
</tr>
<tr>
<td>zone derived estimate(s)</td>
<td>inhalation</td>
<td>12293700.42441</td>
</tr>
<tr>
<td>ART</td>
<td>inhalation</td>
<td>100.0</td>
</tr>
</tbody>
</table>

---

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Using external models (1)
Using external models (2)

---

Inhalation | exposure NF (LCiZ) (TiO2 NP’s)

<table>
<thead>
<tr>
<th>Concentration estimate(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protective equipment used</td>
</tr>
<tr>
<td>Population presence</td>
</tr>
</tbody>
</table>

Add concentration estimate(s)

<table>
<thead>
<tr>
<th>source/model</th>
<th>route</th>
<th>peak conc.</th>
<th>long-term conc.</th>
<th>unit</th>
<th>use</th>
<th>PPE effectiveness</th>
<th>peak estimate</th>
<th>long-term estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>zone derived estimate</td>
<td>Inhalation</td>
<td>12293700.42441</td>
<td>12150766.75497</td>
<td>particles/cm³</td>
<td>not applied</td>
<td>1.2E7 particles/cm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ART</td>
<td>inhalation</td>
<td>100.0</td>
<td>100.0</td>
<td>mg/m³</td>
<td>not applied</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure Scenario Library</td>
<td>Inhalation</td>
<td>16285.0</td>
<td>16285.0</td>
<td>particles/cm³</td>
<td>not applied</td>
<td>1.2E7 particles/cm³</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Exposure Scenario Library

Use the GUIDEnano Exposure Scenario Library and search for a similar exposure scenario to derive an exposure estimate from.

Relevant parameters extracted from the GUIDEnano case to search in the Exposure Scenario Library:

- Activity (exposure contributing scenario): Production of TiO2 NP formulation
- NOAA and substance characteristics:
  - Physical state of the NOAA: solid
  - Name of the NOAA used: Titanium Dioxide
- Activity emission potential:
  - Applied level of energy: sMedium

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Production Of Printing Inks, Emptying Bags In Filling Station

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IOM
GUIDEnano (Project funded by the European Union’s Seventh Framework Programme)
Grant Agreement No: 244057
IOM Research Avenue, North, Pcnktet, Edinburgh, EH10 5JF, United Kingdom
## Final exposure estimate

### Workers in factory

#### Exposure scenario

**description**
Worker exposure (formulation mixing)

**relevant material:** TiO2 NP’s

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Presence/Contact</th>
<th>Used Concentration Estimates</th>
<th>Exposure Duration</th>
<th>Predicted Conc.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>exposure NF (LCIZ)</strong></td>
<td>2 h a day</td>
<td>inhalation 1.2E7 particles/cm³</td>
<td>8 h</td>
<td>4.8E6 particles/cm³</td>
</tr>
<tr>
<td><strong>exposure Rest of the room (FF)</strong></td>
<td>6 h a day</td>
<td>inhalation 1.2E7 particles/cm³</td>
<td>8 h</td>
<td>4.8E6 particles/cm³</td>
</tr>
<tr>
<td>Dermal contact of TiO2 powder during mixing</td>
<td>2 h 15 min a day</td>
<td>dermal 2.4E6 particles/cm³</td>
<td>8 h</td>
<td>4.8E6 particles/cm³</td>
</tr>
</tbody>
</table>

---

*calIBRAte, user testing sessions. February, 22nd 2018*
Hazard assessment

Workers in factory

- 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)

Exposure relevant material: TiO2 NP's
Workers in factory

repeated dose toxicity (dermal)

Exposure relevant material: TiO2 NP's

STEP 1
Are there regulatory binding or provisional DNEL dermal for the exposure relevant material? (long term exposure) Yes

Describe the safety limit value for the exposure relevant material:

<table>
<thead>
<tr>
<th>Dose descriptor</th>
<th>critical dose</th>
<th>unit</th>
<th>duration</th>
<th>exposure relevant material</th>
<th>source / comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNEL</td>
<td>5.0</td>
<td>mg/cm²</td>
<td>long-term</td>
<td>TiO2 NP's</td>
<td></td>
</tr>
</tbody>
</table>
Workers in factory

STEP 2

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

<table>
<thead>
<tr>
<th>guide line</th>
<th>name study</th>
<th>studied material</th>
</tr>
</thead>
<tbody>
<tr>
<td>STIS</td>
<td>STIS - short term inhalation studies (subacute)</td>
<td>TiO2 NP’s used in tox study</td>
</tr>
</tbody>
</table>

Available studies

<table>
<thead>
<tr>
<th>Score</th>
<th>Override</th>
<th>Accepted</th>
<th>Study Effect Level(s)</th>
<th>DNEL(s)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.78</td>
<td>0.9</td>
<td>Yes</td>
<td>subacute NOAEL 1.3 mg/m3</td>
<td>long-term DNEL 0.0005889 mg/m3</td>
<td>22.22x</td>
</tr>
</tbody>
</table>

STEP 3b, Default values based on generic grouping
### STIS - short term inhalation studies (subacute) [STIS xyz]

<table>
<thead>
<tr>
<th>General information</th>
<th>Studied / administered material(s)</th>
<th>Species used</th>
<th>Observed Effects</th>
<th>Quality</th>
</tr>
</thead>
</table>

Indicate the **study relevant substance/(nano)material** and if it's contained within a vehicle/carrier material also indicate the **substance as administered**.

If the material you want to refer to is not yet defined, add it to the list of (nano)materials and fill in all available properties.

Is a vehicle/carrier substance used to administer the study relevant material?  **No**

Indicate the study relevant material: TiO2 NP’s used in tox study 📄
### 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

<table>
<thead>
<tr>
<th>Guide Line</th>
<th>Name Study</th>
<th>Studied Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>STIS</td>
<td>STIS - Short term inhalation studies (subacute)</td>
<td>TiO2 NP's used in tox study</td>
</tr>
<tr>
<td>OECD 413</td>
<td>Subchronic Inhalation Toxicity: 90-day Study</td>
<td>TiO2 NP's used in tox study</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Available Studies</th>
<th>Score</th>
<th>Override</th>
<th>Accepted</th>
<th>Study Effect Level(s)</th>
<th>DNEL(s)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STIS</strong></td>
<td></td>
<td></td>
<td>Yes</td>
<td>subacute NOAEL 1.3 mg/m³</td>
<td>long-term DNEL 0.0005889 mg/m³</td>
<td>22.22x</td>
</tr>
<tr>
<td>similarity</td>
<td>0.78</td>
<td>0.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>quality</td>
<td>1.0</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>relevance</td>
<td>0.3</td>
<td>0.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **OECD 413** | | | No | | | |
| similarity | 0.78 | 0.78 | | | | |
| quality | 0.0 | 0.0 | | | | |
| relevance | 0.5 | 0.5 | | | | |


**SIMILARITY assessment:** Park et al (submitted)

**RELEVANCE assessment (for mutagenicity):** Catalán et al. (2017) Nanotoxicology, 11, 964.
**DNEL Derivation**

<table>
<thead>
<tr>
<th>Available studies</th>
<th>Score</th>
<th>Override</th>
<th>Accepted</th>
<th>Study Effect Level(s)</th>
<th>DNEL(s)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>STIS</td>
<td></td>
<td></td>
<td></td>
<td>subacute NOAEL 1.3 mg/m³</td>
<td>long-term DNEL 0.0005889 mg/m³</td>
<td>22.22x</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effect Level</th>
<th>Type</th>
<th>Factor</th>
<th>What does it address</th>
<th>Options for uncertainty reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>subacute NOAEL 1.3 mg/m³</td>
<td>'relevance'</td>
<td>uncertainty 3.33x</td>
<td>uncertainty due to relevance of the study in relationship to this hazard endpoint</td>
<td>uncertainty = 1 / relevance score</td>
</tr>
<tr>
<td>'similarity override'</td>
<td>uncertainty 1.111x</td>
<td></td>
<td>uncertainty due to dissimilarity between exposure relevant and the studied material</td>
<td>uncertainty = 1 / override similarity score for now</td>
</tr>
<tr>
<td>'allometric scaling'</td>
<td>modification 4.0x</td>
<td></td>
<td>Extrapolation of dose based on differences in body weight.</td>
<td></td>
</tr>
<tr>
<td>'toxicokinetics/dynamics'</td>
<td>variability 2.5x</td>
<td></td>
<td>Correction for interspecies differences (other than allometric scaling), i.e. toxicokinetic differences not related to metabolic rate (small part) and toxicodynamic differences (larger part).</td>
<td>can not be reduced</td>
</tr>
<tr>
<td>'exposure time per day (inhalation)'</td>
<td>modification 1.333x</td>
<td></td>
<td>Differences in exposure time per day between exposure scenario and study considered i.e. 6h 6th exposure study is used for a scenario involving 16h or 24h exposure for workers or consumers.</td>
<td>Reduction not possible</td>
</tr>
<tr>
<td>'intraspecies differences'</td>
<td>variability 5.0x</td>
<td></td>
<td>Variability between humans taking into account differences in sensitivity. Such variability is always present in a population.</td>
<td>Reduction not possible</td>
</tr>
<tr>
<td>'study duration'</td>
<td>uncertainty 6.0x</td>
<td></td>
<td>Determines whether study duration is long enough to even assess endpoint and if so, is used to correct for the differences in duration between study and exposure scenario, e.g. when a 28day study is used for chronic exposure.</td>
<td>Reduction is possible based on evidence that increasing exposure does not increase the incidence or severity of adverse effects, particularly for local effects in the respiratory tract (considered concentration- rather than dose dependent).</td>
</tr>
<tr>
<td>'correction activity workers (inhalation)'</td>
<td>modification 1.49x</td>
<td></td>
<td>Differences in respiratory activity between experimental animals and workers (during 8 hours light activity at work the respiratory rate becomes higher than standard).</td>
<td>Reduction not possible</td>
</tr>
</tbody>
</table>

**Factors overview**

Hazard endpoint: repeated dose toxicity (inhalation)

Study: STIS/1

**DNEL Calculation**

- **Derived DNEL**
  - long-term DNEL 0.0005889 mg/m³
Workers in factory

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)

Lowest DNEL is used

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

<table>
<thead>
<tr>
<th>Guide line</th>
<th>Name study</th>
<th>Studied material</th>
</tr>
</thead>
<tbody>
<tr>
<td>STIS</td>
<td>STIS - short term inhalation studies (subacute)</td>
<td>STI02 NPs used in tox study</td>
</tr>
<tr>
<td>OECD 413</td>
<td>Subchronic Inhalation Toxicity: 90-day Study</td>
<td>STI02 NPs used in tox study</td>
</tr>
</tbody>
</table>

Available studies

<table>
<thead>
<tr>
<th>Study Effect Level(s)</th>
<th>DNEL(s)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>subacute NOAEL 1.3 mg/m³</td>
<td>long-term DNEL 0.0005889 mg/m³</td>
<td>22.22x</td>
</tr>
</tbody>
</table>

STEP 4
Final safety limit value for this endpoint:

<table>
<thead>
<tr>
<th>Type</th>
<th>Final safety limit value</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNEL</td>
<td>long-term DNEL 0.0005889 mg/m³</td>
<td>22.22x</td>
</tr>
</tbody>
</table>

CALIBRATE, user testing sessions. February, 22nd 2018
Eco hazard endpoints

Fresh water species, near outlet

Exposure relevant material: TiO2 NP’s

STEP 1
Is there a safety limit value already available for the exposure relevant material? Yes

Describe the safety limit value for the exposure relevant material:

<table>
<thead>
<tr>
<th>Dose descriptor</th>
<th>critical dose</th>
<th>unit</th>
<th>duration</th>
<th>exposure relevant material</th>
<th>source / comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNEC</td>
<td>10.6</td>
<td>µg/l</td>
<td>long-term</td>
<td>TiO2 NP’s</td>
<td>Nanotoxicology, 10:4, 436-444, DOI: 10.3109/1743</td>
</tr>
</tbody>
</table>

Final safety limit value for this endpoint:

Type: PNEC
PNEC: 10.6 µg/l
Uncertainty: 0.0x
Risk Characterization Ratio (RCR) = \frac{\text{Exposure Estimate}}{\text{Final Safety Limit Value}}

Exposure related:
- variability factors
- uncertainty factors

<table>
<thead>
<tr>
<th>Exposure Estimate</th>
<th>Final Safety Limit Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>'relevance'</td>
<td>uncertainty</td>
</tr>
<tr>
<td>'similarity override'</td>
<td>uncertainty</td>
</tr>
<tr>
<td>'allometric scaling'</td>
<td>modification</td>
</tr>
<tr>
<td>'toxicokinetics/dynamics'</td>
<td>variability</td>
</tr>
<tr>
<td>'exposure time per day (inhalation)'</td>
<td>modification</td>
</tr>
<tr>
<td>'intraspecies differences'</td>
<td>variability</td>
</tr>
<tr>
<td>'study duration'</td>
<td>uncertainty</td>
</tr>
<tr>
<td>'correction activity workers (inhalation)'</td>
<td>modification</td>
</tr>
</tbody>
</table>
Eliminating uncertainty in the hazard outcome is unlikely to lower the risk to an acceptable level.

Try to reduce the exposure concentration.

Eliminating uncertainty in the hazard outcome might lower the risk to an acceptable level.

Try to find an additional relevant long-term ecotox study of a different trophic level.
Scenario without gloves: 
- Dermal contact of TiO2 powder during mixing (TiO2 NPs)
- Protective equipment used: Gloves - Neoprene (unsupported)

Scenario with gloves: 
- Dermal contact of TiO2 powder during mixing (TiO2 NPs)
- Protective equipment used: Gloves - Neoprene (unsupported)
## Output report

**caLIBRAtate, user testing sessions. February, 22nd 2018**

**GUIDEnano**

*Tox21 analyzed data*

### Table 1: Analysis Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter A</td>
<td>0.123</td>
<td>m</td>
</tr>
<tr>
<td>Parameter B</td>
<td>4.567</td>
<td>m</td>
</tr>
<tr>
<td>Parameter C</td>
<td>3.141</td>
<td>m</td>
</tr>
</tbody>
</table>

### Graph 1: Data Trends

- **x-axis**: Time (in days)
- **y-axis**: Values of Parameter B

### Graph 2: Comparative Analysis

- **x-axis**: Different conditions
- **y-axis**: Comparison of Parameter C

---

**Note:** Further details and analyses are provided in the comprehensive output report.