Guidelines

on the

Precautionary Matrix for Synthetic Nanomaterials

Version 1.1

Schweizerische Eidgenossenschaft
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Contents

1 Context

Synthetic nanomaterials are not specifically covered by present legislation. But in principle all areas of regulation implicitly include synthetic nanomaterials and nanoparticles. This is the conclusion of both the Swiss and the European authorities. Responsibility for safe handling of synthetic nanomaterials lies with industry (producers, processors) and trade.

However, up until now there have been no special regulations for synthetic nanomaterials either in Swiss or in European Union legislation. The scientific and methodological prerequisites (e.g. special testing requirements) have not been in place to enable us to define requirements going further than the current general provisions to protect health and the environment.

This situation results in considerable uncertainty concerning actions and investments made by businesses, and it makes it difficult to have a public debate on the opportunities and risks presented by nanotechnology.

In view of this general situation, the Federal Council adopted the Swiss Action Plan Synthetic Nanomaterials1. This action plan envisages the development of a precautionary matrix for products and applications using synthetic nanomaterials, as the central measure to increase the extent to which industry takes responsibility in this area.

The precautionary matrix helps trade and industry to identify possible sources of risk in the production, use and disposal of synthetic nanomaterials.

Using a classification of risk potential should show what action is appropriate:

“Class A”: The nanospecific risks can be classified as low. No further clarification is necessary.

“Class B”: Possible nanospecific risks cannot be excluded. Further clarification of the risks is needed, or if necessary risk reduction measures must be taken in relation to manufacture, use and disposal, with a precautionary approach in mind.

For further clarification of risks, the investigations carried out by the manufacturer on human exposure, inputs into the environment and the effects of nanomaterials or – if applicable – data from the literature may also be used.

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[1] This can be downloaded free of charge at: www.umwelt-schweiz.ch.ch/div-4002-e

2 Objective and Area of Application

2.1 Objective

The present precautionary matrix allows the estimation of “nanospecific risk potentials” for synthetic nanomaterials and for their applications for workers, consumers and the environment, based on selected parameters[2]. However, the approach should not in any way be compared with doing a risk assessment.

Potentially dangerous applications can be identified with the help of the matrix, and measures to protect health and the environment can be taken in cooperation with industry. In this way the precautionary matrix is an instrument, which can be used in the context of duty of care and self-supervision by trade and industry for the production and marketing of synthetic nanomaterials. The precautionary matrix should enable industry to assess the risk potential of existing or new products and processes. The matrix comes with a structured approach to assess the risk potentials, and allows the most important sources of risk to be identified. Thus it also provides the basis for early decision-making for or against new projects.

Comprehensible classification of the risk potential allows the approach to the opportunities and risks presented by nanotechnologies to be differentiated and seen objectively, and it contributes to making the public debate objective.

2.2 Area of application

In the precautionary matrix it is assumed that nanospecific risks only arise if particles can be released, which are on the nanoscale in two dimensions (nanorods) or in three dimensions (nanoparticles)[3]. In the precautionary matrix these two types of particles are consistently referred to as **nanoparticles and nanorods (NPR)**.

The precautionary matrix focuses exclusively on nanomaterials or applications, which contain synthetic NPR. Nanospecific risks of surface structures and coatings where the thickness is in the nanometre range are not covered by the precautionary matrix if they do not contain any NPR. Regardless of whether a nanomaterial is present, particles in the nanometre range of size can also be produced by abrasion or combustion, and by the loosening of fragments (nano thin layers) from coatings. The resultant risks are dealt with in connection with fine /very fine particulate matter and are not recorded by the precautionary matrix. Risks to health or to the environment which are not nanospecific e.g. resulting from the toxicity of the chemical composition of a NPR (classical “chemical toxicity”) are not covered by the precautionary matrix. These risks must be assessed by conventional standard procedures.

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[2] The scientific and technological basis for a solid assessment of the risks presented by synthetic nanomaterials for human beings and for the environment are still largely lacking. In the area of the environment the input of nanomaterials into different compartments and their distribution between compartments have not been clarified. Also, only a small amount is known about possible harmful effects of nanoparticles on the body, as test systems have not yet been established.

[3] In the precautionary matrix, the ISO nomenclature and definitions are used (Technical Specification ISO/TS 27687, Nanotechnologies — Terminology and definitions for nanoparticles, Proof, © ISO 2007). However, for the matrix the nanoscale is extended to 500nm (rationale see section 4.3.1).

The precautionary matrix estimates the risk potentials – through the whole life cycle – for the health of workers and consumers, and for the environment. The following processes are taken into account in the life cycle of nanomaterials (see Figure 1):

- Research and development (industrial or university)
- Production (including storage, packaging and transport)
- Use
- Waste disposal

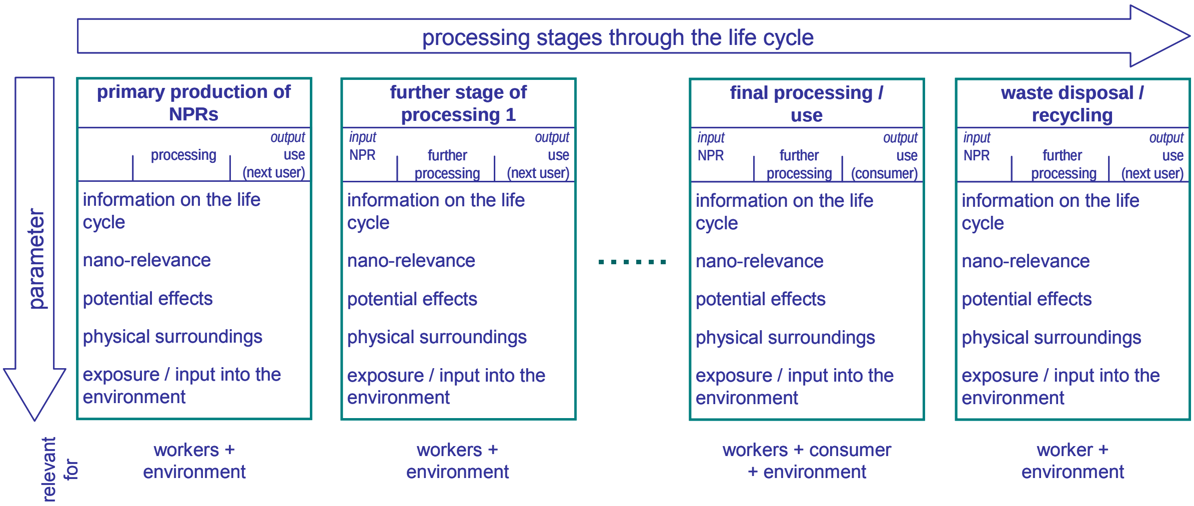

Figure 1: the stages of processing as part of the whole life cycle

Primary production and all steps of further processing during the life cycle are relevant for workers and for the environment; during this part of the life cycle, consumers do not have to be considered in the precautionary matrix. However, in the final processing of a product containing NPR the use of the product by consumers has to be taken into account. In any case where a final product is manufactured for use by a consumer, the matrix must be filled in for workers, consumers and for the environment. In principle, for each new step in the process a separate precautionary matrix must be filled in (including specific waste disposal and recycling).

The precautionary matrix is based on a limited number of evaluation parameters. The potential effect[4] is estimated by the reactivity and stability[5] of the NPR. The probability and degree of exposure of human beings and input into the environment are examined through data on the physical surroundings of the NPR, the amount marketed and the emission of the NPR from production or use. The precautionary matrix is made up of modules for these evaluation parameters. This structure ensures that new scientific information on effects, the

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[4] Capacity of the NPR to act upon their surroundings (human beings, environment)

[5] In the context of the precautionary matrix, stability of the NPR is to be understood as the persistence of the NPR as such in the surroundings in question (e.g. resistance to dissolving, chemical or physical change, sintering to bulk material, breakdown etc.).

exposure of human beings or inputs into the environment can be taken into account at any time.

A precautionary matrix only applies for a certain type of NPR in clearly defined surroundings. If the physical surroundings (e.g. solvent, matrix / substrate, state of aggregation etc.) change, then a new precautionary matrix has to be filled in. A new matrix also has to be filled in if during use the original NPR change into defined new NPR, for instance through rapid dissolving of a coating.

3 Approach to filling in the Precautionary Matrix

The matrix is to be filled in according to the procedure described below, and evaluated for possible risks for human health and for the environment. More detailed explanations and help on how to fill in the matrix and to the evaluation are given in chapter 4 “Development and metrics of the precautionary matrix”. The evaluation is always done linked to processing steps. Therfore, each processing step requires a separate filled-in matrix. This enables industry to identify risky processing steps and to avoid them if appropriate. By considering all processing steps leading to a product, it is possible to estimate the overall risk potential in relation to its production.

Therefore, it may be necessary for a company to fill in several precautionary matrices, depending on the number of processing steps used. The total risk potential in the company is given by the total of the risk potential of the individual processing steps in that company. For this it is important to classify the sub-areas with the highest risk potential.

Approach:

1. **Make an inventory of materials / products / applications**, which should be tested for nano-relevance and potential risks. Materials / products / applications for which it seems doubtful whether nanomaterials are involved, should be included.
2. **Check the nanorelevance** of each material / product / application listed using the parameters as described in section 4.3.1. Exclude materials / products / applications that are not nano-relevant. It is recommended that 500 nm be used as the limit of the nanoscale, in order to avoid excluding any nano-specific risks.

   If the same material / product contains several NPR, or if several are used in the same application, then a separate matrix must be filled in for each NPR If the NPR can change specifically in the body or in the environment (e.g. dissolving of a coating, oxidation etc.) and could be present together with these new forms, then a separate matrix must be filled in for each of these NPR. If there are insufficient data to establish nano-relevance, then it must be decided who must supply these data (supplier…).
3. **Find and divide up (process) steps** for all nano-relevant materials / products / applications, which are covered for assessment by the matrix (no change in the physical surroundings of the NPR). A separate matrix must be filled in for each step.
4. **Establish the position in the chain of added value** of each (process) step found, using Figure 1. Decide for which groups (workers, consumers, the environment) the matrix must be filled in.

   If appropriate, separate matrices must be filled in for workers with different activity profiles in the same (process) step, or for different groups of consumers.
5. **Fill in general information in the matrix**.
6. **Fill in the technical part of the matrix,** as far as possible according to the parameters described in chapter 4 for information on the life cycle (section 4.3.2), the potential effect (section 4.4) and exposure of human beings or input into the environment (section 4.5).

7. **Determine the sources of information**: name the contact person in charge in case any data or information may be missing (e.g. suppliers, research departments, universities etc.).
8. **Obtain information** using the relevant questions from the matrix.
9. **Finish the matrix**, delimit the relevant sources of risk (section 4.6) and determine the classification (section 4.7).
10. **Clarify any need for action** and if appropriate initiate measures (activation of further clarification, additional measures, protection measures, measures to provide information, communication etc.).

4 Structure and Metrics of the Precautionary Matrix

This chapter describes the structure of the precautionary matrix using parameters, and shows how they are linked together. The tables illustrate queries and possible responses in the precautionary matrix (grey background) and the resulting numerical values for the estimation of risk potential.

4.1 Plan

The risk potential is defined as a function primarily depending on the potential effect (W) and on the potential exposure of human beings or on potential inputs into the environment (E). "Specific framework conditions" (S) is introduced as an additional parameter. These take account of uncertainties due to lack of understanding of past events and of the future life of the nanomaterials, or due to lack of clarity in the system under consideration (impurities or inaccurate estimation of size distribution for NPR, etc.).

Risk potential = f (W, E, S1, S2)

The following symbols are used:

W:	Potential effect (section 4.4)
E:	Exposure of human beings / input into the environment (section 4.5)
S1:	Nano-relevance (section 4.3.1)[6]
S2:	Information about the life cycle (section 4.3.2)

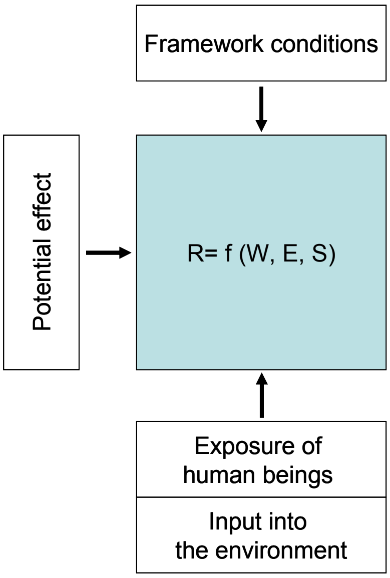

Figure 2: Concept for estimation of the risk potential

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[6] A system is considered to be nano-relevant if nano-specific risks have to be taken into account.

Potential effect, exposure of human beings, input into the environment and specific framework conditions are each evaluated using a parameter selected for the class, and related together to determine the risk potential. To do this both tables of relationships and corresponding parameter-dependent functions are used.

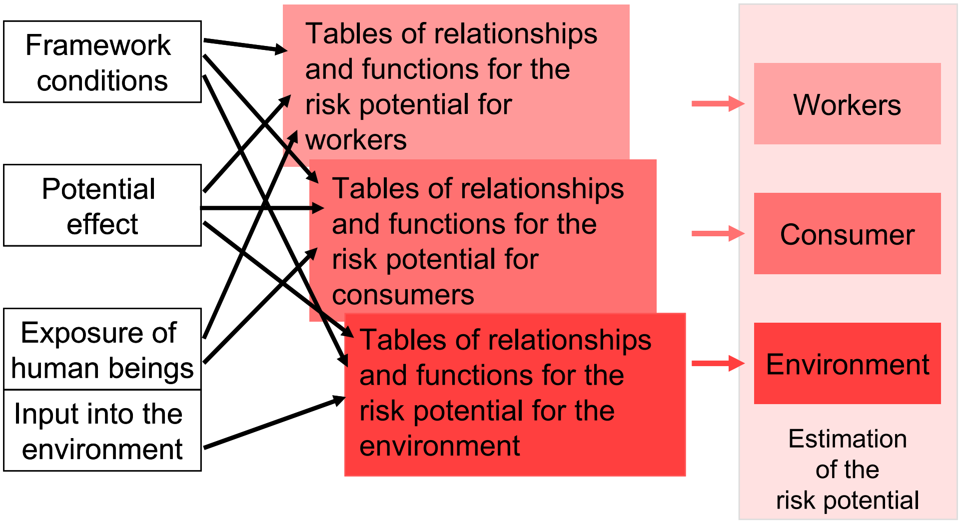

Figure 3: Parameters for estimation of the risk potential

Risk potentials areclassified by sub-division into:

- “normal use” (NG)
- “worst case” (WC)[7]

using the relevant parameters referring to workers (A), consumers (V) and the environment (U).

In order to differentiate sufficiently between the two classes in the final assessment of risk potential, for input parameters a three-fold greater resolution was chosen, i.e. from 1 to 9 (zero is used if a value is not relevant). The numbers 1, 5 and 9 are currently used to represent low, medium and high rating of the parameter in question.

In all cases in which it is not possible to do an assessment according to the guidelines in the matrix (e.g. low, medium, high), because the information is not available, the value must be used which would finally give the highest risk potential.

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[7] As relevant worst case scenarios for the precautionary matrix, only accidents during production, storage, packaging and transport, which lead to an increase in exposure in the workplace and environmental pollution through inadequate waste disposal of the NPR are considered. It is not possible to include natural disasters and attacks in the matrix. Abnormal use of materials and products is the responsibility of workers and consumers, so it is not considered in the matrix. Effects of major accidents on the population are not considered.

4.2 Parameters

The parameters, their sub-divisions and their assignment to the areas of specific framework conditions, potential effect, and exposure / input into the environment are summarised in Table 1.

Specific framework conditions	**Nano-relevance**	S1
	Order of size of the primary particles (NPRs) in the materials (free, bound, aggregated or agglomerated)	S1.1
	Under the possible physiological conditions does deagglomeration of agglomerates to primary particles or agglomerates (<500nm) occur?	$S1.2_{A,V}$
	Under the possible environmental conditions does deagglomeration of agglomerates to primary particles or agglomerates (<500nm) occur?	$S1.2_{U}$
	Information on the life cycle	S2
	Is the origin of the starting materials known?	S2.1
	Is there an evaluated precautionary matrix for the starting materials?	S2.2
	Is the future life cycle of the synthetic nanomaterials known?	S2.3
	How accurately is the material system known or can disturbing factors (e.g. impurities) be estimated?	S2.4
Potential effect	**Potential effect**	W
	Redox activity and / or catalytic activity of the NPRs present in the nanomaterial (uncoated or coated)	W1
	Stability (half-life) of the NPRs in the nanomaterial (uncoated) or of their coating under physiological conditions	$W2_{A,V}$
	Stability (half-life) of the NPRs in the nanomaterial (uncoated) or of their coating under environmental conditions	$W2_{U}$
Exposure of human beings / input into the environment	**Physical surroundings**	E1
	Potential for release related to exposure of human beings	$E1_{A,V}$
	Potential for release related to the environment	$E1_{U}$
	Exposure of human beings	E2
	Possible amount of NPR which an employee handles per day	E2.1
	Possible amount of NPR with which an employee comes in contact in the worst case	E2.2
	Frequency with which an employee handles the NPR	E2.3
	Amount of NPR which the consumer handles daily, via the utility product	E2.4
	Frequency with which a consumer uses the utility product	E2.5
	Input into the environment	E3
	Annual amount of NPR disposed of as waste (via wastewater, exhaust air, solid waste), which is not subjected to specific waste disposal	E3.1
	Annual amount of NPR in utility products	E3.2

Table 1: Metrics of the parameters used

4.3 Specific framework conditions (S)

4.3.1 Nano-relevance (S1)

Parameters S1.1 and S1.2 examine the nano-relevance of the system. This is determined from the size of the primary particles, which are present – free, bound or as aggregates or agglomerates – in the nanomaterial that is being evaluated (S1.1).

The division into three ranges of particle size reflects the following:

- There is a range of particle sizes in which there is no longer any nano-relevance. The evaluation criterion for this is the range of sizes where particles are no longer recognised by macrophages (threshold around 500nm).
- There is a range of sizes in which the nanoscale character has a dominant physical and chemical influence on the properties[8]
- There is a grey zone between these ranges, which cannot yet be accurately delimited using data that are currently available. When using the precautionary matrix, it is recommended to include this range to estimate nano-relevance.

Order of sizes of primary particles (NPR) contained in the materials (free, bound or as agglomerates)	>1nm, <100nm	>100nm, <500nm	>500nm
S1.1	1	1	0

Table 2: Nano-relevance

The maximum of the size distribution is used to measure the size of primary particles[9].

If the primary particles (<500nm) are in an aggregated or agglomerated form > 500nm, then for “nano-relevance” it is decisive whether under the ambient conditions these aggregates or agglomerates can disintegrate into primary particles or smaller agglomerates (< 500nm)[10]. If there are stable agglomerates as well as free primary particles, then parameter S1.2 must in all cases be set as 1.

Stability under physiological conditions is important for assessing the health risk ($S1.2_{A,V}$), and stability under environmental conditions is important for assessing the environmental risk ($S1.2_{U}$).

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[8] This goes back to the nanoscale range of 1-100nm defined by ISO

[9] For a more detailed consideration, the exact size distribution must be used. For practical reasons, this is not done here.

[10] Even for stable agglomerates >500nm, structural elements (nanoscale branches) can be produced, which have nano-specific toxicity when in contact with biological tissues. To deal with these cases in the precautionary matrix see appendix 5.2.

Under possible physiological conditions does deagglomeration[11] of agglomerates (or aggregates) to primary particles or agglomerates (<500nm) occur?	yes	no
S1.2$_{A,V}$	1	0 (1)[10]
Under possible environmental conditions does deagglomeration of agglomerates (or aggregates) to primary particles or agglomerates (<500nm) occur?	yes	no
S1.2$_{U}$	1	0

Table 3: Agglomerates

S1 is given by the product of S1.1 und S1.2:

$$\mathbf{S1 = S1.1 \cdot S1.2}$$

4.3.2 Information about the life cycle (S2)

Parameters S2.1 to S2.3 evaluate the uncertainties that result from lack of knowledge of the previous history of the nanomaterials and of their future life cycle, this also includes knowledge of other likely effects on the nanomaterial during its life cycle. S2.4, as an additional parameter, takes account of lack of clarity about the system under consideration, which includes impurities, inaccuracies in the estimation of the size distribution for the NPR etc.

The sum of parameters S2.1 to S2.4 gives factor S2:

$$\mathbf{S2 = S2.1 + S2.2 + S2.3 + S2.4}$$

Is the source of the starting materials known?	yes	partly	no
S2.1	0	3	5
Has a precautionary matrix been evaluated for the starting materials?	yes	partly	no
S2.2	0	3	5
Are the subsequent steps in the life cycle of the nanomaterials known?	yes	partly	no
S2.3	0	3	5
How accurately is the material system known, or can disturbing factors such as contaminants be estimated?	precisely	not precisely	not known
S2.4	0	3	5

Table 4: Information about the life cycle

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[11] To decide whether deagglomeration occurs, it is recommended that the agglomerates be subjected to ultrasound treatment and then tested using the usual standard procedures, to see whether original primary particles can be detected. If that is the case, then the answer to deagglomeration is yes.

4.4 Potential effect (W)

The potential effect of NPR on health and the environment is estimated by:

1. Redox activity and / or catalytic activity of the NPR present in the (uncoated or coated) nanomaterial (W1)
2. Stability of the NPR present in the nanomaterial (uncoated) or their coating under the relevant physiological conditions ($W2_{A,V}$) or environmental conditions ($W2_U$)

At present there are no recognised methods to determine the **redox activity** or **catalytic activity** of NPR. If there are no specific data for the NPR, then - as a good approximation - the bulk properties of the materials can be used for reference information for particles larger than 100nm.

In the present context **stability** takes into account the resistance of the synthetic NPR used as such to dissolving, chemical or physical change, sintering or breakdown of the particles. The latter is for instance the case if a coating dissolves under physiological conditions.

The conditions (and hence the stability) in physiological surroundings and for different environmental compartiments can theoretically differ from each other. For this reason two sperate parameters ($W2_{A,V}$ and $W2_U$) are used. If there is no evidence that the stability differs between the two surroundings, then $W2_{A,V}$ and $W2_U$ are evaluated by the same value. This is given by the available data for either physiological or environmental conditions. If there are no data on the stability, it can be estimated by the solubility in water of the bulk materials.

Redox activity and / or catalytic activity of the NPR present in the nanomaterial (uncoated or coated)	Low	medium[12]	high
W1	1	5	9
Stability (half-life) of the NPR present in the nanomaterial (uncoated) or their coating under physiological conditions	Hours	days to weeks	months
$W2_{A,V}$	1	5	9
Stability (half-life) of the NPR present in the nanomaterial (uncoated) or their coating under environmental conditions	Hours	days to weeks	months
$W2_U$	1	5	9

Table 5: Potential effect

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[12] Because of their special toxicokinetics NPR could get to places in the organism, which are not normally accessible for the basic chemical substances, in soluble form. If the NPR get to these places in solution, there may be locally high concentrations of these chemical substances, with new toxic effects. In the present context, this possible influence on the potential effect is not considered as there are not currently sufficient data.

If there is a coated NPR[13], then the following cases have to be distinguished[14]:

- If the coating is stable, then the precautionary matrix is filled in based on W1 and W2 for the coated NPR.
- If the coating is conceived in such a way that when used it dissolves very rapidly, without any expected impact on the properties of the NPR, then the potential effect is to be based on parameters W1 and W2 for the resultant uncoated NPR.
- If the coating dissolves in use or application, during a period which leads to the co-existence of coated and uncoated NPR, then in addition to the precautionary matrix for coated particles an additional one must be filled in for uncoated particles. To estimate the risk potential for health and the environment of the material under consideration, the precautionary matrix which identifies a higher risk potential is to be considered as determinant.

In the case of soluble NPR (W2=1) the chemical substance could exhibit greater biological availability than its non-nanoscale form. This could lead to an increased acute toxicity, which is recognised by classical toxicity tests for chemical substances. Therefore, it has been decided not to include this possible impact on the potential effect in the precautionary matrix.

The total potential effects $W_{A,V}$ on human beings and W_U on the environment are estimated using the following equations:

$$\mathbf{W_{A,V} = W1 \cdot W2_{A,V}}$$
$$\mathbf{W_{U} = W1 \cdot W2_{U}}$$

4.5 Exposure of human beings / input into the environment (E)

To estimate the exposure of human beings or input into the environment, two groups of parameters are used:

1. the physical surroundings of the NPR in the nanomaterial or in its application as a measure of the availability of the NPR (E1)
2. the extent of the exposure of human beings (E2) or of the input into the environment (E3)

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[13] In the present precautionary matrix coating includes all other kinds of surface functionalization

[14] These considerations apply in a similar way if during the production or use of the NPR, new defined NPR can be produced by chemical reactions (e.g. oxidation)

4.5.1 Physical surroundings

The potential availability of the NPR is different depending on the physical surroundings of the NPR in the nanomaterial or on its application (Table 6). Only one of the given surroundings can be selected per matrix. Selecting the physical surroundings assigns predefined values (Table 6) for availability in relation to the exposure of human beings ($E1_{A,V}$) and input into the environment ($E1_U$).

Physical surroundings	**$E1_{A,V}$**	**$E1_U$**
Air	1	1
Liquid media as aerosols <3 µm	1	1
Liquid media (exposure via mouth, throat, stomach and intestine), aerosols >3 µm	0.1	1
Liquid media (exposure via the skin)	0.1	1
Solid matrix, not stable under conditions of use	0.1	1
Solid matrix, stable under conditions of use, NPR mobile	10^{-2}	10^{-2}
Solid matrix, stable under conditions of use, NPR not mobile	10^{-4}	10^{-4}

Table 6: Physical surroundings

In the case of human exposure, for the evaluation of NPR in the air and in liquid media a distinction is made between possible exposure of the lungs ($E1_{A,V}$ =1) and other target organs ($E1_{A,V}$ = 0.1). No such a distinction is relevant for the environment.

If the NPR are within or bound to a solid matrix (plastic, ceramic, metal), the evaluation is done regardless of the exposure path, using the stability of this matrix referring to the particular conditions of use[15] and referring to the strength of the binding of the NPR to the matrix[16]. The latter is only relevant for stable and very stable matrices.

In the estimation of exposure, parameters $E1_{A,V}$ and $E1_U$ have a multiplicative effect on the extent of exposure.

4.5.2 Exposure of human beings

For workers and consumers, exposure is estimated by the amount of NPR with which those people come in contact per day, and the frequency at which this occurs.[17] The parameters linked to this are evaluated as shown in Table 7.

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[15] An example of an "unstable" matrix could be ski wax, and for a "very stable" matrix a bicycle frame

[16] If the NPR are not in the presence of a solubilizer in the matrix , they can be designated as strongly bound. Surface-bound NPR cannot be classified *a priori.* Clarification is needed in such cases.

[17] It is also necessary to consider here that in practice personal protective equipment is often not used or is inadequate.

Possible amount of NPR with which a worker[18] comes into contact per day[19]	<25µg	<250µg	>250µg
E2.1	1	5	9
Possible amount of NPR with which a worker comes into contact in the "worst case"	<250µg	<2500µg	>2500µg
E2.2	1	5	9
Frequency with which a worker handles the NPR(s)	monthly	weekly	daily
E2.3	1	5	9
Amount of NPR which a consumer handles daily through the utility product	<25µg	<250µg	>250µg
E2.4	1	5	9
Frequency with which the consumer uses the utility product	monthly	weekly	daily
E2.5	1	5	9

Table 7: Exposure of human beings

The extent of exposure is then estimated taking account of the availability of the NPR as a function of the physical surroundings (section 4.5.1), separately for workers and consumers:

Estimation of the exposure of workers

$$\mathbf{E_A = E1_{A,V} \cdot E2.1 \cdot E2.3}$$

in the worst case also: $\mathbf{E_A^{WC} = E1_{A,V} \cdot E2.2}$

The following symbols are used:

$E1_{A,V}$: Physical surroundings specific for target groups “workers / consumers” (section 4.5.1)

E2.1: Possible amount of NPR with which a worker comes into contact per day

E2.2: Possible amount of NPR with which a worker comes into contact in worst case

E2.3: Frequency with which a worker comes in contact with the NPR

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[18] For cases where various workers are subject to markedly different exposure, it is recommended that separate precautionary matrices be filled in for these workers

[19] For the derivation of the given value see appendix 5.1

Estimation of the exposure of consumers

$$E_V = E1_{A,V} \cdot E2.4 \cdot E2.5$$

The following symbols are used:

$E1_{A,V}$: Physical surroundings specific for target groups “workers / consumers” (section 4.5.1)

E2.4: Amount of NPR with which a consumer comes into contact

E2.5: Frequency with which a consumer comes into contact with NPR

4.5.3 Input into the environment

The environmental inputs during the production phase (including manufacture, processing, packaging and transport) and during the consumption phase are considered separately. In the consumption phase, two different scenarios also have to be considered (use with and without specific waste disposal).

The following diagram shows how to deal with the possible environmental inputs using the precautionary matrices that are needed:

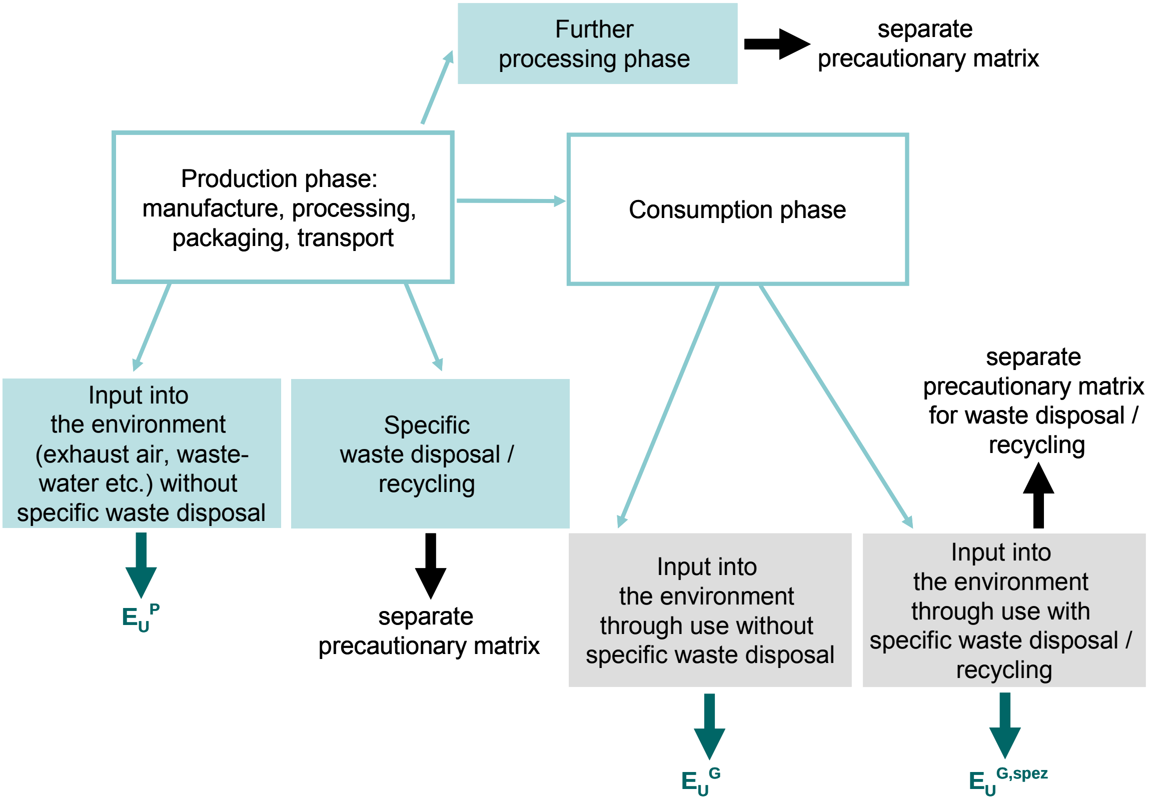

Figure 4: Scenarios of environmental exposure

Estimation of the input into the environment

1. Production phase (manufacture, processing, packaging, transport)

During the phase of production of nanomaterials there can be input of NPR into the environment via exhaust air, wastewater or unspecific waste disposal. In the precautionary matrix, this is assessed by the decrease in NPR during the process considered (E3.1):

$$\mathbf{E_U^P = E3.1}$$

The following symbols are used:

E_U^P: Input into the environment during the production phase

E3.1: Amount of NPR disposed of as waste (in wastewater, exhaust air, solid waste) per year, which is not subject to specific waste disposal

Any input during specific waste disposal, recycling or further processing takes place in a separate process step and must be estimated using its own precautionary matrix.

2. Use phase

For use two scenarios have to be distinguished:

a) In case of use without specific waste disposal (e.g. of utility products) it is difficult to estimate the input into the environment. Therefore this is designated as “worst case” in the matrix. The estimation is done based on the total amount of NPR in the marketed utility products (E3.2). Input into the environment is estimated without including the physical surroundings ($E1_U$) since, when looked at in the long term, all NPR are introduced into the environment, independently of their physical surroundings.

$$\mathbf{E_U^G} = \mathbf{E3.2}$$

The following symbols are used:

E_U^G: Input during use, without special waste disposal

E3.2: Amount of NPR in utility products per year

b) For use followed by specific waste disposal, only inputs during use are considered. Exposure is estimated by the total amount of NPR in the marketed utility products (E3.2) taking account of the physical surroundings ($E1_U$).

$$\mathbf{E_U^{G,spez} = E1_U \cdot E3.2}$$

The following symbols are used:

$E_U^{G,spez}$: Input during use, with special waste disposal

$E1_U$: Physical surroundings, specific for the environment (section 4.5.1)

E3.2: Amount of NPR in utility products per year

The environmental inputs via a specific means of waste disposal or recycling after use represent an individual process step. Its risk potentials have to be evaluated with separate recautionary matrices.

The parameters relevant for the environment are evaluated as follows:

Amount of NPR disposed of as waste (in wastewater, exhaust air, solid waste) per year, which are not subject to specific waste disposal[20]	< 5kg	< 500kg	> 500kg
E3.1	1	5	9
Amount of NPR in utility products per year	< 5kg	< 500kg	> 500kg
E3.2	1	5	9

Table 8: Input into the environment

4.6 Estimation of the risk potentials

To estimate the risk potentials (R), the values determined for potential effect (W) and for exposure of human beings / input into the environment (E) are multiplied together, then S2 is added and the result is multiplied by S1:

$$R = (W \cdot E + S2) \cdot S1$$

Risk potential for workers $R_A = (W_{A,V} \cdot E_A + S2) \cdot S1_{A,V}$

$R_A^{WC} = (W_{A,V} \cdot E_A^{WC}) + R_A$

Risk potential for consumer $R_V = (W_{A,V} \cdot E_V + S2) \cdot S1_{A,V}$

Riks Potential for the environment: $R_U^P = (W_U \cdot E_U^P + S2) \cdot S1_U$

$R_U^{G,spez} = (W_U \cdot E_U^{G,spez} + S2) \cdot S1_U$

$R_U^G = R_U^{WC} = (W_U \cdot E_U^G + S2) \cdot S1_U$

The following symbols are used:

R_U^P: risk potential during production

$R_U^{G,spez}$: risk potential during use with specific waste disposal

R_U^G: risk potential during use without specific waste disposal

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[20] The basis for the values given was the REACH threshold amounts (1-10t, 10-100t, 100-1000t) modified using the adaptations from Appendix 5.1 to adjust from bulk materials to nanomaterials (with the surface as the decisive parameter).

4.7 Classification

When evaluating a precautionary matrix with the metrics used here, a total number of points is obtained, which falls within a certain range. The position within this range allows one to classify the nanospecific risks using the following divisions into risk classes A and B:

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

For cases where the specific framework conditions do not make any additional contribution (S2=0) and the physical surroundings allow maximum availability of the NPR (E1=1), the minimum and maximum values are as follows:

For workers and consumers:

- Low redox activity (W1=1) and stability ($W2_{A,V}$ =1), low extent of exposure (E2=1): 1 point
- High redox activity (W1=9) and stability ($W2_{A,V}$ =9), high extent of exposure (E2=81): 6561 points

For the environment:

- Low redox activity (W1=1) and stability ($W2_U$ =1), low input into the environment (E3=1): 1 point
- High redox activity (W1=9) and stability ($W2_U$ =9), high input into the environment (E3=9): 729 points

In this case, the deviation in maximum values between health and the environment by a factor of 9 is almost compensated for by the different evaluation of the physical surroundings ($E1_{A,V}$ und $E1_U$). For this reason, the classification is done using the same limits in points in both cases.

5 Appendix

5.1 Basis for estimating E2.1 and E2.3

To determine the threshold values for assessing parameters E2.1 and E2.3, the maximum workplace concentration value for diesel soot in the workplace (Suva, Grenzwerte am Arbeitsplatz 2007 - www.suva.ch/waswo) was used as reference. This value is 100 µg /m^3 for workplace exposure (8 hours workday), related to the elemental carbon (EC) core of the particle, which can get into the alveoli. Since the density of these particles is very low, the amount of them can very well be used as the threshold value for daily human exposure: the same amount of denser particles (i.e. the most of all particles) means fewer particles in the same volume, and so an overestimate of exposure. This is accepted consciously so that the risk of exposure to NPR will on no account be underestimated.

The average volume of air breathed by a person carrying out normal physical effort can be calculated, according to Freijer et al., 1997, by:

$$Q_{inh} = 2.3 \cdot B_w^{0.65} \, m^3 / \, day$$

Where B_w is body weight in kg. To convert this to a value for 8 hours, the volume obtained must be divided by 3, since the equation applies to a 24-hour day.

Using an assumed average value of 70 kg the volume of air breathed during 8 hours is about 12 m^3. Multiplying this by 100 (µg/m^3) gives an acceptable highest quantity of 1200 µg of particles of elementary carbon per working day, with which a worker can come in contact.

With reference to the density of the NPR, as shown above diesel soot represents a favourable extreme case for assessing all NPR. However, the size of the diesel soot particles (assumption: environmental limit for particles that can get into the alveoli: 2.5µm) is too large to allow them to be applied unrestrictedly for NPR. According to H. Hofmann[21] a bulk quantity of a substance can be extrapolated to an analogous quantity of nanoparticles. Adapting this approach to diesel soot particles the adaptation factor for nanoparticles is given as follows:

$$M_{nano} = M_{bulk} \, (D_{nano}/D_{bulk});$$

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[21] Personal communication

The following symbols are used:

M_{nano}: equivalent amount of the material as nanoparticles

M_{bulk}: amount of bulk material

D_{nano}: diameter of the nanoparticles in nm

D_{bulk}: diameter of the particles of the bulk material in nm

If we put in the following values: M_{bulk} = 1200 µg (as above), D_{nano} = 50 nm, D_{bulk} = 2.5 µm, then this gives an equivalent amount of 24 µg. For general purposes this value is rounded up to 25 µg.

This means that, starting from the threshold value for diesel soot, making certain assumptions (see above), a worker can come in contact with a tolerable amount of 25 µg nanoparticles. For particles of higher density and greater diameter than the values assumed, exposure will be increasingly overestimated.

This approach represents a rough approximation, which has to be further refined and adapted in terms of the values during practical use of the matrix.

The amounts of particles given for E2 only apply in the air, but they can be taken in the first approximation for particles in all surroundings (air, liquid and solid matrixes). Differentiation of exposure according to this parameter has to be done through E1. However, by this there can be marked overestimations of the potential exposure for liquid and solid surroundings, and this has to be checked using practical examples.

5.2 Assessment of stable agglomerates in the precautionary matrix

When assessing the nano-relevance of a system, both the size of the primary particles and the ability of the system to create agglomerates are important.

Three cases must be distinguished:

1. The primary particles create agglomerates, which are not stable under the conditions of utilisation, and disintegrate into NPR <500nm. In the precautionary matrix, this case is treated as nano-relevant (S1.2=1).
2. The primary particles create agglomerates, which are stable under the conditions of utilisation and do not disintegrate into NPR <500nm. The NPR are not produced in some way or integrated into a utility product, which leads to exposure of the lungs. In the precautionary matrix, this case is dealt with as not nano-relevant (S1.2=0).
3. As in 2, however, the NPR are in some way produced or integrated into a utility product, which leads to exposure of the lungs (agglomerates with a size range of 500nm - 3µm). In the lungs, even with stable agglomerates >500nm structural elements (nanoscale side branches) can appear, which, in contact with lung tissue, show nanospecific toxicity. In this case the NPR are evaluated as nano-relevant (S1.2=1), a precautionary matrix must be filled in with EI (physical surroundings) = air.

Flow diagram for the evaluation of nano-relevance:

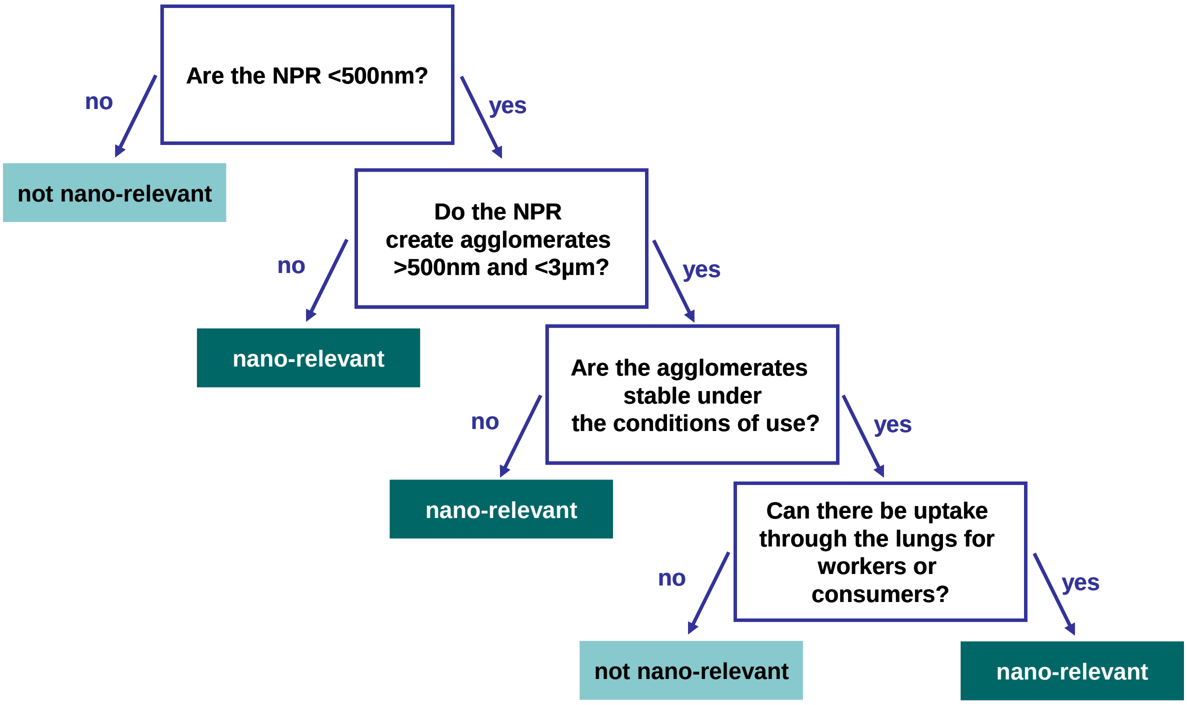

Figure 5: Evaluation of nano-relevance

Notes: