ETH zürich

Guideline: Safe Handling of Nanomaterials in the Lab

Nanomaterials are produced and used at several ETH Zurich laboratories. Due to the widely varying properties and, thus, the hazard potential of nanomaterials, the special safety measures collected in this guideline must be observed when handling them. The recommendations formulated here refer to a research laboratory scale, i.e. from a few grams to a maximum of 1 kilogram.

Welding smoke particles; carbon nanotubes; titanium dioxide nanocoatings (source: BauA)

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Scope

This guideline applies for all ETH Zurich institutes and research groups working with nanomaterials.

Legal basis

Current legislation in the chemical, food, environmental and pharmaceutical sectors also applies to nanomaterials. In Switzerland, the *Chemikalienverordnung* (Ordinance on Chemicals), the *Biozidprodukteverordnung* (Ordinance on Biocidal Products), the *Pflanzenschutzmittelverordnung* (Ordinance on Plant Protection Products) and *Lebensmittelrecht* (Food Law) contain specific requirements for nanomaterials. Further nanospecific legal adaptations will be developed in the implementation of the "Action plan for synthetic nanomaterials".

- *Bundesgesetz über den Schutz vor gefährlichen Stoffen und Zubereitungen*, ChemG (Swiss Federal Act on Protection Against Dangerous Substances and Preparations)
- *Verordnung über den Schutz vor gefährlichen Stoffen und Zubereitungen/Chemikalienverordnung*, ChemV (Ordinance on Protection Against Dangerous Substances and Preparations/Ordinance on Chemicals)
- *Verordnung über das Inverkehrbringen von und den Umgang mit Biozidprodukten/Biozidprodukteverordnung*, VBP (Ordinance on the Placing on the Market and Handling of Biocidal Products/Ordinance on Biocidal Products)
- *Verordnung über das Inverkehrbringen von Pflanzenschutzmitteln/Pflanzenschutzmittelverordnung*, PSMV (Ordinance on the Placing on the Market of Plant Protection Products/Ordinance on Plant Protection Products)
- *Verordnung über die in Lebensmitteln zulässigen Zusatzstoffe/Zusatzstoffverordnung*, ZuV (Ordinance on the Additives Permitted in Foodstuffs/Additive Ordinance)
- *Bundesgesetz über die Arbeit in Industrie, Gewerbe und Handel/Arbeitsgesetz*, ArG (Swiss Federal Act on Work in Industry, Trade and Commerce/Labour Act)
- Bundesgesetz über die Unfallversicherung, UVG (Swiss Federal Act on Accident Insurance)
- *Verordnung über die Verhütung von Unfällen und Berufskrankheiten*, VUV (Ordinance on the Prevention of Accidents and Occupational Diseases)
- Labour Act of 13/3/1964 (Art. 6, Art. 35) and the commentary on Ordinances 3 and 4 of the Labour Act (commentary on 3 and 4 of the ArG)
- *Wegleitung zum Vorsorgeraster für synthetische Nanomaterialien* (Commentary on the precautionary matrix for synthetic nanomaterials). *Bundesamt für Gesundheit und Bundesamt für Umwelt (*Federal Office of Public Health and Federal Office for the Environment), Berne 2018, Version 3.1

Explicit authorisation regulations exist for nanomaterials in the following areas:

- Pharmaceuticals, plant protection products and biocidal products are subject to an authorisation procedure.
- Novel nanomaterials must be approved by the *Bundesamt für Lebensmittelsicherheit und Veterinärwesen*, BLV (Federal Food Safety and Veterinary Office) before they can be placed on the market.
- New chemicals are subject to a registration procedure according to the Ordinance on Chemicals (ChemV) as well as a registration according to REACH.
- Use as cosmetics.
- Use in foodstuffs and as a component of ingredients and additives.
- Use in packaging materials.
- Medical devices are assessed by the manufacturers on their own responsibility. For products with higher risks, a compliance assessment entity must be involved.

In Switzerland, there is also a notification duty for hazardous substances or ingredients regarding their identity and classification, as well as a general labelling obligation for hazardous substances.

Safety, Security, Health and Environment

1. Definitions

For nanomaterials, the definition according to the EU Recommendation of 2011 applies: "*A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm. In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50% may be replaced by a threshold between 1 and 50%.*"
Examples of such materials are:

- Nanoplates – one dimension on the nanoscale
- Nanorods – two dimensions on the nanoscale
- Nanoparticles – three dimensions on the nanoscale.

According to the Swiss Ordinance on Chemicals and Plant Protection, the following definition applies: "*A material containing particles in an unbound state or as an aggregate or as an agglomerate, where one or more external dimensions is in the size range 1-100 nm, or a material where the specific surface area by volume is greater than 60 m^2/cm^3. A material is only considered a nanomaterial if it is deliberately produced to utilise the properties arising from the defined external dimensions of the particles it contains, or from the defined surface area by volume of the material. Fullerenes, graphene flakes and single-wall carbon nanotubes with one or more external dimensions below 1 nm are considered to be nanomaterials.*"

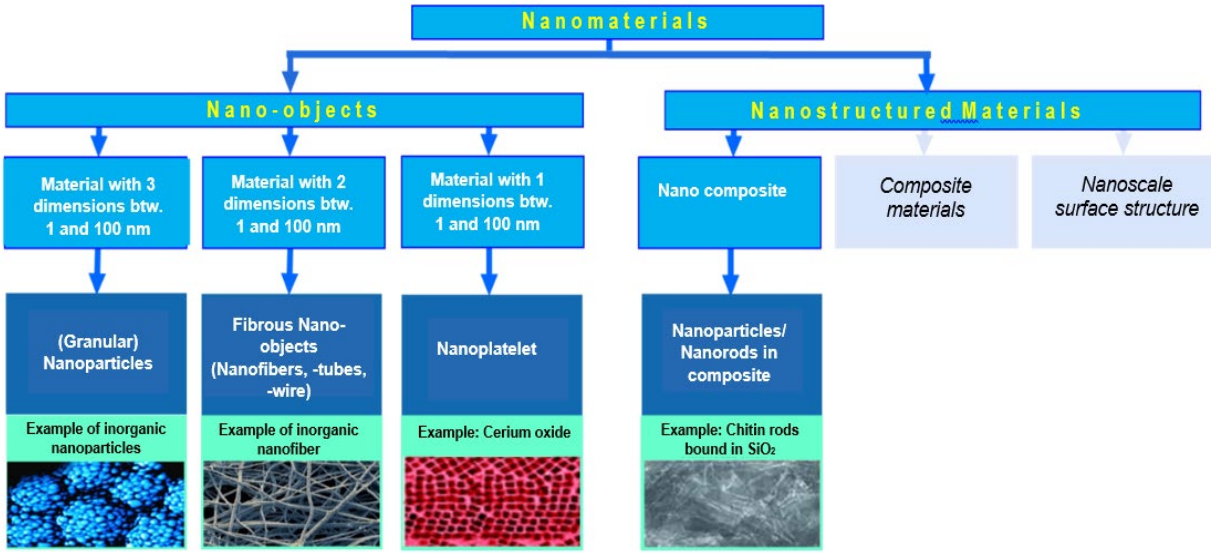

Figure 1: Summary of) the definition of nanomaterials and nano-objects (source: Swissnanocube.ch – Modul «Sicheres Arbeiten mit Nanomaterialien»

Up to now, the data basis for risk assessments and toxicity information for nanomaterials is rather poor, with the current exception of special nanomaterials such as bio-resistant rigid nanofibres, e.g. carbon nanotubes (CNT) and carbon nanofibres (CNF) with dimensions based on WHO fibres. Such substances can have an asbestos-like effect. For precautionary reasons, they therefore are considered as possibly carcinogenic substances. The only exemption of that rule is, if the producer proved through studies that the given fibres are not cancerogenic or do not fulfill the WHO criteria. In addition, the required protective measures must be specified in the safety data sheet. This also applies to fibres, which have not been subjected to morphological tests! Some examples of nanomaterials classified as carcinogenic are arsenic or arsenic compounds (e.g. in quantum dots), cadmium or cadmium compounds (e.g. in quantum dots), chromium (VI) compounds, nickel or nickel compounds (e.g. nickel sulphide or nickel oxide) and crystalline silicon dioxide (quartz).

2. Human uptake and elimination routes

Free nanoparticles can enter the human body via the following routes, listed in descending order:

- Via the air when breathing in (inhalation)
- Through contaminated hands via the digestive tract (incorporation)
- Exposure via the skin (skin absorption)
- Across the placenta to the fetus (passing the placental barrier in the womb)).

Free and powdered nanoparticles are able to float in the air for up to 300 hours. This ability prompts inhalation as the major uptake route. In addition, possible uptake routes of nanomaterials in the human body depend largely on the form in which they are present in the environment:

Nanomaterials	Practical example	Uptake risk without protective measures
Free nanoparticles (incl. agglomerates and aggregates)	Working with powdered nanoparticles	high
Nanoparticles bound in another substance	Nanoparticles as reinforcement in plastics	moderate – low
Nanoparticles dispersed in a liquid (suspension)	Spray application, vigorous stirring, etc.	high

Once in the body, regardless of the uptake route, the mononuclear phagocyte system (MPS) takes up most nanoparticles, transports them away and finally ensures their excretion from the body. This system is a network of cells that are distributed throughout the body in the organs. The cells of the MPS have the task of inactivating and eliminating dead cells, bacteria, viruses and intruding small particles. Nanoparticles also belong to this group of particulate “intruders”. The elimination rate via the MPS also depends on the surface properties of the nanoparticles. Thus, approximately 90% of the non-surface-treated nanoparticles in the body are recognised by the MPS, taken up by its cells and disposed of or eliminated from the body. Conversely, this results in a poorer elimination of surface-treated nanoparticles.

3. Risk assessment of nanomaterials

For the majority of new, synthetically manufactured nanoparticles, a complete risk analysis is difficult to carry out given the current state of knowledge. Nevertheless, a risk assessment must be carried out before any work with nanomaterials can begin.
In principle, for nanomaterials the same risk assessment methodology can be applied as for conventional chemicals but with due consideration of various nanospecific features:

- Nanomaterials can reach other organs via the bloodstream than their corresponding “macro materials” and can cause toxic effects.
- At present, it is not possible to estimate the bioaccumulation potential of a nanomaterial based on its physical and chemical properties. Therefore, an experimental determination of the bioaccumulation potential is necessary.
- Not all test methods developed for conventional chemicals are suitable for testing properties of nanomaterials
- Existing QSAR methods as well as read across approaches are not suitable for nanomaterials.
- Existing models for predicting the environmental behavior of an conventional chemical are inapplicable for nanomaterials.

Which data are necessary for a risk assessment must be decided on a case-by-case basis. The possible chemical hazard needs always to be considered. In order to verify it, the following points must be observed:

- The potential hazardousness of the material must be identified and tested under controlled conditions, e.g. in the laboratory.
- The exposure or the amount of material with which humans, animals or the environment come into contact must be accurately measured and determined.

Based on the results, the level of individual risk is then estimated for the different exposure scenarios.

Since this procedure cannot be carried out for every newly synthesised nanomaterial (e.g. because it is only produced on the smallest laboratory scale), it must be assumed in cases of doubt that the nanomaterial is harmful to health and the environment. Consequently, such a nanomaterial must be handled considerately: For such new substances for which the knowledge of their hazardous properties is insufficient, the goal is to reduce exposure to a minimum.

In principle, valid limit values, for example, the general dust limit values for the alveolar and inhalable dust fraction or substance-specific limit values, must be complied with.
Below you find a brief and concise guide to risk assessment (see [6]):

Risk class	Risk category			
	Properties of the nanomaterial	Inhalability	Exposure level	Exposure duration
High	1) Soluble + insoluble with CMR properties (acute, chronic, toxic, corrosive, sensitising, organ-damaging) 2) Insoluble, non-phagocytisable or phagocytisable with harmful properties	1) Powder form: open manipulation, even with air extraction 2) Liquid form: spraying or misting, even with air extraction	Limit value exceeded or no limit value available and concentration of nanoparticles clearly above the background concentration (>double)	Daily exposure possible (working days only); incidents with release
Medium	1) Insoluble without harmful properties (if phagocytisable) 2) Soluble with harmful properties (irritant, danger of aspiration)	Abrasion of granules, splashes of liquids	Limit values complied with or concentration of nanoparticles max. up to double the background concentration	Occasional (>daily) exposure possible
Low	Soluble without harmful properties	Firmly bound or agglomerated – release of nanoparticles unlikely; closed process; laboratory: fume hood or glove box	Limit value clearly not reached or concentration of nanoparticles similar to background concentration (max. +10%)	Exposure during normal work almost impossible

It also helps to use a risk assessment based on the precautionary matrix for synthetic nanomaterials from the Federal Office of Public Health. For information on this, see the following **link→.**

4. Preventive protective measures

Once the risk assessment has been carried out, the defined preventive protective measures must be implemented in accordance with the **STOP model** (highest priority: S, lowest priority: P):

Substitution

Replace hazardous substances with more harmless substances:

- Replace toxic raw materials with less toxic ones.
- Replace powdered nanoparticle preparations with those containing nanoparticles in a bound form, thus making release more difficult and less likely (dispersions, pastes, granulates, compounds, etc.).
- Replace spray applications with methods having a low aerosol output (brushing, dipping).

Technical protective measures = collective protection

Whenever possible, closed systems or facilities should be used for the production of and work with unbound nanoparticles (exception: very small µg quantities).

I. Structural and technical protective measures (room requirements)

- Use of closed apparatus and material transfer systems.
- If this is not possible, install source exhaust for dust and aerosols.
- Room ventilation and exhaust air filter system for the extracted air (HEPA filter H14, then connection to chemical/process exhaust air) – **no exhaust air recirculation** (recommended: air change rate of 5–8 x room volume per h).
- Separation of working areas and zones with adjustment of room ventilation (slight negative pressure (0.1-0.2 bar pressure difference).

II. Technical protective measures related to a specific experiment

- To be evaluated with regard to the particular experiment and hazard analysis, e.g. when working in a glove box use additionally “sticky mats” in the entrance area to prevent carry-over, connect experimental setup directly to a filter system.

Organisational protective measures

- Minimise the exposure time.
- Minimise the number of exposed persons.
- Avoid generation of dust or aerosols (e.g. no “open” weighing or refilling).
- Restrict access to the room.
- Clean only by suctioning using a suitable device (HEPA filter) or preferably wipe with a damp cloth. No blowing off (e.g. with compressed air pistol)!
- Instruct personnel about hazards and protective measures (operating instructions) – define and record clear responsibilities.
- Establish occupational hygiene rules:
  - Clean workstations, equipment and clothing, protected storage of clothes not used for work (= street wear).
  - Personal hygiene measures including skin protection and skin care (suitable washing facilities and products, etc.).
  - Personal protective equipment and work clothes must be cleaned by the employer.
  - Inform and instruct personnel in good hygienic practice.
- Regular inspection and maintenance of the closed working systems as well as exhaust and ventilation systems.
- Appropriate storage of nanomaterials and safe collection of nanowaste (e.g. vetilated cupboard or fume hood); see Chapter 5.

Personal protective measures = Individual protection Respiratory protection:

- At least: fibrous filter masks (made of glass fibres or cellulose) with medium or high filter capacity (FFP2, FFP3).
- For (granular) substances creating dust: Use full or half masks with P2 or P3 filters, particle filter devices with fan and hood or helmet (TH2P, TH3P), particle filter devices with fan and full or half mask (TM2P, TM3P), possibly also particle filtering half masks (FFP2, FFP3).
- For bio-resistant toxic or fibrous nanomaterials: use half masks with P3 filters or FFP3 particle-filtering half masks; for longer tasks, fan-assisted respiratory protective masks with TM2P or TM3P particle filters. Not all carbon nanotubes are likely to have asbestos-like effects and require such a high level of protection; a case-by-case assessment is necessary.
- Ensure that the mask fits tightly on the face; all wearers must check that the mask fits properly.

Eye protection:

- Closed, tight and well-fitting safety goggles – full protective eyewear recommended.

Protective clothing:

- Protective gloves (recommendation when using disposable gloves: wear two sets of gloves on top of each other, first virus protective gloves and then chemical protective gloves) – the overlap with the protective suit (protection against hazardous dust (type 5, EN 13982-1)) is very important, see figure 2.

Figure 2: Protective clothing for handling nanoparticles. Sources for pictures: left: ETH SGU. Middle and right: www.sapros.ch.

- Protective clothing/protective suit with hood (disposable if possible): non-woven membrane materials (e.g. Tyvek or polyethylene), no woven materials (e.g. lab coat made of cotton). In case of dust occurrence: Wear dust-proof protective clothing (type 5).
- It is essential to put on and take off the gloves correctly without carrying over nanomaterials and dust.

5. Disposal of nanomaterials

At ETH all types of nanomaterials must be disposed of as hazardous waste at the **hazardous waste disposal facilities** →. Needed containers can be obtained free of charge at the hazardous waste facilities. →.

Disposal via waste water or ordinary domestic waste is generally prohibited!

When handing over hazardous nano waste attention should be paid to:

- Liquid (dissolved) or paste-like nanomaterials:
  - Collect in defined closed containers.
- Solid nanomaterials (also with unstable matrix):
  - Collect in defined closed containers.
- Papers, cleaning cloths, PPE and other items with loose nano-contamination:
  - Collect in (antistatic) plastic bag.
  - Put the filled bag into a second bag or another tight container, close it and label it accordingly.
- Powdered nanomaterials/nanomaterials creating dust:
  - Dispose in tightly closed containers as hazardous waste.
- Explicitly declare toxic substances (e.g. arsenic, cadmium, etc.) on the disposal label.
- Store in a fume hood or a similar suitable place.
- Dispose as soon as possible at one of ETH Zurich hazardous waste disposal facilities.

References and legal basis:

[1] SUVA checklist 67077 – *Gesundheitsgefährdende Stäube*

[2] *Technische Regeln für Gefahrstoffe – Tätigkeiten mit Nanomaterialien* (. TRGS 527; January 2020 issue

[3] *Wegleitung zum Vorsorgeraster für Synthetische Nanomaterialien*. Federal Office of Public Health (FOPH) and Federal Office for the Environment (FOEN), Berne 2018, Version 3.1

[4] ISO/TS 80004-2:2015(en) Nanotechnologies – Vocabulary – Part 2: Nano-objects

[5] ISO/TR 27628:2007, Workplace atmospheres – Ultrafine, nanoparticle and nano-structured aerosols – Inhalation exposure characterization and assessment

[6] *Bundesanstalt für Arbeitsschutz und Arbeitsmedizin* (BAuA) /*Verband der Chemischen Industrie e.V. (*VCI): *Empfehlung für die Gefährdungsbeurteilung bei Tätigkeiten mit Nanomaterialien am Arbeitsplatz* (2012)

[7] Recommendation on the definition of a nanomaterial (2011/696/EU)

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