Material Safety Data Sheet

according to 1907/2006/EC, Article 31

DATE: 02.08.2013

1. Identification of substance and of the company/undertaking

1.1 Product identifier

Substance Name: Zinc Oxide (powder)
Chemical formula: ZnO
CAS No.: 1314-13-2
EC No.: (EINECS) 215-222-5
Index Number (CLP Regulation): 030-013-00-7
REACH Registration No.: NA

1.2 Relevant identified uses of the substance and uses advised against

Application of the substance / the preparation: Zinc Oxide is used as an additive into numerous materials and products including rubber, ceramics, chemical products, compounds, paints, glass, catalysts, cosmetics.

- Sector of Use category: Industrial use (SU3), Formulation [mixing] of preparations and/or re-packaging (excluding alloys) (SU10). Professional use (SU22).
- Chemical Product category: Coatings and paints (PC9a), Cosmetics, personal care products (PC39).
- Process category: Use in closed batch and other processes (synthesis) where opportunity for exposure arises (PROC4).
- Environmental Release category: Formulation of preparations (ERC2)
- Article category: Paints and varnishes (HS CODE: 320890)

Uses advised against: Consumer use (SU21), Manufacture of food products (SU4)
Reasons why uses advised against: The use of powder by the general public and in food products is advised against due to the high risk of human end environmental exposure.

1.3 Details of the supplier of the Safety Data Sheet

Manufacturer/Supplier: NA
Street address/P.O. Box: NA
Country ID/Postcode/Place: NA
Telephone number: NA
Email address of competent person for the SDS: NA
National Contact: NA

1.4 Emergency telephone number

Opening hours: NA
2. Hazards identification

2.1 Classification of the substance

2.1.1 Classification according to Regulation (EC) No 1272/2008 [CLP]

Aquatic Acute 1, H400
Aquatic Chronic 1, H410

2.1.1.1 Self classification

In case of Zinc Oxide nanoparticles it should be also taken under account, that:

- Any very fine metal particles (nanopowder) may cause eye irritation (suggested: hazard category: “Eye Irrit. 2”, hazard statement code: H319).
- Any very fine metal particles (nanopowder) may cause respiratory irritation (suggested: hazard category: “STOT SE 3”, hazard statement code: H335).
- Any very fine metal particles (nanopowder) may cause skin irritation (suggested: hazard category: “Skin Irrit. 2”, hazard statement code: H315).

2.1.2 Classification according to Directive 67/548/EEC

Classification: N; R50-53
S- phrase; S60, S61

2.1.3 Additional information

Any additional information

2.2 Label elements

Labelling according to Regulation (EC) No 1272/2008 [CLP]

Hazard pictograms:
Suggested pictograms:

Signal word:
GHS09: Warning.

Hazard statements:

Suggested hazard statements:
Very toxic to aquatic life (H400).
Very toxic to aquatic life with long lasting effects (H410).
Causes serious eye irritation (H319).
May cause respiratory irritation (H335).
Causes skin irritation (H315).
Precautionary statement
Avoid release to the environment (P273).
Wear protective gloves/protective clothing/eye protection (P280).
Avoid breathing dust (P261).
Store in a well-ventilated place. Keep container tightly closed (P403 + P233).

2.2 Other hazards
Nano ZnO, as a powder, during handling can form dust. Catalytically active zinc oxide dust is more toxic when treated with ultraviolet light. Aside from these considerations, Zinc oxide dust is considered to be of low toxicity and is classified as a nuisance particulate by the ACGIH. However, inhalation fumes or very fine dust may cause "zinc fume fever", which is characterized by flu-like symptoms with metallic taste, coughing, weakness, fatigue, muscular pain, and nausea, followed by fever and chills. Onset of symptoms occurs about 4-12 hours after exposure.

3. Composition/information on ingredients

3.1 Substances

<table>
<thead>
<tr>
<th>Identification name</th>
<th>Index number in CLP Annex VI</th>
<th>CAS number</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc oxide</td>
<td>030-013-00-7</td>
<td>1314-13-2</td>
<td>≥ 99.9</td>
</tr>
</tbody>
</table>

3.2 Mixtures
NA

4. First aid measures

4.1 Description of first aid measures
Following inhalation: Remove victim to fresh air and keep at rest in a position comfortable for breathing. If required, provide artificial respiration. Seek immediate medical advice.

Following skin contact: No health effect expected. Wash with plenty of soap and water. If skin irritation occurs get medical advice/attention.

Following eye contact: Do not allow victim to rub eye(s). Rinse cautiously with lukewarm, gently flowing water for several minutes, while holding eye(s) open. Remove contact lenses, if present and easy to do. Continue rinsing. If irritation persists, immediately obtain medical attention. Do not attend to manually remove anything stuck to the eye.
Following ingestion: If irritation or discomfort occurs, seek medical treatment.

Self-protection of the first aider: The first responder should wear appropriate personal protection devices, at least a mask to avoid inhalation of powder in air.
Following ingestion: If irritation or discomfort occurs, seek medical treatment.

Self-protection of the first aider: The first responder should wear appropriate personal protection devices, at least a mask to avoid inhalation of powder in air.

4.2 Most important symptoms and effects, both acute and delayed

1. Nausea, vomiting
2. Cough
3. Abdominal pain.
4. Diarrhoea.
5. Itchy and watery eyes.
6. Skin irritation or ulceration.
7. Metallic taste
8. Inhalation of fume may cause metal fume fever. The fume is irritating to the respiratory tract. The effects may be delayed. See Notes.

4.3. Indication of any immediate medical attention and special treatment needed

No further relevant information available.

5. Fire fighting measures

5.1 Extinguishing media:

Suitable extinguishing media: Fire extinguishing powder, dry sand.

Unsuitable extinguishing media: Do not use direct water streams.

5.2 Special hazards arising from the substance or mixture:

When heated to decomposition it emits toxic fumes of zinc oxide.

5.3 Advice for fire-fighters:

Wear self-contained respirator.
Wear fully protective impervious suit.
6. Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures:
Wear protective equipment. Keep unprotected persons away. Ensure adequate ventilation. Close-fitting safety goggles may be necessary in some circumstances to prevent eye contact with dust or fume.

6.1.1 For non-emergency personnel:
Leave affected area.

6.2. Measures for environmental protection:
Clean up in a way that doesn’t disperse the powder into air. Do not allow product to reach sewage system or any water course. Inform respective authorities in case of seepage into water course or sewage system. Do not allow material to be released to the environment without proper governmental permits.

6.3. Measures for cleaning/collecting:
Powder should be mechanically cleaned up in a way that doesn’t disperse it into air. Treat or dispose of waste material in accordance with all local, regional, and national requirements.

6.4. Additional information:
See Section 7 for information on safe handling
See Section 8 for information on personal protection equipment.
See Section 13 for disposal information.

7. Handling and storage

7.1 Precaution for safe handling:
Protective measures:

Measures to prevent fire: May explode when mixed with chlorinated rubber. Zinc Oxide and Magnesium can react explosively when heated.

Measures to prevent aerosol and dust generation: Ensure good ventilation/exhaustion at the workplace. Use appropriate filters (HEP > H13).

Measures to protect the environment: Keep container tightly sealed.

Advice on general occupational hygiene: Avoid inhalation and contact with skin, eyes and clothing. Avoid prolonged or repeated exposure. Always practice good personal hygiene.

No special precautions are necessary if used correctly.
7.2 Conditions for safe storage, including any incompatibilities:

Zinc oxide gradually absorbs carbon dioxide upon exposure to air.

Technical measures and storage conditions:

Store containers in a cool dry location, away from direct sunlight, sources of intense heat, or where freezing is possible.

Store containers away from incompatible chemicals (refer to Section 10, Stability & Reactivity). Inspect all incoming containers before storage, to ensure containers are properly labeled and not damaged.

Have appropriate extinguishing equipment in the storage area.

Packaging materials: No special requirements.

Requirements for storage rooms and vessels: Storage areas made of fire-resistant materials is recommended.

Storage class: NA

Further information on storage conditions

Keep container tightly closed when not in use.

Empty containers may contain residual particles; therefore, empty container should be handled with care.

Never store food, feed, or drinking water in containers, which held this product. Do not store this material in open or unlabeled containers.

7.3 Specific end-uses:

Zinc oxide powder used for preparation of paints and varnishes.

8. Exposure controls and personal protection

8.1 Control parameters

Occupational exposure limits values: (http://limitvalue.ifa.dguv.de)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Zinc oxide, dust</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAS No.</td>
<td>1314-13-2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Country</th>
<th>Limit value - Eight hours</th>
<th>Limit value - Short term</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ppm</td>
<td>mg/m³</td>
</tr>
<tr>
<td>Australia</td>
<td>10 (1)</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Canada - Ontario</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Canada - Québec</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>
This project is implemented through the CENTRAL EUROPE Programme co-financed by the ERDF.

### Table 1: Limit Values of Zinc Oxide

<table>
<thead>
<tr>
<th>Country</th>
<th>Limit value - Eight hours</th>
<th>Limit value - Short term</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ppm</td>
<td>mg/m³</td>
</tr>
<tr>
<td>Australia</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Austria</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
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<td>10</td>
</tr>
<tr>
<td>Canada - Québec</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>European Union</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Germany (DFG)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hungary</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>New Zealand</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Poland</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Singapore</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>South Korea</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Spain</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

### Remarks

- Australia: (1) This value is for inhalable dust containing no asbestos and < 1% crystalline silica.
- Canada - Ontario: (1) respirable aerosol
- Germany (DFG): calculated as Zn
- USA - NIOSH: (1) ceiling limit value (15 min)
Information on monitoring process:

PN-EN 14042:2004: „Powietrze na stanowiskach pracy. Przewodnik użytkowania i stosowania procedur do oceny narażenia na czynniki chemiczne i biologiczne”.

8.2 Exposure controls

8.2.1 Appropriate engineering controls:

- Avoid work procedures producing dusts.
- Minimise the number of exposed workers and the duration and intensiveness of the exposure.
- Keep away from heat.
- Work in ventilated enclosures (e.g., glove box, laboratory hood, process chamber) equipped with high-efficiency particulate air filters (Section 7.1).
- Where operations cannot be enclosed, use adequate ventilation to maintain the concentration of silver dust in working environment below the exposure limit(s) outlined in Section 8.1 of this Safety Data Sheet.
- Provide local exhaust ventilation (e.g., capture hood, enclosing hood) equipped with HEPA filters and designed to capture the contaminant at the point of generation or release.
- Supply sufficient replacement air to make up for air removed by the exhaust system.
- Provide safety equipment such as eyewash fountains, first aid kits and safety showers.

Substance/mixture related measures to prevent exposure during identified uses: NA.

Structural measures to prevent exposure: Provide hand washing facilities and information that encourages the use of good hygiene practices. Prohibit dry sweeping or use of compressed air or portable blowers or fans for clean up. Use wet wiping and vacuum cleaners equipped with HEPA filters. Damp cleaning methods with soap or cleaning oils is preferred. Work area should be cleaned at the end of each work shift (at a minimum).

Organisational measures to prevent exposure: Integrated management systems are implemented at the workplace e.g. ISO 9000/9001, ISO-ICS 13100, or alike, and are, when appropriate, IPPC-compliant. Such management system would include general industrial hygiene practice e.g.:
- information and training of personnel on prevention of exposure/accidents,
- procedures for control of personal exposure (hygiene measures),
- regular cleaning of equipment and floors, extended workers instruction-manuals,
- procedures for process control and maintenance,
- personal protection measures (see below).
Technical measures to prevent exposure: Properly operating chemical fume hood designed for hazardous chemicals and having proper face velocity between 0.4 and 0.6 m/sec (80-120 feet/minute). Constant velocity hoods are a better design than compensating hoods. Filtering cabinet connected to ventilation system to the outside. General ventilation of laboratory environment. If engineering controls are not feasible then the use of a proper respirator mandatory.

8.2.2 **Personal protection equipment:** The usual precautionary measures for handling chemicals should be followed. Keep away from foodstuffs, beverages and feed. Remove all soiled and contaminated clothing immediately. Wash hands before breaks and at the end of work.

8.2.2.1 **Eye and face protection:** If eye contact while using product may be anticipated, wear appropriate safety glasses with side shields or chemical goggles as described by European Standard EN166.

8.2.2.2 **Skin protection:** Substance may have drying effect on skin. Maintain good industrial hygiene. Protection recommended for workers suffering from dermatitis or sensitive skin. Wear protective clean body-covering to minimize skin contact. Either a lab coat or clothing suitable for chemical operations is recommended. In handling a large quantity of powder a Tyvek type jump suit should be considered. In handling a large quantity of dispersion a Tychem type jump suit should be considered.

**Hand protection:** Disposable gloves usually made of lightweight synthetic material such as Nitrile is recommended to guard against potential mild irritants. In handling a large quantity of powder laminated PVA gloves and polycoated Tyvek should be considered.

**Other skin protection:**

8.2.2.3 **Respiratory protection:**

In case of exposure to dust, and in any case if such exposure is above regulatory limits (see above), wear a personal respirator in compliance with national law and European Standard EN 149. Generally, a half respirator with an organic vapour cartridge and particulate filter (NIOSH type P95 or R95 filter) for up to ten times the exposure limit. A full-face piece respirator with an organic vapour cartridge and particulate filter (NIOSH P100 or R100 filter) for 50 times the exposure limit.

Proposed specific personal protection are presented in Tables below.

<table>
<thead>
<tr>
<th>Protective Measure</th>
<th>Nano-Powders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory Protection</strong></td>
<td>Moderate to Heavy Handling of Powders</td>
</tr>
<tr>
<td></td>
<td>Powered Air Purifying Respirator (PAPR)</td>
</tr>
<tr>
<td></td>
<td>Manufacturer: 3M</td>
</tr>
<tr>
<td></td>
<td>Model or NIOSH No.: GVP Series Cartridge</td>
</tr>
<tr>
<td></td>
<td>Type: 3M HEPA (99.97%)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Light Handling of Powders</strong></td>
</tr>
<tr>
<td></td>
<td>Dust Mask Respirator: 3M or Moldex N100 (99.97% efficient)</td>
</tr>
<tr>
<td><strong>Skin Protection</strong></td>
<td>Use nitrile disposable gloves.</td>
</tr>
<tr>
<td><strong>Eye Protection</strong></td>
<td>Safety glasses with side shield.</td>
</tr>
</tbody>
</table>
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| Clothing | Clothing or uniforms normally acceptable for working in a chemical operation. For Heavy Handling of powders Tyvek disposable suit is required. |

8.2.2.4 Thermal hazards: NIF

8.2.2 Environmental exposure controls:

Substance/mixture related measures to prevent exposure during identified uses: NIF

Structural measures to prevent exposure: Use an absorbent walk-off mat where the personnel will exit the access controlled area. Hand washing, showering, changing and cleaning clothes facilities should be provided to prevent the inadvertent contamination of other areas (including take-home) caused by the transfer on clothing and skin.

Organisational measures to prevent exposure: NE

Technical measures to prevent exposure: Filtered ventilated air before release to the outside.

9. Physical and chemical properties:

9.1 Information on basic physical and chemical properties:

a) Appearance:
Physical state: Solid powder (nanomaterial)
Colour: White
Granulometry:
  i) Average particle size (Transmission Electron Microscope image analysis): 26 ± 0.8 nm (SD=1.47).
  ii) Aggregation / agglomeration (Nanoparticle Tracking Analysis): dispersion in water: average particle size 88 nm (SD 31), D10 55 nm, D50 81 nm, D90 128 nm.
  iii) Aggregation / agglomeration (Dynamic Light Scattering): dispersion in water: average particle size 83 nm, polidisperssion: 0.154
  iv) Shape Transmission Electron Microscope image analysis: semi-spherical nanoparticles.

b) Odour: Odourless

c) Odour threshold: NA
d) pH: NA
e) Melting point: NR; ZnO decomposes at 1975 °C.
f) Initial boiling point and boiling grange: NR; decomposes before boiling.
g) Flash point: NA
h) Evaporation rate: NA
i) Flammability (solid, gas): Non-combustible solid, but potentially flammable in dust or powder.
j) Upper/lower flammability or explosive limits: NIF
k) Vapour pressure: NA (solid)
l) Vapour density: NA (solid)
m) Relative density: (at 20 degrees C) 5.1 g/cm$^3$.

n) Crystal structure: Wurtzite (hexagonal)
o) SSA BET: 42 m$^2$/g

n) Solubility:
Water: 1.6 – 5 mg/L.
Soluble in acetic acid, mineral acids, ammonia, ammonium, carbonate, fixed alkali hydroxide solution. Insoluble in alcohol.

Dissolution of Zinc Oxide NPs depends on particle size. Enhanced dissolution was found for smaller particles with the enhancement observed in Zn$^{2+}$(aq) concentrations. Size dependence was observed even though the nanoparticles aggregated with hydrodynamic diameters on the order of 1-3 µm. Results obtained at circumneutral pH (pH 7.5) during 24 hours are presented in Table below.

Content of Zn$^{2+}$ dissolved in water (pH 7.5) during 24 h, registered for ZnO nanoparticles.

<table>
<thead>
<tr>
<th>Particle diameter (d) nm</th>
<th>[Zn$^{2+}$] mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 ± 2</td>
<td>32 ± 1</td>
</tr>
<tr>
<td>7 ± 2</td>
<td>15 ± 1</td>
</tr>
<tr>
<td>15 ± 4</td>
<td>14 ± 1</td>
</tr>
<tr>
<td>17 ± 3</td>
<td>12 ± 1</td>
</tr>
<tr>
<td>24 ± 3</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>47 ± 7</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>130 ± 21</td>
<td>6 ± 1</td>
</tr>
</tbody>
</table>

Dissolution rate of NPs is higher than of bulk-size ZnO particles. In nanopure water solubility rates were 7.43 mg/L·h and 5.56 mg/L·h for 20 nm NPs and bulk-size ZnO particles, respectively.

o) Partition coefficient: n-octanol/water: NA

p) Auto ignition temperature: NA

q) Decomposition temperature: 1975 °C

r) Viscosity: NA

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$^a$ Density of bulk material is 5.6 g/cm$^3$

$^b$ Amount of dissolved Zn$^{2+}$ reached steady state within ca. 6 hours.
s) Explosive properties: Product does not present an explosion hazard. Reacts violently with aluminium powder, magnesium powder and chlorinated rubber (on heating at 215°C). This generates fire and explosion hazard.

t) Oxidising properties: Zinc Oxide reacts with carbon monoxide or hydrogen to produce elemental zinc. Upon heating with magnesium, zinc oxide is reduced explosively.

9.2 Other Information:

u) Dustiness:
Method: EN 15051 standard rotating drum test method (CEN, 2006).
Material: ZnO particles with primary particle size of 250-300 nm
Results: Inhalable 142 mg/kg (Very low), Thoracic 72 mg/kg (Low), Respirable 11 mg/kg (Low)\(^5\)

v) Surface charge: Zeta potential in water: 35 mV

w) High photocatalytic activity under UV illumination\(^6\), \(^7\)

10. Stability and reactivity

10.1 Reactivity:
Zinc oxide is amphoteric, that is it reacts with both acids and alkalis. With acid it reacts to form familiar compound such as zinc sulfate. With alkali it forms zincates. Zinc oxide reacts with fatty acids such as stearic directly by mixing and heating the components above the acid melting point. Zinc oxide also undergoes solid state reactions (calcination) at moderately elevated temperatures. Zinc oxide calcines with other oxides such as silica and magnesia\(^8\).

10.2 Chemical stability: Decomposition will not occur if used and stored according to specifications. Zinc oxide exposed to air absorbs both water vapor and carbon dioxide. This results in the formation of basic zinc carbonate.

10.3 Possibility of hazardous reactions: Reacts violently with aluminium powder, magnesium powder and chlorinated rubber (on heating at 215°C). This generates fire and explosion hazard. Slow addition of zinc oxide to cover the surface of linseed oil varnish resulted in heat generation and ignition.

10.4 Conditions to avoid:
Avoid wet atmosphere. Avoid dust generation and incompatibles.

10.5 Incompatible materials: Acids, Bases. I.e. Acetylene, ammonia, strong hydrogen peroxide solutions, strong acids, oxalic acid, tartaric acid, bromoazide, chlorine trifluoride, and ethyleneimine.

10.6 Hazardous decomposition products: Metal oxide fume.
11. Toxicological information

11.1 Information on toxicological effects

The toxicological properties of Zinc Oxide have not been fully investigated. Zinc Oxide can produce delayed pulmonary edema.

**Acute toxicity**

*Cytotoxicity*[^9]

**Method:** In vitro.
**Species:** Human bronchoalveolar carcinoma-derived cells (A549)
**Routes of exposure:** contact with ZnO NPs (diameter of 70 and 420 nm) dispersed in cell culture medium: Ham’s F-12 medium supplemented with 5% fetal bovine serum, 100 units/mL penicillin, and 100 lg/mL streptomycin.
**Exposure time:** 6, 12 and 24 h.
**NOEL:** around 8 µg/mL
**EC50 values of 70 and 420 nm ZnO particles:** 13.6 and 14.2 mg/mL, respectively.
**Results:** Exposure to both sizes of ZnO particles leads to dose- and time-dependent cytotoxicity reflected in oxidative stress, lipid peroxidation, cell membrane damage, and oxidative DNA damage.

**Oral toxicity**

**Case study 1[^10]**

**Method:** In vitro. OECD Guideline 423 (2001).
**Species:** Rat/Sprague-Dawley (Crl:CD(SD)
**Test substance:** NPs of ZnO (primary particle size: 20 nm).
**Dose levels:** 2,000 mg/kg bw as 20% (W/V) aqueous suspension.
**Dose volume:** 10 mL/kg bw
**Vehicle:** Water for injection.
**Route:** Oral (gavage)
**Exposure:** Single application
**Observation period:** 14 days
**LD50:** > 2000 mg/kg bw.

**Case study 2[^11]**

**Method:** In vitro.
**Species:** mouse
**Route:** Oral
**Results:** LD50 = 7950 mg/kg (OECD 401).

**Case study 3[^12]**

The mice gastrointestinally administrated with 5 g/kg body weight of NPs with diameter of 60 nm showed severe symptoms of lethargy, anorexia, vomiting, and diarrhea in the beginning days after treatment. One week later, all the symptoms gradually disappeared. At 2 and 6 days after
administration, one female and one male mice treated with ZnO NPs were dead, respectively. Two mortalities were preceded by anorexia, lethargy, body-weight losses, and lustreless skin. Further post-mortem investigation demonstrated that the mortalities were caused by severe aggregation of zinc particles obstruction in the intestine. Blood-element test showed that in the PLT and RDW-CV significantly increased, and HGB and HCT significantly decreased compared to the controls, which indicated that N-Zn powder could cause severe anemia.

Inhalation: mouse: LC50 = 2500 mg/m³.

Eye irritation: draize test, rabbit, eye: 500 mg/24h (mild).

Eye irritation: draize test, rabbit, skin: 500 mg/24h (mild).

Skin Irritation
Method: Guide to marketing and manufacturing of cosmetics and quasi drugs in Japan.
Species/strain: Guinea pig/Hartley
Test substance: NPs of ZnO (primary particle size: 20 nm).
Dose level: 25% or 40% dispersion in ethanol.
Dose volume: 0.05 mL, once a day for three consecutive days.
Exposure: Intact skin (open)
Study period: Up to three days
Results: There were no signs of systemic toxicity and no mortality. Slight erythema was observed in one of three animals in the 40% test substance group on day 3 of the administration. No other abnormal dermal changes were observed at any time during the administration and observation periods. No abnormal dermal changes were observed at any time during the administration and observation periods in the 25% test substance group.

Chronic toxicity:

In vivo oral ingestion studies: NOAEL = 50 mg Zn/day (based on human clinical studies).

In vivo inhalation studies
Exploratory 5-day lung toxicity study
Method: Exploratory study with inhalation exposures according to ODCE Guideline 412.
Species/strain: Rat/Wistar
Test substance: ZnO NPs (30-200 nm) coated with triethoxycaprylylsilane
Route: Inhalation
Concentrations: 0, 0.5, 2.5, 12.5 mg/m³
Exposure period: Five days
Frequency of exposure: 6 hours/day
Type of exposure: Head-nose
Recovery period: About 14 days
Results: ZnO induced a concentration-related inflammation reaction in the lung. In addition to the inflammation reaction, necrosis was detected in the lung and the nose. As ZnO is soluble in lung fluid and zinc ions are cytotoxic at higher concentrations necrosis can be attributed to the zinc ions dissolved from the ZnO particles. Likewise, elevated zinc levels were detected in various organs, most likely due to zinc ions dissolved from the ZnO particles.
Skin corrosion/irritation:

Exploratory in vivo study on repeated dose dermal toxicity\textsuperscript{10}
Method: modified OECD Guideline 410
Species: Sprague-Dawley rats
Test substance: ZnO NPs with size of 20 nm (according to manufacturer); 63 nm by SEM
Evaluation, 224.7 nm by DLS in aqueous solution.
Dose applied: 75, 180, and 360 mg/kg bw.
Skin area: 10% of the total body surface
Route: Topical application
Exposure time: 6 hours per day for five days per week for a 28 day period.
Results: There was a significant decrease in the collagen content of the skin and the tail. The loss was higher in the skin than in the tail. There was an inverse dose relationship with the higher doses inducing a lower decrease. A maximum decrease was more than 50%.

Skin sensitisation:

Human repeat insult patch test\textsuperscript{10}
Guideline/method: According to internal laboratory methodology.
Species: Human
Group size: 50 volunteers (six males and 44 females)
Test substance: ZnO NPs with crystal size of 48 nm
Concentration: 25% in corn oil (0.2 mL dispensed on occlusive, hypoallergenic patch)
Vehicle: Corn oil
Route: Dermal occlusive application by patch
Procedure: Induction: Nine consecutive 24 hour exposures on Monday, Wednesday and Friday for three consecutive weeks.
Rest period: 10–14 days
Results: None of the 50 investigated volunteers showed any skin reaction at any time. All volunteers were consequently scored with grade 0.

Serious eye damage/irritation: Powder: irritant effect

Germ cell mutagenicity:

Case study \textsuperscript{10}
Comet assay in human nasal mucosal cells
Route: In vitro
Method: According to published protocol
Species/strain: Human nasal mucosal cells obtained from ten surgery patients
Test substance: ZnO nanoparticles (<100 nm, surface area 15–25 m\textsuperscript{2}/g)
Dose levels: Diluted nanoparticle suspension at end concentrations of 0.01, 0.1, 5, 10 and 50 μg/mL
Vehicle: Distilled water
Exposure: Single exposure of 24 hour.
Results: Under the experimental conditions the used ZnO nanoparticles induced DNA damage in human nasal mucosal cells and, consequently, ZnO nanoparticles was genotoxic (clastogenic and/or mutagenic) in these cells. The SCCS agrees with the conclusion that the used ZnO nanoparticles were genotoxic in the comet assay with primary human nasal mucosal cells.
Case study 210

Comet assay in human nasal mucosal cells
Route: In vitro
Method: According to published protocol
Species/strain: Human nasal mucosal cells.
Test substance: ZnO nanoparticles (<100 nm, surface area 15–25 m²/g).
Dose levels: 500 μL of diluted nanoparticle at end concentrations of 0.1, and 5 μg/mL
Vehicle: Distilled water
Exposure: Repeated 3 consecutive exposures of 1 h with a washing step in between
Study period: 27 hours
Results: DNA fragmentation increased after 24 hr of regeneration. In contrast, DNA damage which was induced by the positive control, methyl methanesulfonate, was significantly reduced after 24-hr regeneration. Results suggest that repetitive exposure to low concentrations of ZnO nanoparticles results in persistent or ongoing DNA damage.

Carcinogenicity: CAS# 1314-13-2: Not listed by ACGIH, IARC, NTP, or CA Prop 65.

Reproductive toxicity: Information on the developmental and reproductive toxicity in humans following inhalation exposure to ZnO was unavailable.

Summary of evaluation of the CMR properties: NIF

STOT-single exposure: NIF

STOT-repeated exposure: NIF

Aspiration hazard: NIF

Additional toxicological information: To the best of our knowledge the acute and chronic toxicity of this substance is not fully known.

12. Ecological information:

12.1 Toxicity

Do not allow material to be released to the environment without proper governmental permits.

Acute (short term) toxicity:

Fish13:
Method: In vitro.
Species: Adult Zebrafish (Danio rerio)
Routes of exposure: Ingestion; ZnO nanoparticles dispersed in aerated single-distilled water.
This project is implemented through the CENTRAL EUROPE Programme co-financed by the ERDF

<table>
<thead>
<tr>
<th>Average diameter [nm]</th>
<th>Diameter range [nm]</th>
<th>Hydrodynamic diameter [nm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPs</td>
<td>30</td>
<td>16-157 nm</td>
</tr>
</tbody>
</table>

Effective Dose: LD = 30 mg/L, LC50 = 4.92 mg/L
Exposure time: 96 h

Results:
1. Toxicity of ZnO NPs was similar to toxicity of bulk particles (96-h LC50 = 3.31 mg/L). The toxicity of ZnO NPs could attribute to the combination of NPs themselves, the ∙OH generated and Zn$^{2+}$ ions.
2. Oxidative stress and tissue damage were induced in the liver and gut by NPs through superfluous ROS as indicated by the biomarkers SOD, CAT and GHS. All biomarkers measured in liver tissue were sensitive to 5 mg/L ZnO NPs. The malondialdehyde levels in the liver of fish exposed to 5 mg/l of ZnO NPs was elevated (204% of control).

Metazoa

Method: In vitro.
Species: L1 larvae of Nematode Caenorhabditis elegans (strain Bristol N2)
Routes of exposure: Contact wit suspensions of NPS or bulk ZnO nanoparticles (0.4-8.1 mg/L) in ultrapure water.
Exposure time: 24 h

Characteristics of particles and LC50 values for NPs and bulk ZnO

<table>
<thead>
<tr>
<th>Particle</th>
<th>SSA (m$^2$/g)</th>
<th>Diameter (nm)</th>
<th>Hydrodynamic diameter (nm)</th>
<th>LC50 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nano-ZnO</td>
<td>54</td>
<td>20</td>
<td>759</td>
<td>2.2</td>
</tr>
<tr>
<td>Bulk ZnO</td>
<td>3.3</td>
<td>532</td>
<td>737</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Results: Compared to the control, exposure to 1.6 mg L$^{-1}$ and 4.1 mg L$^{-1}$ ZnO NPs and bulk ZnO significantly reduced the growth of C. elegans, the number of eggs inside the worm and offspring per worm. However, the effect on growth and number of eggs inside the worm was not significantly different among ZnO NPs, bulk ZnO

Zebrafish embryo

Method: In vitro.
Species: 3-3.5 (hpf) embryo-larval of Zebrafish (Danio rerio)
Routes of exposure: Contact wit suspension of 30 nm ZnO nanoparticles (1-100 mg/L) in water (E3 medium).
Exposure time: 96-h post fertilization
LC = 50 mg/L.
Results: ZnO NPs retarded the embryo hatching (1-25 mg/L), reduced the body length, caused tail malformation.

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* According to TEM images
* Particle size distribution in solutions, measured by nano-sizer.
**Crustacea**

Method: In vitro  
Species: *Daphnia magna*  
Routes of exposure: nanoparticles with different diameter were dispersed in three different test media.  
Effective Dose: EC50 close to the 1 mg/L  
Exposure time: 48 h  
Results: In general, the toxicity in the acute tests was independent of particle size (non-nano-scale or nano-scale), coating of particles, aggregation of particles, the type of medium or the applied pre-treatment of the test dispersions.

**Algae/aquatic plants**

Species: *Pseudokirchneriella subcapitata* (formerly known as *Selenastrum capricornutum* and *Rhopidocelis subcapitata*)  
Routes of exposure: contact with liquid test medium containing NPs of with diameter of 50–70 nm.  
Exposure time: 72 h  
Results: NOEC = 0.017 mg metal/l  
EC50 = 0.042 mg metal/l

**Bacteria (own research)**

Method: In vitro. LUMISTOX DIN EN ISO 11348-3  
Species: marine bacteria *Vibrio ficheri*  
Routes of exposure: water with 20.4% sucrose with 50/5/0.5/0.05/0.005 ppm of ZnO nanoparticles with mean diameter 26 nm.  
Exposure time: 30 min  
Results: NOEL = 5 ppm  
EC50 = 52 ppm

**Chronic (long term) toxicity**

*Fish*: NIF  
*Algae/aquatic plants*: NIF  
*Other organisms*: NIF

### 12.2 Persistence and degradability

Abitic degradation: NIF  
Physical- and photo-chemical elimination: NA  
Biodegradation: NA

### 12.3 Bioaccumulation potential

Partition coefficient n-octanol/water: NA  
Bioconcentration factor (BCF): ND
12.4  Mobility in soil
Known or predicted distribution to environmental compartments: ND
Surface tension: NA
Adsorption/desorption: NA

12.5  Results of PBT and vPvB assessment: NA

12.6  Other adverse effects: NIF

12.7  Additional information:
Because of its colloidal properties, it is expected that ZnO binds to complexing and sorbing agents present in soil, suspended matter of sediment.

13. Disposal considerations

13.1  Waste treatment methods

13.1.1  Product/packaging disposal:
The generation of waste should be avoided or minimised wherever possible. Solutions and any by-products should at all times comply with the requirements of environmental protection and waste disposal legislation and any regional local authority requirements. Consult state, local or national regulations to ensure proper disposal.

Product
EWC code 060316: Metallic oxides other than those mentioned in 060315.
Keep waste separate. Because of possible pollution, remove as industrial waste or hazardous waste

Packaging
EWC code 150110: Packaging containing residues of or contaminated by dangerous substances.
Keep waste packaging separate. Consult state, local or national regulations to ensure proper disposal.

13.1.2  Waste treatment-relevant information: Consult state, local or national regulations to ensure proper disposal.

13.1.3  Sewage disposal-relevant information: Disposal via wastewater treated in a common wastewater treatment plant is preferred to disposal via landfill.

13.1.4  Other disposal recommendations: There are no specific informations about disposal of wastes containing Zinc Oxide. However, it is suggested to avoid release of solid material into the environment.
14. Transport information

Land transport ADR/RID (cross-border)
ADR/RID class: 9

Maritime transport IMDG
IMDG Class: 9

Air transport ICAO-TI and IATA-DGR
ICAO/IATA Class: 9

14.1 UN number: UN307718
14.2 UN proper shipping name: Environmentally hazardous substances, solid, n.o.s. (Zinc Oxide nanopowder).
14.3 Transport hazard class: 9
14.4 Packing group: III
14.5 Environmental hazards: hazardous to the aquatic environment.
14.6 Special precautions for user: Do not let this chemical enter the environment.
14.7 Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code: NR

It is suggested to use a secondary seal, such tape seal, or a wire tie to prevent a removable closure from inadvertently opening during transport. The outer package should be filled with shock absorbing material that can protect the inner sample container from damage, absorb liquids that might leak from the inner container during normal events in transport, if applicable.

15. Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture:

EU Regulations:

Authorisations and/or restrictions on use: Not determined/listed
Authorisations: Not determined/listed
Restriction on use: For use only by technically qualified individuals.

15.2 Chemical Safety Assessment: Chemical Safety Assessment has not been carried out.
16. Other information

Notes:
Reacts with hydrochloric acid to produce zinc chloride and with sulphuric acid to produce zinc sulphate. Zinc oxide reacts with hydrogen fluoride to produce zinc fluoride etrahydrate. It reacts with carbon monoxide or hydrogen to produce elemental zinc. Upon heating with magnesium, zinc oxide is reduced explosively. Zinc oxide powder reacts violently with chlorinated rubber at 215°C. Reacts slowly with fatty acids in fats and oils to produce lumpy masses of zinc oleate and stearate. When mixed with a strong solution of zinc chloride or with phosphoric acid, zinc oxide forms a cement-like product, due to the formation of oxy-salts.

It is a sparingly soluble salt with near neutral pH, properties which render it less toxic than zinc sulphate or zinc chloride. Most toxicological reports involving zinc oxide are of "metal fume fever" following occupational inhalation of zinc oxide dust and/or fume.

Studies of zinc oxide inhalation have shown a dose dependent reversible increase in the neutrophil, lymphocyte and macrophage counts of bronchoalveolar lavage fluid and a reversible restrictive pulmonary function defect accompanying the typical features of "metal fume fever".

Zinc oxide fume inhalation causes "metal fume fever". Symptoms may occur up to 24 hours post exposure with cough, dyspnoea, sore throat, chest tightness, headache, fever, rigors, myalgia, arthralgia and sometimes a metallic taste, nausea, vomiting and blurred vision. Chest X-ray may show transient ill-defined opacities but there are typically no delayed sequelae.

Zinc oxide acts as a catalyst in alkylation, oxidation, hydrogenation and desulphurisation reactions.

This information is based on our present knowledge. However, this shall not constitute a guarantee for any specific product features and shall not establish a legally valid contractual relationship.

Indication of changes: Non

Abbreviations and acronyms:
EC No: European Commission number
EINECS: European Inventory of Existing Commercial Chemical Substances
REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals
CAS No: Chemical Abstracts Service number
SU: Sector of Use category
PC Chemical Product category
PROC: Process category
TARIC CODE: Integrated Tariff of the European Communities
CLP regulation: Classification, Labelling and Packaging
STOT SE: Specific Target Organ Toxicity Single Exposure
STOT RE: Specific Target Organ Toxicity Repeated Exposure
HEPA: High Efficiency Particulate Air (filter)
NIOSH: National Institute for Occupational Safety and Health
OSHA: Occupational Safety and Health Administration
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ICS: International Classification for Standards
ISO: International Organization for Standardization
SD: Standard Deviation parameter
D10, D50, D90: particle diameter where that 10%, 50% and 60% of all particles are finer (smaller)
DI water: Deionized water
SSA: Specific Surface Area
BET: Multi-point Brunauer–Emmett–Teller (BET) method
NPs: Nanoparticles
CMR: Carcinogenic, Mutagenic or Toxic for Reproduction
RTECS: Registry of Toxic Effects of Chemical Substances
OECD: Organisation for Economic Co-operation and Development
ADR: Accord européen sur le transport des marchandises dangereuses par Route (European Agreement concerning the International Carriage of Dangerous Goods by Road)
RID: Règlement international concernant le transport des marchandises dangereuses par chemin de fer (Regulations Concerning the International Transport of Dangerous Goods by Rail)
EWC: European Waste Catalogue codes.
IMDG: International Maritime Code for Dangerous Goods
IATA: International Air Transport Association
ICAO: International Civil Aviation Organization
GHS: Globally Harmonized System of Classification and Labelling of Chemicals
LD: Lethal dose
LD50: Lethal dose, 50 percent
LC50: Lethal concentration, 50 percent
EC50: Effective-concentration
NLEC: No Lethal Effective-concentration
NOEL: No-Observed Effect Level
NOEC: No-Observed effect concentration
NOAEL: No Observed Adverse Effect Level
NE: Not established
NA: Not applicable
NIF: No Information Found
ND: No Data

Relevant R-phrases and/or H-statements (number and full text):

H400 - Very toxic to aquatic life.
H410 - Very toxic to aquatic life with long lasting effects.
H319 - Causes serious eye irritation.
H335 - May cause respiratory irritation.
H315 - Causes skin irritation.
R50 - 53 Aquatic Acute 1, Aquatic Chronic 1: very toxic to aquatic organisms, May cause long-term adverse effect In aquatic environment.
S60 – This material and its container must be disposed of as hazardous waste.
S61 – Avoid release to the environment. Refer to special instructions/safety data sheet.
Key literature references and sources of data:

2 http://www.cdc.gov/niosh/npg/npgd0557.html
4 Dissolution and aggregation of zinc oxide nanoparticles at circumneutral pH; a study of size effects in the presence and absence of citric acid, R-A-Thilini Perera Rupasinghe, Theses and Dissertations, University of Iowa (2011).
10 OPINION ON Zinc oxide (nano form) COLIPA S 76, Scientific Committee on Consumer Safety, SCCS, The SCCS adopted this opinion at its 16th plenary meeting of 18 September 2012.
Disclaimer

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