Edited by René Zimmer, Rolf Hertel, Gaby-Fleur Böl

BfR Delphi Study on Nanotechnology

Expert Survey of the Use of Nanomaterials in Food and Consumer Products

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Table of Contents

Preface

The early detection of health risks in consumer-related areas is the responsibility of the Federal Institute for Risk Assessment (BfR) and is part of its daily work. Without the early detection of risks, the consistent, transparent application of the precautionary principle is not possible. In this context the subject nanotechnology is also of relevance for BfR. New materials manufactured using nanotechnology are increasingly finding their way into production processes and consumer products. Questions about the safety and the potential risks of nanotechnology are becoming increasingly pressing.

This prompted BfR in 2006 to carry out the interdisciplinary research project “Delphi Study on Nanotechnology - Expert Survey of the Use of Nanomaterials in Food and Consumer Products”. The goal of this project was to pre-structure the technology area, nanotechnology, on the basis of potential risks through the involvement of various social groups and, in this way, to lay the foundations for future BfR risk assessments of nanotechnology applications. The Delphi method was adopted in this work. This method is frequently used for the purposes of technology forecasting but also for the early detection of unclear risks of new technologies. It is based on structured group surveys and draws on both the participants’ knowledge and intuitive information.

In the Delphi survey around 70 experts from research, industry, public authorities and non-governmental organisations were systematically questioned in two survey rounds about the potential risks of nanotechnology for consumers. The feedback from the first round gave the experts an opportunity to compare their personal impressions with the range of opinions held by the participants. The project identified nanomaterials that are already being or could potentially be used, and attributed them to concrete applications. Based on the knowledge available on exposure and hazards, the applications were then classified according to the level of probable risk and strategies for risk reduction were developed. At two later expert workshops the results were analysed and compiled in a risk barometer.

I would like to thank the experts who bundled the “weak signals” along the lines of early risk detection in the context of this project in order to forecast, amongst other things, future developments and potential risks of nanotechnology applications. The results are a first pointer as to the areas in which consumer health may be at risk and where institutional action may be necessary.

Professor Dr. Dr. Andreas Hensel
President of the Federal Institute for Risk Assessment

1 Introduction

Nanotechnologies are deemed to be the key technologies of the 21st century. The hopes and expectations placed in them as the driver of innovation are enormous. “Key technologies are the passport to the future”, say Federal Minister Annette Schavan in her preface to the “Nano Initiative – Action Plan 2010”. In the 2010 Action Plan the German Federal Government has set out the main areas of its cross-ministry high tech strategy. The core is the implementation of the results of nanotechnological research in diverse innovations, the introduction of other sectors and companies to nanotechnologies, and the timely coordination of various areas of policy in order to dismantle obstacles to innovation. This Action Plan is accompanied by a comprehensive dialogue programme involving the various sectors, the sciences and the public at large. Scientific risk assessment, the safe and responsible handling of consumer information, consumer protection and health and safety at work are seen as a special challenge. The emphasis will likewise be on questions of standardisation and test strategies. The support measures of the federal government, therefore, also include interministerial research activities on timely risk evaluation and assessment.

The Federal Institute for Risk Assessment in Berlin (BfR) is the competent independent federal institution in Germany. In this context it has developed, together with the Federal Institute for Occupational Safety and Health (BAuA) and the Federal Environmental Agency (UBA), a research strategy to identify the potential risks of nanotechnology. The goal of this research strategy is to structure this research area, to develop methods for the measurement and characterisation of nanoparticles, to collect information on exposure, toxicological and eco-toxicological effects, and to promote the development of a risk–based test and evaluation strategy. In parallel to this BfR conducted a Delphi survey in 2006 of experts in the area of nanotechnology. The goal was to identify nanomaterials that are already used or could be used, to assign them to concrete applications and to draw conclusions from this information about consumer exposure. The project had several goals in terms of its findings:

- Expert knowledge on scientific risk assessment is sourced from different angles and examined for consistency. Possible differences in the data sources used and in evaluation are to be rendered visible.
- The findings can provide insight into the level of knowledge in the various groups and identify where evaluations of topics differ so greatly that a public controversy is to be expected.
- From the evaluations theme areas are identified where there is a specific need for research and action on the basis of which priorities can be derived for BfR’s action and communication strategies.

2 The Delphi method as an instrument of early risk detection

Classical Delphi methods were already developed in 1964 by RAND Co. and were originally intended for the evaluation of defence technologies (Gordon & Helmer 1964). The Delphi method consists of a structured communication process within a specific group. The process effectively pools individual knowledge or assessments which means that even complex topics or technology forecasting and evaluation can be handled by the group (Linestone & Turoff 1975). Delphi surveys have been used since the 1970s above all as a forecasting tool within the framework of technology impact assessments for risk assessment purposes and aim to reduce uncertainties about knowledge and knowledge assessments, probable occurrences and action options by conducting a survey of a larger group of experts. Other approaches focus more on the aspect of scientific and technical development potential and examine obstacles, the timeline up to market maturity or market penetration (Cuhls *et al.* 1998).

The classical Delphi method has the following structure. Experts are sent a standardised questionnaire and are asked to complete it. The survey can be repeated several times. The evaluations of the prior survey Rounds are disclosed and experts are thus given an opportunity to adjust their own assessment (Aichholzer 2002). Modern Delphi methods are normally staged in two Rounds to keep down the costs (Grunwald 2002, p. 211). This is also the case for this research project.

The Delphi method is founded on the assumption that experts assess risks on the basis of information which may be of differing quality (own research, primary and secondary literature, media reports, experience etc) and which comes from different assessment contexts (scientific discipline, interests, values, attitudes, etc). The exchange of knowledge over several Rounds has the advantage that feedback processes are possible which encourage participants to re-examine their own evaluation. As a rule, the spectrum of assessments is reduced, trends become clearer. Some Delphi surveys seek to achieve consensual assessment over several Rounds. This research project aims to bring the assessments closer together over the two Rounds, and to identify areas of agreement and disagreement. The question techniques used in classical Delphi methods are based on the evaluation of specific facts or statements/scenarios that describe future applications. In a Delphi method experts are asked to indicate the degree of their own informedness or the reliability of their assessment. No use was made of this explicit evaluation in the case of the Nano Delphi. The category “don’t know” was consistently included for all questions and participants also had an opportunity to make qualitative comments and remarks. At the same time, this touched on the basic problem that in classical Delphi methods the reasons for individual assessments are not recorded. More recent approaches (Webler & Renn 1991; Renn 1994) address this problem and develop more interactive forms like the group Delphi method in which additional workshops are staged in order to record the reasons for the evaluations.

3 BfR Expert Delphi Survey on Nanotechnology

3.1 Objective

Nanotechnologies are used in a number of sectors and encompass various production methods, substances and products. Given the broad nature of the subject matter, BfR – in line with its scientific competence – focused its research efforts on the consumer applications food, cosmetics and consumer products (textiles and surface coatings). The objective of the Delphi method can be described as follows:

Generation of expert assessments whether potentially damaging effects of nanotechnologies could arise from:

- the nature of nanoparticles/nanomaterials themselves (e.g. their chemical reactivity),
- the characteristics of products made from nanoparticles/nanomaterials or
- aspects of the production process that are revealed in the end product.

In this context the estimation of experts was also to be taken into account concerning

- which nanotechnology applications are already being used now or will be used in the future in the defined areas,
- which risks and undesirable consequences are expected and
- which application is likely to lead to risks in particular for consumers.

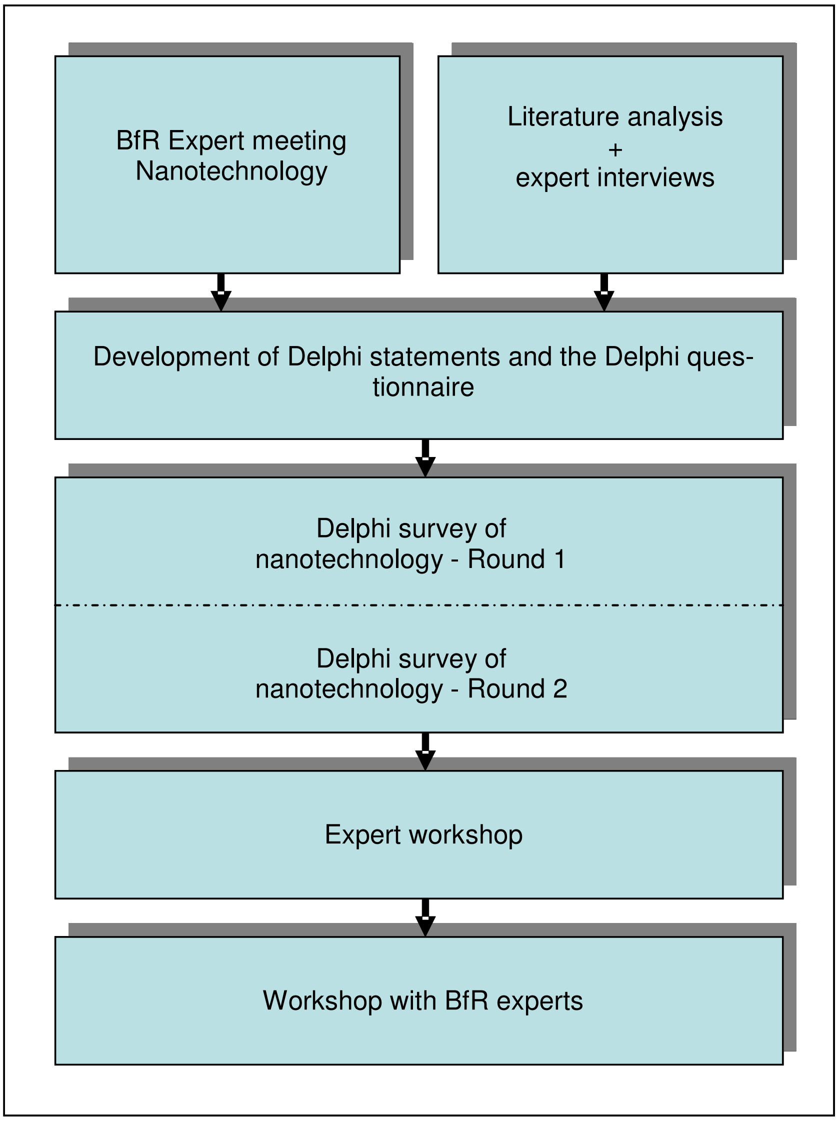
Another task was to determine the need for action by BfR and to depict the results as a risk barometer that highlights risk trends. The risk barometer was discussed with BfR experts.

3.2 Design

The BfR Delphi study on nanotechnologies in the areas of food, cosmetics and consumer products was set up as a multi-phase process and was conducted in 2006. Fig. 1 gives an overview.

The study began with the BfR expert meeting (Nanotechnology, its products and risks for the consumers) on 26 March 2006. An invitation was extended to experts from various disciplines and the expert meeting looked at nanotechnologies in food, cosmetics, surface coatings and textiles. Furthermore, the experts were selected in such a way that there was an even balance between industry and science. The target groups for the event were the staff of senior federal authorities (who used the event, amongst other things, to build on their knowledge), representatives of associations and companies, environmental organisations and consumer associations. The meeting came to the conclusion that nanomaterials or nanotechnologies are already used in diverse ways in the production of consumer products but that many risk assessment questions have still to be answered. The development of suitable test strategies to identify health risks constitutes a particular challenge.

Fig. 1: Design of the BfR Delphi study on nanotechnology



The following experts attended the expert meeting Nanotechnology at the Federal Institute for Risk Assessment:

- Dr. Gerhard J. Nohynek, L'OREAL Worldwide Safety Department – "Der Einsatz von Nanopartikeln in der kosmetischen Industrie" (Nohynek 2006)
- Prof. Dr. Dr. Jürgen Lademann, Humboldt University Berlin, Charité – "Risikobewertung von Nanopartikeln in kosmetischen Produkten" (Lademann 2006)
- Prof. Dr. Tilman Butz, Leipzig University, Physics and Geosciences Faculty – "Die Haut als Barriere für Nanopartikel – Das NANODERM-Projekt" (Butz 2006)
- Prof. Dr. Peter Schurtenberger, Freiburg University, Physics Department – "Nanotechnologie in der Lebensmittelindustrie" (Schurtenberger 2006)
- Dr. Axel Siegner, neosino nanotechnologies AG – "Neue Nahrungsergänzungsmittel durch Nanotechnologie" (Siegner 2006)
- Dr. Peter Wick, EMPA, Materials – Biology Interaction – "Einblick in die Nanotoxikologie: erste cytotoxikologische Ergebnisse von Nanopartikeln" (Wick 2006)

- Prof. Dr. Horst-Christian Langowski, Fraunhofer Institute for Process Engineering and Packaging IVV – “Anwendung der Nanotechnologie in Materialien für den Lebensmittelkontakt” (Langowski 2006)
- Dr. Dirk Hegemann, EMPA, Functional Fibers and Textiles – “Funktionale Textilien dank Nanotechnologie” (Hegemann 2006)
- Prof. Dr. Wolfgang Bremser, Paderborn University, Chemistry and Technology of Coasting Substances – “Nanotechnologie bei der Beschichtung von Oberflächen” (Bremser 2006)

The BfR expert meeting as well as several expert interviews and literature studies were the basis for the development of the actual Delphi questionnaire. In February 2006 the Interdisciplinary Research Unit on Risk Governance and Sustainable Technology Development (ZIRN) at Stuttgart University was commissioned, together with BfR, to carry out the Delphi survey and the two workshops. The next step was to build up a qualified pool of addresses of 100 experts. The experts came from the areas science, industry, non-governmental organisations (NGOs), networks[1] as well as insurance companies, and work in nanotechnology in one or more of the theme areas food, cosmetics and consumer products (surfaces and textiles). The selection criterion used was technical competence for the specific theme area. If at all possible, experts were selected who had already been involved in evaluating and assessing nanomaterials in conjunction with risk questions and/or were involved in dialogue projects and conferences on the potential risks of nanotechnologies.

The questionnaire was designed in such a way that the applications food, cosmetics, surfaces and textiles were covered as well as the basic questions on economic development, toxicity and exposure, regulation and further action options for dealing with nanomaterials (see questionnaire in the Annex). The survey was conducted in two Rounds. As a rule, the experts only answered questions on areas in which they had technical expertise and indicated in this in the questionnaire.

Following an inter-agency pre-test in June 2006 involving experts from BfR and the Federal Institute for Occupational Safety and Health (BAuA), the first round of this Delphi survey was staged from 3 to 22 July 2006. The experts were contacted as the representatives of their organisations. As a rule the participants had the task of coordinating the response to the questionnaire within their organisations. On average 2-3 experts from each of the respective institutions completed the questionnaire. In one case several departments were involved in completing the questionnaire. Out of the 100 experts contacted, 71 returned a completed questionnaire. This relatively high return quota for surveys of this kind was achieved by various means ranging from personal contacts, telephone pre-contacts, letters sent together with the questionnaire by email and personal follow-up right up to the submission of the completed questionnaire. The reasons given for not participating were listed in order of frequency of the responses: overly small time window, too much work or too little expertise in the areas examined. Some experts exceeded the time window without reacting or giving any reasons and two experts thought that the questions were not useful.

The second Delphi round was conducted from 4 to 26 October 2006. The results from Round 1 were made available to the participating experts together with the second questionnaire (cf. questionnaire in the Annex). At the same time, the experts in Round 2 were again asked for their estimation in order to render visible changes in assessments over the course of time. The second round of the Delphi survey was used in order to put more in-depth questions as some assessments in the first round showed major variances or a lack of clarity in the questions from Round 1 had become visible. Out of the 71 experts contacted who had partici-

[1] The category “network” is used for individuals who are key figures in nanotechnology working groups or nanotechnology networks and, therefore, have nanotechnology expertise of relevance for this study.

pated in Round 1, 56 responded. This corresponds to a return quota of 78% in Round 2. With a return quota of 56% for 100 participants over two Rounds, the quota in this Delphi survey is far higher than the quotas normally achieved in these studies. This can be attributed, amongst other things, to the topical nature of the subject, the interest of the experts in generating common knowledge and their willingness to cooperate.

After Round 2 of the Delphi survey an expert workshop, based on the structure of the group Delphi method, was held. The expert workshop was intended mainly as a forum for dialogue and the number of participants was, therefore, limited to 12. The goal was to examine the qualitative reasons given and to widen knowledge across stakeholders. The participants were selected on the basis of competence, their responses in the questionnaires and with a view to having the broadest possible range of attitudes. Furthermore, the stakeholder groups were to be appropriately represented. Participation was as follows:

- Industry (3 participants),
- Science (3 participants),
- NGOs (environmental organisations 2 participants, consumer associations 1 participant),
- Insurance companies (1 participant),
- Public authorities (2 participants).

As the theme areas food, cosmetics and consumer products were also to be represented but it was not possible to secure an industry and science representative for each area, experts with overarching knowledge or scientists with in-depth knowledge of these theme areas (e.g. textile abrasion) were selected. At the workshop the results with very great variance in the assessments were discussed in depth, substantiated and documented. Some of the open questions could also be clarified, e.g. on inhalational or dermal exposure to nanomaterials, test criteria for nanomaterials or stakeholder differences. No representative was available for the application food which had already been under-represented in the Delphi survey.

3.3 Socio-demographic data and stakeholder distribution

3.3.1 Gender distribution

In Round 1 54 of the experts who participated in the Delphi study were men and 17 were women. In order to achieve a balanced distribution of gender, preference was given to women when both male and female participants with the same qualifications were available from the same organisation. Nonetheless, in Round 1 a ratio of just under 2:3 was achieved and the gender distribution in Round 2 remained almost the same: 43 men and 13 women.

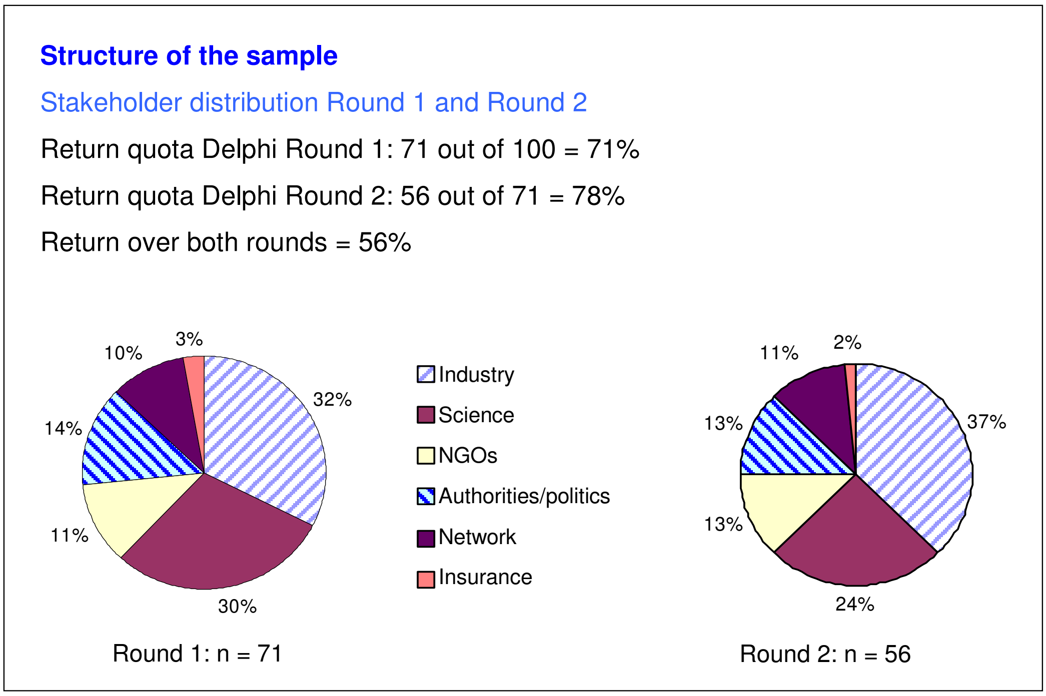
3.3.2 Stakeholder distribution

In line with the agreements with the client, BfR, a sample with 3 stakeholder groups of approximately equal size was established (see Fig. 2).

- The first group of experts came from research-based and application-oriented industry and worked in the four theme areas food, cosmetics, surfaces and textiles (industry: 23 representatives in Round 1, 21 representatives in Round 2).
- The second group encompassed scientists whereby efforts were made to ensure a balanced distribution between basic scientific researchers and application-related researchers for the four themes areas (science: 21 representatives in Round 1, 14 representatives in Round 2). The largest drop was observed in the group of scientists. Negative replies were received because of the ongoing university term and the large number of scientific conventions

- A third, highly heterogeneous group consisted of experts who are mainly involved in their institutions in the risk assessment of nanotechnologies and the applications of interest here (27 representatives in Round 1, 21 representatives in Round 2). 10 representatives of public authorities and political parties were assigned to this group in the first Delphi Round, in Round 2 seven people responded. The BfR, as the client, did not take part in the survey. 8 experts from environmental organisations, consumer protection groups and trade unions (all NGOs) took part in Round 1 and 7 in Round 2. From the area of networks 7 people took part in Round 1, six in Round 2. Insurance companies had 2 representatives in Round 1; in Round 2 only 1 insurance company took part in the survey. The common feature of this group is that the participants primarily looked at the risk questions of nanotechnologies or have corresponding knowledge as the central key figures in nanotechnology networks.

Fig. 2: Stakeholder distribution after Delphi survey 1 and Delphi survey 2



For the evaluation discussion focused on the extent to which the major drop in the size of the science group had had a major impact on the results from Round 2. Whereas the group of risk experts (NGOs, public authorities, networkers and insurance companies) remained almost constant despite some negative replies (38% in Round 1, 39% in Round 2), the scientist group fell by 6%. The industry group had the lowest number of negative replies and had a share of 30% in Round 2 corresponding to a growth of 5%. The percentage strengthening of industry could have led to the assumption that a less critical assessment would be undertaken in Round 2 or that a polarisation of assessment between industry and "critics" would have become more obvious. The opposite is the case. What is typical of the Delphi method is that, on presentation of the results from Round 1 coupled with a request for renewed assessment, experts tend to confirm existing trends. This applies in this case both to the positive and also negative evaluations undertaken for Delphi Round 1. The evaluations from Round 1, which show a polarisation, tended to be more differentiated in Round 2. Unclear assessments from Round 1 were not clarified to any major degree in Round 2 either.

The following section gives the assignment of individual stakeholders to specific applications. The number of experts who answered is given in brackets.

Industry:

- Manufacturers of raw materials who produce nanomaterials for more than 1 application (5 in Round 1/5 in Round 2),
- Food (3/3),
- Cosmetics (8/8),
- Surfaces (2/1),
- Textiles (2/1),
- Overarching industry associations (2/2),
- Other (1/1)

Science:

- Toxicology /Inhalation biology (6/4),
- Environmental research (3/2),
- Surface coatings (4/3),
- Textiles (2/1),
- Food (1/1),
- Experts from disciplines that cover the different applications (e.g. ITAS Karlsruhe, Fraunhofer IAO) (5/3)

NGOs, trade unions and consumer protection groups:

- Environmental organisations (4/4),
- Trade unions (2/1),
- Consumer protection groups (2/2),

The group of public authorities and politics mainly consisted of representatives on the federal level:

- Senior federal authorities/ministries/politics (10/7)

No distinction can be made in the case of networks and insurance companies.

When it comes to the choice of experts it should also be noted that imbalances in the stakeholder weighting can be attributed above all to the respondents' response behaviour. This was particularly noticeable in the area of food where it was very difficult to get experts to participate in the Delphi survey. It was also difficult to increase the number of participants from NGOs or consumer associations.

4 Nanomaterials

When defining a research orientation, the suspected risk should be given high priority. Both the individual risk, which describes the level of the individual risk as well as the population risk which takes into account the number affected, are relevant parameters which should play a major role when selecting the main focus of research. In order to describe a risk, information is needed, amongst other things, about the degree to which humans and the environment come into contact with nanomaterials (exposure) as well as information on a substance's dose-dependent toxicological and ecotoxicological properties. Only when both these parameters can be combined, is it possible to proceed to risk description and assessment. The degree and probability of damage are important parameters. This means that nanomaterials that present a larger toxic/ecotoxic action potential and/or show higher exposure to man and the environment are of special importance and should be given priority in the assessment. If no further information is available on exposure, then the annual production volume of a substance can be used to estimate it.

Nanomaterials are seen as the products of a new technology although a large number of nanostructured materials which are currently on the market have ranked amongst established chemicals for some decades. There are also truly new nanomaterials which have only been developed in recent years. A number of new nanomaterials are expected for the future. Compared with established industrial chemicals the increased need for information on the risks of nanomaterials is partially justified by the fact that nanotechnology is seen as a new technology and that there are new risk scenarios for which we have no experience and where there is a special public interest.

4.1 Hazard

The term "hazard" describes the potential contained in the triggering of a risk (for instance substance, technology or behaviour) to constitute a possible threat to life, health and the environment (Jaeger *et al.* 2001; IRGC 2005). Instead of the word "hazard" the term "hazard potential" is frequently used in German in order to stress the possibility of a danger (Schütz *et al.* 2003, p. 24).

In the meantime a whole series of basic substances with a nanostructured form are available on the market. They include titanium dioxide, silicon dioxide, zinc oxide, aluminium oxide, iron oxide, ceroxide, silver, carbon black, carbon nanotubes, fullerenes etc. In particular the free, non-soluble nanomaterials which are ingested via various pathways are of special toxicological importance. There is no systematic compilation that records the morphological and chemical changes of the various substances. As, at the present time, it cannot be ruled out that changes may alter not only technical properties but also toxicological properties, there is a need for a systematic, differentiated overview. This kind of information is essential in order to identify those nanomaterials in a risk-oriented procedure which are to be given priority when it comes to assessment and examined more extensively. Parameters like solubility, size, surface, shape, degree of agglomoration/aggregation, surface modification or reactivity, number concentration and others are discussed as parameters which may have an effect on toxicological properties.

4.1.1 Toxicity of selected nanomaterials in various aggregate states

In the first set of questions on toxicity, experts were confronted with various nanomaterials and were asked to respond to the following questions, "*In your opinion do these nanomaterials have a toxic potential in the following aggregate states?"* The categories indicated were: "as volatile particles", "in an aerosol", "naturally aggregated", "coated", "in a liquid medium/in a solvent" and "embedded in the matrix". If none of the options were chosen, this could mean that the participant had no knowledge of the substance or that it has no toxic potential. Hence, the table only checks the existing knowledge of toxic potential but does not record a lack of knowledge.

This set of questions was answered in Round 1 by 64 of the 71 participating experts. Some participants only commented on individual substances about which they had more extensive knowledge. As, against the backdrop of a change in population per substance, no exact representation of assessment is possible, absolute numbers were used. They indicate a trend for the substances where a certain number of experts see a toxic potential in a specific aggregate state. The results also provide some indication about how well documented some individual substances are.

Prior to looking at this table, some information should be given about the terms used. The term “volatile particle” should encompass nanomaterials which are present as “ultrafine dust”. Although the term passed the internal public authority pre-test, at the following workshops it was recommended that the term “free nanoparticles” should be used. What is problematic here is the demarcation to aerosols which is why, based on the level of knowledge available today, the two were combined in the category of “airborne nanoparticles”. The uncertainty regarding the definitions used, which flared up several times in the course of the project term, reflects a general definition problem which can be observed not just within the pre-test group but across all stakeholder groups. The questions are presented in their original form and were not amended at a later stage.

Table 1: Estimation of the existence of a toxic potential of nanomaterials depending on the aggregate state (number of mentions as “toxic”).

	as volatile particles	in an aerosol	naturally aggregated	coated	in a liquid medium	in a matrix
Silicon dioxide	26	28	4	9	8	1
Titanium dioxide	32	29	5	10	12	2
Zink dioxide	32	28	8	8	14	3
Chromium(III)-oxide	22	29	11	12	15	4
Nickel oxide	24	30	14	13	17	7
Aluminium oxide	21	25	4	7	9	3
Iron oxide	21	26	4	7	10	3
Silicates	17	23	8	6	6	2
Inorganic dye pigments	19	28	7	5	11	3
Organic dye pigments	17	25	6	5	11	3
Carbon nanotubes	25	31	13	7	15	4
Fullerenes	25	26	7	8	18	2
Polymers	15	18	4	4	8	3
Nanocomposites	13	17	3	4	5	1
Silver	17	21	10	7	11	4
Vitamins	6	8	4	3	6	1
Degradable materials: Lipid compounds, biopolymers	7	9	4	6	2	5
Nanotones/layered silicates	10	16	5	4	6	3

Table 1 shows that the experts thought that out of all the aggregate state combinations “aerosols” and the category “volatile (free) particles” had the highest toxic potential. In the table the mentions are presented in columns. This meant that “nanomaterials in an aerosol” were assigned toxic potential a total of 417 times and “nanomaterials as volatile (free) particles” 349 times. Other categories “in a liquid medium” (n= 184), “coated” (n= 125), “naturally aggregated” (n= 121) and “in a matrix” (n= 54) followed much further behind.

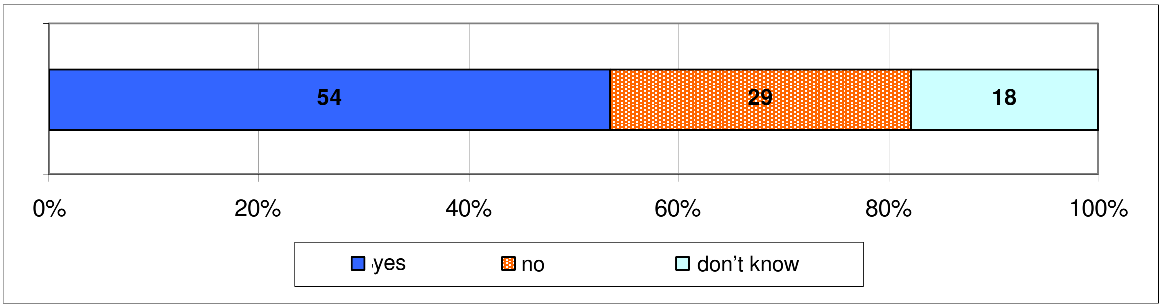
These results reveal a trend whereby the experts interviewed here see nanomaterials in the form of aerosols or volatile/free particles as being a group with particularly high toxic potential. The experts are of the opinion that coatings, natural aggregations of nanoparticles or the incorporation of the particles into a liquid or solid medium considerably reduce the toxic potential of nanomaterials.

In order to examine whether any major aggregate states in which nanomaterials may occur are missing in Table 1, the experts in the second survey round were asked to check the following list for completeness and, where appropriate, to add to it:

- as volatile (free) particles
- in an aerosol
- naturally aggregated
- coated
- in a liquid medium/in a solvent
- embedded in a matrix

The assessment by the experts confirmed the list of criteria examined in survey Round 1 (Fig. 3).

Fig. 3: Responses to the question: Is the list of criteria sufficient to describe the aggregate state of nanomaterials? (n= 46 responses)



Explanation: percentages rounded up

4.1.2 Toxic potential of individual nanomaterials

This set of questions analysed whether, beside a particularly problematic aggregate state, substances can also be identified which must be deemed to be particularly toxic independently of the aggregate state. To this end, the mentions for the individual nanomaterials were pooled beyond the aggregate states. This estimation may be relevant when individual substances are the focus of assessments within the framework of regulations and no distinction is made on the basis of the aggregate state.

Nickel oxide is in first place in Table 2. Independent of the nanoparticulate form this is the substance which can cause sensitisation when in contact with skin and cancer when ingested (labelling of dangerous substances from Directive 67/548/EEC, Annex I, R: 49–43). Otherwise the results show that no general statement about the toxicity potential of the substance independently of its aggregate state can be made on the basis of these findings. What is noticeable is, for instance, that zinc oxide, titanium dioxide and silicon dioxide – the 3 substances which are best described in their nanoparticulate form in the literature and for which experience spanning several years is available – were deemed comparatively frequently to have toxic potential. This contradicts the estimation of experts from the BfR expert meeting and the following expert workshops.

Table 2: Sum of mentions of the toxicity of nanomaterials across all aggregate states

Substance	Sum of mentions
Nickel oxide	105
Carbon nanotubes	95
Chromium(III)-oxide	93
Zinc oxide	93
Titanium dioxide	90
Fullerenes	86
Silicon dioxide	76
Inorganic dye pigments	73
Iron oxide	71
Silver	70
Aluminium oxide	69
Organic dye pigments	67
Silicates	62
Polymers	52
Nanotones/layered silicates	44
Nanocomposites	43
Degradable materials: lipid compounds, biopolymers	33
Vitamins	28

4.1.3 Criteria for toxicity potential

The next step was to ask experts about the possible causes of the toxic potential of nanomaterials. When designing the questionnaire the criteria "solubility", "size" (indicated in the range for instance < 70 nm), "shape" and "surface and reactivity" were deemed to be particularly important and therefore included.

Table 3 gives the results for the individual materials. With 310 mentions across all materials the specific "surface and reactivity" is linked the most frequently with possible toxicity. "Shape" (113 mentions) and "solubility" (110 mentions) are selected less frequently. What is noticeable here is the number of mentions for carbon nanotubes in conjunction with the criterion "shape" which was mentioned 18 times. This is based on the assumption that carbon nanotubes - because of their long fibre-like shape - could have an effect similar to that of asbestos fibres (Poland *et al*. 2008).

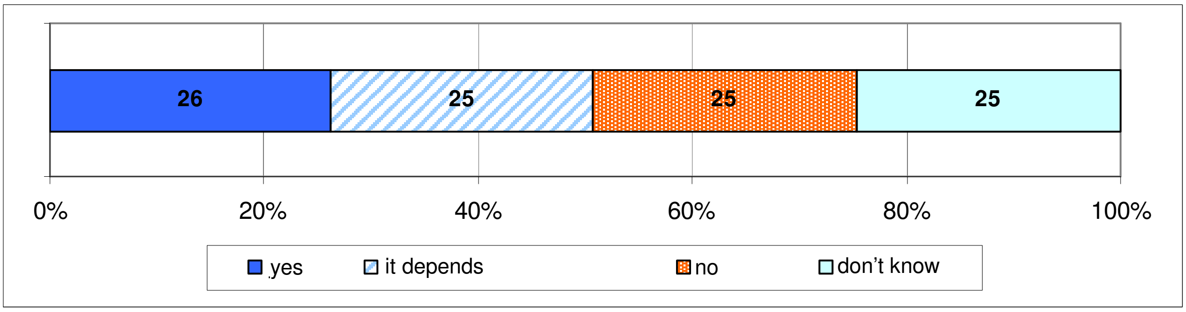
Table 3: Possible causes of the toxicity of nanomaterials (number of mentions)

	Solubility	Shape	Surface & reactivity
Silicon dioxide	4	10	19
Titanium dioxide	4	8	27
Zinc dioxide	8	6	25
Chromium(III)-oxide	7	6	21
Nickel oxide	9	8	23
Aluminium oxide	4	5	18
Iron oxide	6	6	21
Silicates	3	7	16
Inorganic dye pigments	9	5	19
Organic dye pigments	12	5	18
Carbon nanotubes	6	18	17
Fullerenes	7	9	21
Polymers	5	6	11
Nanocomposites	2	5	14
Silver	9	4	18
Vitamins	7	1	6
Degradable materials: lipid compounds, biopolymers	5	1	6
Nanotones/layered silicates	3	3	10
Total mentions	**110**	**113**	**310**

In many discussions in a scientific and political context it is pointed out that the smallness of the nanoparticles was the decisive factor for them being more toxic than larger particles of the same material. Hence the experts were asked whether they could indicate a critical size range as the cause of possible toxicity. From the comparatively few responses it was not possible to obtain a comprehensive picture. For 10 of the 18 substances only 4 up to 7 of the 71 experts expressed an opinion. Furthermore, for instance for the particle size of zinc oxide, for which 15 mentions were recorded, 4 were in the range between 41 and 60 nm and 5 mentions between 81 and 100 nm. The broad range of responses and the low number of responses do not permit any statements about a trend. Experts do not seem to be able to agree on the problematic particle sizes.

In order to examine whether particle size is at least then a relevant criterion for possible toxicity when it comes to distinguishing between nano and microparticles the experts were asked to evaluate a theory whereby nanoparticles were more toxic than microparticles. Here, too, no agreement was reached. 26% of the respondents agreed with the statement and 25 disagreed (Fig. 4).

Fig. 4: Evaluation of the theory: As nanoparticles are more toxic than microparticles, their inhalation leads to new toxicities (n=65 responses)



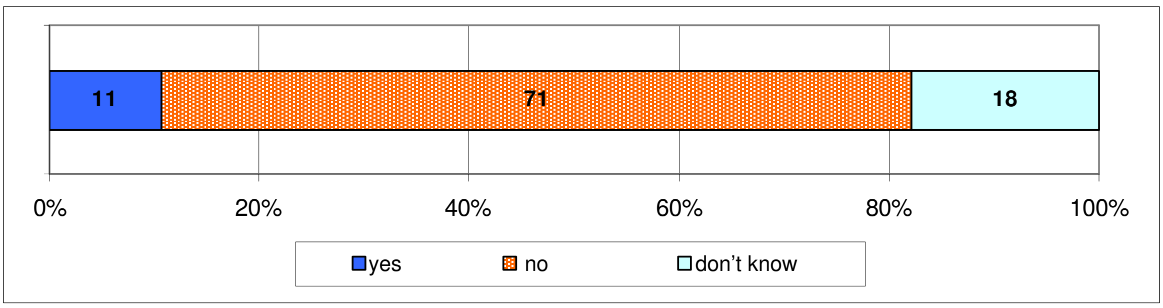
Explanation: percentages rounded up

In order to determine whether the criteria presented in Round 1, which could be of importance potentially for the toxicity of nanomaterials, are sufficient, the experts in the second survey Round were asked to review the following criteria:

- Solubility
- Size (indication in range, e.g. < 70 nm)
- Shape
- Surface and reactivity

Regarding the list of criteria to assess toxicity, a need for addition criteria was seen (Fig. 5). 71% of the respondents said “no”. There was a clear wish for a case-by-case examination in which a defined number of criteria should be taken into account.

Fig. 5: Responses to the question: Is the list of criteria sufficient to assess the toxicity of nanomaterials? (n=46 responses)



Explanation: percentages rounded up

As only a few qualitative comments were made in the questionnaires in Delphi Round 2 concerning which criteria should be added, this question was discussed at the next expert workshop. The experts from industry, science, NGOs, consumer associations, public authorities and insurance, who attended the workshop, jointly developed the following 18 test criteria:

General test criteria for nanomaterials:

- Dose
- Length of exposure
- Substance/substance group
- Degradability, persistence, latency period, formulation
- Shape
- Solubility (in water and biological liquids *in vivo*)
- Crystallinity and crystal phase
- Purity and contamination of the substance
- Size, size distribution

Additional nanospecific test criteria:

- Degradability, persistence, latency period, accumulation (does this change in the case of nanomaterials?)
- Pharmaceutical form (aerosol, suspension, emulsion, dispersion, composite)
- Tendency towards aggregation, agglomeration/stability of the aggregates, agglomerates
- Exposure pathway
- End point
- Solubility (in water and biological liquids *in vivo*)
- Size, size distribution
- Shape
- Surface (coating, charge, defects) and reactivity

The list of the 18 criteria shows just how complex a robust toxicity assessment of nanomaterials is in the opinion of the experts. It was expressly pointed out that this examination only makes sense in individual cases.

4.1.4 Description of the mechanisms of action

After several possible causes had been identified for the toxic effects of nanomaterials, the experts were asked to make some comments on the mechanism of action. In order to specify in what direction the question should go, the examples genotoxicity and oxidative stress were mentioned. Once again the experts were given a list of nanomaterials which are listed in Table 1. Just over half of the respondents (55%) answered this question. From each stakeholder group at least 50% of the respondents commented on the toxicity of the individual substances and the corresponding mechanisms of action. The contents of the participants' statements differ in some cases markedly. This applies both to the points of view and evaluations between various stakeholders as well as to the views of different experts with the stakeholder groups. The comments on the mechanisms of action of possible toxic effects are presented below for the individual nanomaterials. Multiple mentions within a stakeholder group were deleted in order to improve transparency as the main aim here was to record the various arguments in a qualitative manner. The most important arguments are listed as verbatim quotes in order to avoid interpretations by the authors. The value of the following comments lies in the fact that the entire knowledge spectrum of reliable and unreliable information is covered. Hence the list could serve as a source of information for more in-depth expert dialogues on this subject.

Silicon dioxide

The results show that the stakeholder's assessments are not uniform either within the stakeholder groups or between the various stakeholders. No assessment of the substance silicon dioxide in nanoparticulate form is possible on the basis of these statements. New data material from practice could indeed be helpful in order to examine the mechanism of action in the experiment in a practical context. Cooperation between industry and public authorities would seem to be recommendable based on the results for this section.

Table 4: Qualitative description of the mechanisms of action of nanoscale silicon dioxide

Stakeholder	Quote/Evaluation of the mechanism of action
Industry	"In principle what can be said from the angle of x (manufacturers of raw materials) is that, based on our comprehensive expertise on the physico-chemical properties of synthetic amorphous salicylic acid, they are not nanomaterials. X produces and distributes synthetic amorphous pyrogenous salicylic acids. They have been comprehensively characterised from the toxicological angle. There are no indications of systemic effects. Inflammation reactions in the lungs caused by high inhalational exposure are reversible. A recently conducted epidemiological study in employees involved in the production of synthetic amorphous salicylic acids did not produce any indications of relevant pulmonary changes. More recent work on the solubility of synthetic amorphous salicylic acids in biological media demonstrates their solubility which is a major factor in the mechanism of action." "No elevated, rather lower toxic potential" "Amorphous no toxicity and no chronic damage" "Inert insoluble particles, inflammatory effect"
Science	"Expect no toxicity" "Oxidative stress" "Inflammation" "Shape depends on the production process, may have toxic potential" "Inhalation – systemic intake"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation" "Impairment of mitochondria amongst other things of cellular organelles, membrane damage" "Accumulation of protein in the cell nucleus, blockade or replication and transcription, IL8 cytokines" "Genotoxicity, activation of immune system"
Public authority/politics	"Oxidative stress" "Inflammation" "Rather unproblematic"
Network	" Disruption of cellular metabolism" "Possible oxidative stress and inflammation reactions in the lung tissue"
Insurers	"Analogy silicosis during inhalation"

Titanium dioxide

The results for nanoscale titanium dioxide reveal correlations for mechanisms of action which were already mentioned for silicon dioxide. They also play a role for all of the following substances. They include "oxidative stress" with the highest number of multiple mentions, "inflammation processes" and "genotoxic effects". These three seem to be important mechanisms of action which could apply to almost all nanomaterials as shown by the tables below.

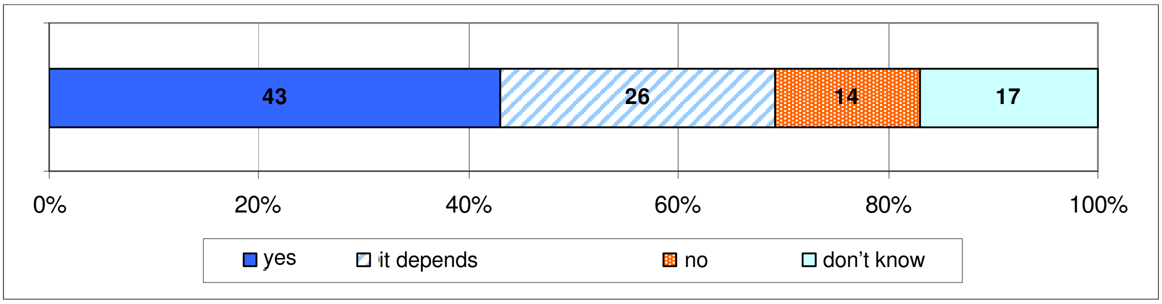
Table 5: Qualitative description of the mechanisms of action of nanoscale titanium dioxide

Industry	"No elevated potential" "Inert insoluble particles, inflammatory effect"
Science	"Mechanism of action not yet known" "Oxidative stress in microgliocytes (Long *et al.* 2006 Environ. Sci. & Technol.)" "Oxidative stress, inflammation reactions"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things the cellular organelles, membrane damage, penetration of broken skin, oxidative stress" "Lung: oxidative stress and DNA damage" "Cytotoxicity, immune system activation, inflammation"
Public authority/politics	"*In vitro tox:* solubility of oxidic NP decisive (Brunner, T. *et al.*, ES&T Web 3/11/06.)" "Oxidative stress" "Inflammation" "Genotoxicity, depending on size" "Differentiation between coated or untreated necessary"
Networks	"Disruption of cellular metabolism" "Possible oxidative stress and inflammation reaction in lung tissue"
Insurers	"Oxidative stress"

The description of the genotoxic effects of titanium dioxide in nanoparticulate form in the comments does not seem to be shared by a majority of experts. If one presents the theory "No genotoxic or photo-genotoxic risks for man are to be feared from the normal use of nanoscale TiO_2 particles" to experts, it is confirmed by 43 of respondents (Fig. 6). 43% of experts are of the opinion that titanium dioxide does not constitute any genotoxic risks for man. Only 14% reject the theory which means that they cannot at least rule out genotoxic effects.

It was added that comprehensive industrial studies already showed in 2000 that there are no risks linked to the conventional use of nanoscale TiO_2 particles and that TiO_2 of the corresponding particle size did not have a genotoxic effect. Comments were made by other respondents that this depended on the particle sizes used and on the modifications to the particle surfaces. Furthermore, no studies were available on inflamed or broken skin.

Fig. 6: Evaluation of the theory: No genotoxic or photo-genotoxic risks for man are to be feared from the normal use of nanoscale TiO_2 particles (n= 65 responses)



Explanation: percentages were rounded up

Zinc oxide

What is noticeable about the descriptions of nanoscale zinc oxide is that only industry indicates low toxic potential. There are a large number of multiple responses particularly from the cosmetics industry.

Table 6: Qualitative description of the mechanisms of action of nanoscale zinc oxide

Industry	"Low potential" "Inert insoluble particles, inflammatory effect"
Science	"Mechanism of action not yet known" "Oxidative stress, inflammation reactions" "Ion channel interaction" "Inhalation – systemic intake"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things the cellular organelles, membrane damage" "Penetration of damaged skin, oxidative stress, DNA damage" "Phototoxic effects (mammalian cells), genotoxicity, allergy potential (inhalation)"
Public authorities/politics	„Oxidative stress" 'Inflammation"
Networks	"Disruption of cellular metabolism" "Possible oxidative stress and inflammation reactions in the lung tissue"
Insurers	"Cell toxicity"

Chromium(III)-oxide

"Chronic toxicity" is listed by the experts for the first time for chromium(III)-oxide. The substances are deemed to be carcinogenic and toxic in all aggregate states and size ranges, i.e. also in the micro range. Otherwise the pattern of mechanisms of action is repeated here.

Table 7: Qualitative description of the mechanism of action of nanoscale chromium(III)-oxide

Industry	"Inert insoluble particles, inflammatory effect"
Science	"Mechanism of action not yet known" "Oxidative stress, inflammation reaction, genotoxicity" "Inhalation – systemic intake"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst things the cellular organelles, membrane damage" "Free oxygen radicals" "Chronic toxicity"
Public authorities/politics	"Oxidative stress" "Inflammation"
Networks	"Disruption of cellular metabolism" "Possible oxidative stress and inflammation reactions in the lung tissue"
Insurers	No details

Nickel oxide

For nickel oxide too, the experts are of the opinion that there are signs of "chronic toxicity" and labelling as a carcinogenic substance. Nickel oxide and chromium(III)-oxide should, however, be distinguished from other nanosubstances like, for instance, silicon dioxide or titanium dioxide, which are deemed to inert in this micro range.

Table 8: Qualitative description of the mechanisms of action of nanoscale nickel oxide

Industry	"Nickel oxide is already labelled as R 49 (Canc. Cat 2)"
Science	"Oxidative stress, inflammation reactions, genotoxicity" "Allergenic potential, carcinogenic potential" "Ion channel interaction" "Inhalation – systemic intake"
NGO/trade unions	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria amongst other things cellular organelles, membrane damage" "Inflammation in the lung, free oxygen radicals and DNA damage" "Chronic toxicity"
Public authorities/politics	"Oxidative stress, inflammation"
Networks	"Disruption of the cellular metabolism" "Carcinogenic potential"
Insurers	Cell toxicity

Aluminium oxide

The profile defined by experts for nanoscale aluminium oxide and iron oxide is almost identical. For both there are comments that "no toxicity" is expected. This indication from science is set against the mechanisms of action already mentioned which crop up for various substances in the responses in the questionnaires. The response behaviour could be an indication that experts are of the opinion that nanomaterials can, in general, trigger these mechanisms of action when they are, for instance, inhaled.

Table 9: Qualitative description of the mechanisms of action of nanoscale aluminium oxide

Industry	"Inert insoluble particles, inflammatory effect"
Science	"Expect no toxicity" "Oxidative stress, inflammation reactions" "Inhalation – systemic intake"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage" "Inflammation in the lungs, free oxygen radicals and DNA damage" "Neurodegenerative diseases, absorption via respiratory pathways possible"
Public authorities/politics	"Oxidative stress, inflammation"
Networks	"Disruption of the cellular metabolism" "Possible oxidative stress and inflammation reactions in lung tissue"
Insurers	No details

Iron oxide

What is new in the case of iron oxide is the reference by experts to "neurodegenerative diseases". Otherwise, the known mechanisms of action are described.

Table 10: Qualitative description of the mechanisms of action of nanoscale iron oxide

Industry	"Inert insoluble particles, inflammatory effect"
Science	"Expect no toxicity" "Oxidative stress, inflammation reactions" "Inhalation – systemic intake"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage" "Inflammation in the lungs, free oxygen radicals and DNA damage" "Neurodegenerative diseases, absorption via respiratory pathways possible"
Public authorities/politics	"Oxidative stress, inflammation"
Networks	"Disruption of the cellular metabolism" "Possible oxidative stress and inflammation reactions in lung tissue"
Insurers	Lung: irritation

Silicates

What is noticeable here is the reference by the circle of public authorities to “chronic inflammation processes” and the indication from insurance representatives that inhalation of nanoscale silicates could lead to clinical pictures similar to the ones observed in the case of the lung disease, silicosis.

Table 11: Qualitative description of the mechanisms of action of nanoscale silicates

Industry	“No elevated potential, rather lower”
Science	“Expect no toxicity“ “Inflammation, oxidative stress” “Inhalation – systemic intake”
NGO/trade union	“Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage“
Public authorities/politics	“Chronic inflammation processes” “Inflammation and oxidative stress”
Networks	“Disruption of the cellular metabolism” “Possible oxidative stress and inflammation reactions in lung tissue”
Insurers	“Analogous silicosis during inhalation”

Inorganic dye pigments

What is noticeable in the response pattern for nanoscale inorganic dye pigments is the uniform observation by industry, science, NGOs and the networks that no general statements are possible and various inorganic dye pigments have very different properties. Here closer examination would be helpful.

Table 12: Qualitative description of the mechanisms of action of nanoscale inorganic dye pigments

Industry	“Can only be answered in a specific manner”
Science	“Mechanisms of action not known” “Oxidative stress, acute toxicity” “Inflammation, oxidative stress” “Various assessments possible depending on the type of pigment”
NGO/trade union	“Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage“ “Depends on the toxicity of the individual substances”
Public authorities/politics	“Oxidative stress”
Networks	“Disruption of cellular metabolism” “Substances differ considerably, a critical property is lung passage with collection in adjacent lymph nodes” “Possible oxidative stress and inflammation reactions in lung tissue”
Insurers	No details

Organic dye pigments

In the case of nanoscale organic dye pigments, too, the vast majority of experts recommend examination on a case-by-case basis.

Table 13: Qualitative description of the mechanism of action of nanoscale organic dye pigments

Industry	"Can only be answered in a specific manner"
Science	"Oxidative stress, genotoxicity" "Not to be indicated as dependant on organic structure" Various assessments possible depending on the type of pigment"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage" "Dependant on the toxicity of the individual substances"
Public authorities/politics	"Genotoxicity" "Oxidative stress"
Networks	"Disruption of cellular metabolism" "Substances differ considerably, a critical property is lung passage with collection in adjacent lymph nodes" "Possible oxidative stress and inflammation reactions in lung tissue"
Insurers	No details

Carbon nanotubes

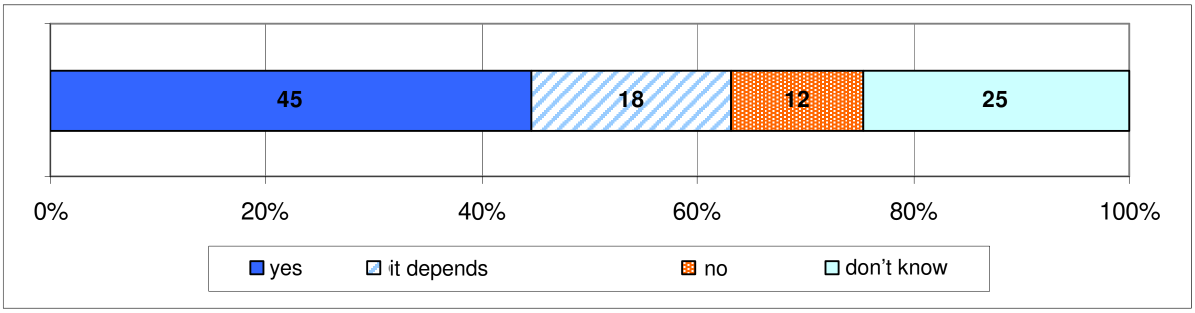
Almost all the stakeholders mention a comparison of carbon nanotubes and asbestos fibres in their comments. Reference is made particularly frequently to the fact that the mechanism of action is unknown. This is perhaps because the scientific studies on carbon nanotubes conducted up to now tend to contradict one another (Poland *et al*. 2008, Zhao *et al* 2008). The results correspond to results on the possible causes for toxicity potential where shape was indicated 18 times as being the cause for the toxicity of carbon nanotubes.

Table 14: Qualitative description of the mechanisms of action of carbon nanotubes

Industry	"Fibre- typical toxicity" "Toxicity potential not clear (inadequate characterisation, influence of impurities, metal, soot)" "Still unclear at the present time"
Science	"Mechanisms of action not known" "Because of their shape nanotubes have a particularly high toxic potential similar to that of asbestos" "Oxidative stress" "Unknown" "Analogy asbestos" "Fibrous, like asbestos"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria " "Asbestos- like effect" "Inflammation, fibrosis and granuloma in the lung caused by metallic catalyst particles, cytokine release, free radicals" "Oxidative stress"
Public authorities/politics	"Oxidative stress, mechanical effect in the case of agglomerated needles"
Networks	"Disruption of cellular metabolism" "Substances vary considerably, one critical property is lung passage with accumulation in adjacent lymph nodes" "Possible oxidative stress and inflammation reactions in lung tissue"
Insurers	"Aggregated inflammatory"

The comparison with asbestos used by the experts was taken up in one theory and presented to the experts for assessment. The theory was "In areas of nanotechnology where nanotubes are used, there may possibly be health consequences similar to those caused by asbestos fibres as the nanotubes may behave like larger respirable fibres, too". 44.6% of the respondents were of the opinion that effects may occur during the inhalation of carbon nanotubes similar to those observed when asbestos fibres are inhaled (Fig. 7). 12.3 % of the experts did not share this opinion. They commented that the flexibility of nanotubes means that simple analogies to asbestos were somewhat questionable. It was far more the case that case-by-case observations were needed which take into account for instance whether carbon nanotubes are embedded in a matrix or in what chemical formulation or morphology particles were available. Furthermore, it was important whether carbon nanotubes are not in fact attacked by the macrophages in contrast to asbestos fibres. Moreover, the aggregation behaviour of carbon nanotubes seems to be different from that of asbestos fibres. The current data situation does not, however, permit any clear statements or definitive assessment.

Fig. 7: Evaluation of the theory: In areas of nanotechnology where nanotubes are used, there may possibly be health consequences similar to those caused by asbestos fibres as the nanotubes may behave like larger respirable fibres, too (n=65 responses)



Explanation: percentages rounded up

Fullerenes

The experts made fewer comments about fullerenes than they did about carbon nanotubes. What is important here is the reference to the lipophilic properties of fullerenes which are referred to repeatedly by NGO representatives. This is set against the research data available up to now that only indicate low toxicity.

Table 15: Qualitative description of the mechanisms of action of fullerenes

Industry	"Data show low toxicity" "Mainly examined up to now in fish"
Science	"Mechanisms of action not known" "Unclear, oxidative stress possible"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage" "Lipophilic brain disorders caused by lipid peroxidation" "Potential crossing of the blood-brain barrier"
Public authorities/politics	"Oxidative stress"
Networks	"Disruption of cellular metabolism"
Insurers	No details

Polymers

The comments on nanoscale polymers differ considerably. On the one hand industry states that polymers were not generally toxic and on the other NGO representatives believe that "death caused by haemorrhagic pneumonia" is possible. One comment from scientists is that it is rather the residues of polymers that are to be viewed critically. The other comments are the same as for the previous substances.

Table 16: Qualitative description of the mechanisms of action of nanoscale polymers

Industry	"Polymers are generally non-toxic" "Can only be answered in a specific manner"
Science	"Area not clearly defined" "Oxidative stress" "Consideration should be given rather to the residues of monomers"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage" "Death caused by haemorrhagic pneumonia not by fresh, non-agglomerated particles"
Public authorities/politics	"Oxidative stress"
Networks	"Disruption of cellular metabolism"
Insurers	No details

Nanocomposites

The few, non-specific answers correspond to the rather subordinate assessment of nanocomposites from the angle of toxic effects (Table 1).

Table 17: Qualitative description of the mechanisms of action of nanocomposites

Industry	"Normally embedded in a matrix and thus freely available" "Can only be answered in a specific manner"
Science	"Area not clearly defined" "Oxidative stress" "As persistent particles inflammatory effect"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage"
Public authorities/politics	"Oxidative stress"
Networks	"Disruption of cellular metabolism"
Insurers	No details

Silver

The comments on the toxic effects of nanoscale silver come from all stakeholder groups. This estimation correlates with the increasingly critical comments about applications with silver in the further course of the survey.

Table 18: Qualitative description of the mechanisms of action of nanoscale silver

Industry	"Less toxic than solutions of silver salts" "When present as inert insoluble particles inflammatory effect"
Science	"Mechanism of action known" "Active catalytically, oxidative stress"
NGO/trade union	"Mainly accumulation" "Translocation over the olfactory nerve of olfactory bulb of the brain, passage of the synapses, in the brain in mitochondria" "Unknown nanoscale effects"
Public authorities/politics	"Impairment of respiratory organs" "Oxidative stress"
Networks	"No risk" "Disruption of the cellular metabolism" "Silver (Ag^+) is acutely toxic, inhibits a series of enzymes" "Possible oxidative stress and inflammation reactions in lung tissue"
Insurers	No details

Vitamins

Comments also differ within the stakeholder groups when it comes to the assessment of nanoscale vitamins. There doesn't seem to be any agreement whether vitamins can be included at all as nanomaterials. Overall, the toxic potential and the mechanisms of action are not linked necessarily to nanoscale but rather to hypervitaminosis.

Table 19: Qualitative description of the mechanisms of action of nanoscale vitamins

Industry	"No nanoparticles" "No toxicity is known for vitamins, better bioavailability because of smaller particles and particle sizes" "Not toxic" "Are normally soluble in body liquids, intrinsic substance properties must be taken into account"
Science	"Mechanism of action known" "Depending on the vitamin toxicity/e.g. vitamin E" "Change in bioavailability may possibly lead to hypervitaminosis"
NGO/trade union	"Mainly accumulation"
Public authority/politics	"Oxidative stress"
Networks	No details
Insurers	No details

Degradable materials: nanoscale lipid compounds, biopolymers

Generally speaking the representatives of industry do not assume any negative mechanism of action for these materials. What is worth noting is the high proportion of responses from the cosmetics industry which are almost all uniform and very comprehensive. For many other substances the cosmetic industry had indicated that they were not used in their area and, therefore, they could not comment. Exceptions are nanoscale silicon dioxide, titanium dioxide and zinc oxide which were each rated as having "no elevated potential" or "low potential".

Table 20: Qualitative description of the mechanisms of action of nanoscale lipid compounds, biopolymers

Industry	"Already dissolve in the uppermost layer of the skin, hence no nanoparticles and no relevance for nano discussions" "Should not be deemed to be nanomaterials in my opinion as these are lipid structures which lose their form in the uppermost layer of the skin and merely serve as a transport vehicle for active ingredients" "Not toxic" "Are normally soluble or degradable in body fluids, no known toxicity, improved bioavailability because of smaller particle and droplet sizes" "Not nano – in my opinion these substances do not come under the definition nano. They are spherical arrangements of phospholipid layers which are similar in structure to the biological cell membranes. Liposomes and nanosomes are used to transport the special active ingredients which are encapsulated in these structures more easily into the skin" "Because of the degradability of these substance classes, cannot assume that they have a nanoform"
Science	"Mechanism of action not yet known" "Potential biologically active substances in degradation, activation of cellular defence"
NGO/trade union	"Mainly accumulation" "Inflammation in the lungs, vascular effects like thrombosis following intravenous administration", "liver effects, local radical oxygen species" "Only degradation products toxic"
Public authority/politics	"Moderate toxicity as free particles" "Oxidative stress"
Networks	No details
Insurers	No details

Nanotones/layered silicates

When it comes to the assessment of nanotones there are differences between the statements of scientists and representatives from networks concerning the question whether fine dust from glass fibres could be problematic. Otherwise, the already known mechanisms like oxidative stress and genotoxicity are listed. Generally speaking the assessment seems to go rather in the direction that, when it comes to the use of nanotones, the benefits outweigh the potential risks.

Table 21: Qualitative description of the mechanisms of action of nanotones/layered silicates

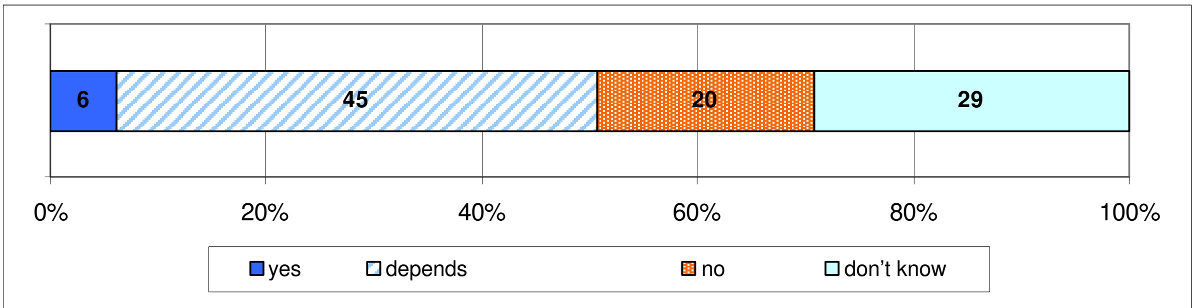
Industry	No further details
Science	"Expect no toxicity" "Non matrix-bound particles to be classified initially on precautionary grounds as risky; also some aggregated particles may be toxic" "Oxidative stress"
NGO/trade union	"Genotoxicity, radical formation, catalytic processes, cytotoxicity, accumulation, impairment of the mitochondria of amongst other things cellular organelles, membrane damage"
Public authority/politics	"Oxidative stress"
Networks	"Disruption of cellular metabolism" "Amongst other things fine dust from glass fibres"
Insurers	"Silicosis"

4.1.5 Factors for the carcinogenic effects of nanomaterials

The previous section already examined various mechanisms of action in detail. Mention was made particularly frequently of oxidative stress, inflammation processes and genotoxic effects as mechanisms of action for the toxic effect of nanomaterials. In this section a closer look is taken at another toxicological end point which hasn't been mentioned so far – the carcinogenicity of nanomaterials. This topic was presented to the experts in the following statement, "After inhalation nanoparticles have a carcinogenic effect".

Figure 8 clearly shows that only 6% of experts confirm this statement. 44.6% of respondents do not at least rule out a carcinogenic effect under certain conditions. 20% do not believe that the inhalation of nanoparticles has carcinogenic effects.

Fig. 8: Assessment of the statement: After inhalation nanoparticles have a carcinogenic effect (n= 65 responses)



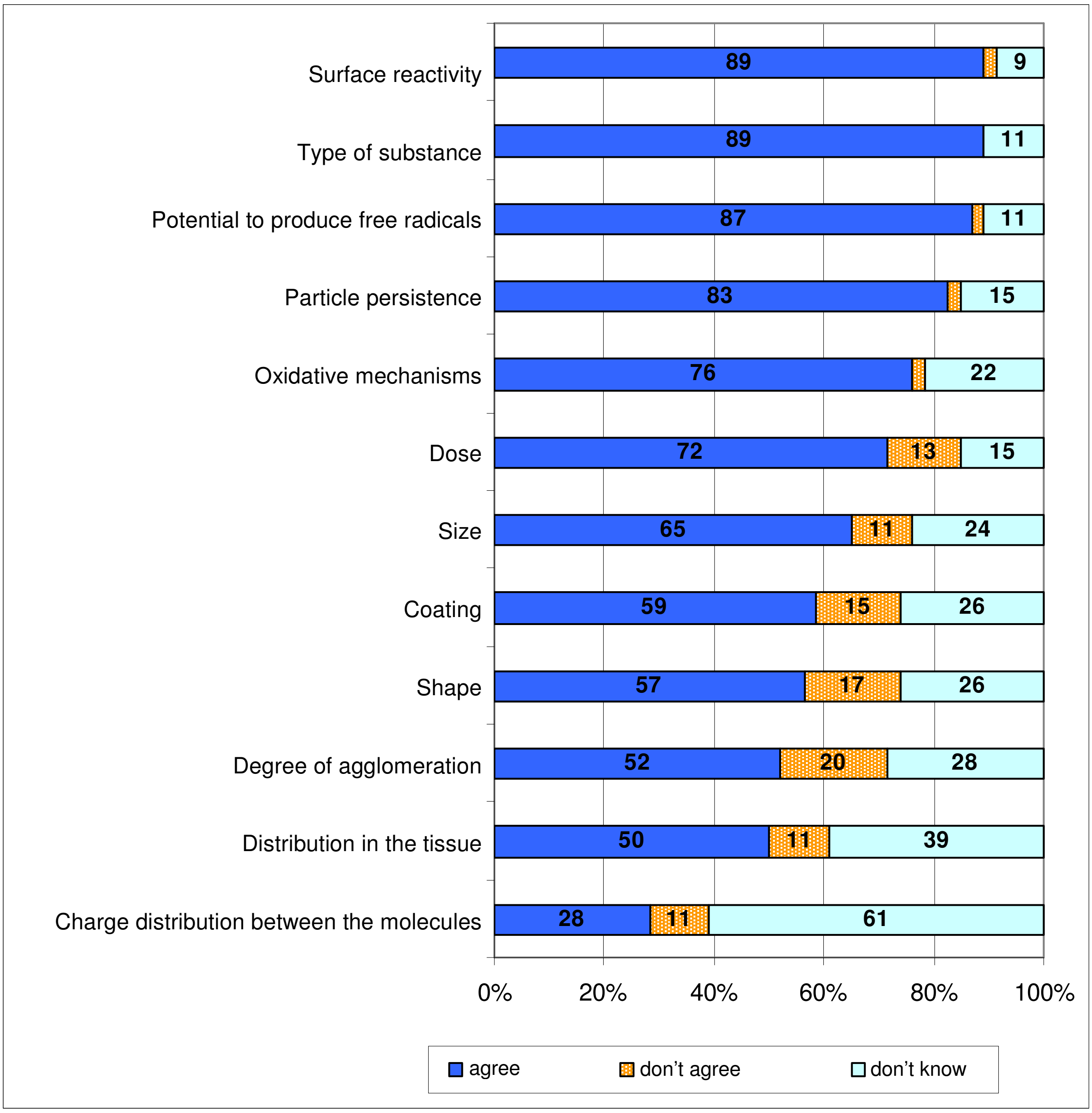
Explanation: percentages rounded up

The following statements give an indication of the various criteria on which the carcinogenic effect of nanomaterials could depend:

- Charge distribution between the molecules
- Distribution in tissue
- Degree of agglomeration
- Shape
- Coating
- Size
- Dose
- Oxidative mechanisms
- Persistence of particles
- Potential to produce free radicals
- Type of substance
- Surface reactivity

These criteria were again assessed by the experts in survey Round 2. The results show that experts mainly regard the surface reactivity of nanomaterials, the type of the respective substance, the potential to produce free radicals, and the persistence of nanoparticles as the main causes of the carcinogenic effects of nanomaterials.(Fig. 9).

Fig. 9: Dependency factors for carcinogenic effects of nanomaterials (n= 46 responses)



Explanation: percentages rounded up

The comments generally went in the direction that nanomaterials do not have any specific carcinogenicity or that the assumption was wrong that nanoparticles had a general carcinogenicity. It was far more the case that carcinogenicity would have to be examined for each specific substance. Reference was also made to the results of a study (Warheit *et al*. 2006) which did not show any correlation with particle size (nano/micro) in conjunction with the inhalation toxicity of quartz sand.

The comments on the question about the dependency factors for carcinogenicity do not reveal significant stakeholder-specific differences. Regarding surface reactivity it was noted that this was possible for instance for TiO_2 but had not yet been proven. One possible cause of chronic inflammation was the reaction with molecules triggered by surface reactivity. A link was seen, in principle, between carcinogenicity and the potential to produce free radicals, too. What was decisive in this context was, however, the concentration of radical forms as well as the site of their formation.

The importance of the substance for possible carcinogenic effects is a subject on which the experts' opinions partly differ. Some of the respondents indicate that not every nanoscale substance has carcinogenic potential. For instance, titanium dioxide and zinc oxide do not have any carcinogenic effects. Another respondent points out that each nanosubstance with a particle size < 70 nm is potentially carcinogenic. The comments regarding the persistence of particles state that at least the particles which remain on the uppermost level of the skin do not have any carcinogenic potential. Furthermore, persistence was only relevant in the case of soluble particles when it comes to quantity. Moreover, it is pointed out that the persistence of particles had already been proven in animals. This was the starting point for chronic inflammation and carcinomas. It is also noted that persistence did increase the duration of exposure but that this was not a condition for carcinogenicity.

In respect of the dose it was repeatedly pointed out that this is not responsible in all cases for carcinogenic effects. What should be taken into account here was, for instance, the substance-dependent threshold of action. On the other hand, it was noted that the dose played a role for each toxic effect. Differentiated consideration was also called for regarding the importance of coating. Firstly, it is pointed out stability is relevant: the more stable the coating, the less carcinogenic it was. On the other hand, a different coating did not necessarily lead to major differences in effect. Nanoscale titanium dioxides, for instance, behaved in a very similar manner despite different coatings on the skin or in their localisation.

4.2 Exposure

In science a distinction is made between the terms “hazard” and “risk”. In this context “risk” means a combination of the scale and probable occurrence of damage. What is decisive here is the weighting of the potential scale of damage against the probability of exposure and related damage. It is assumed that the use of nanomaterials in consumer products will lead to growing consumer exposure. Furthermore, exposure is possible via water, soil and air when nanomaterials reach these environmental compartments. From the angel of consumer health protection knowledge about the occurrence of nanomaterials in household products (articles, products as well as preparations) is of interest. It would, therefore, be helpful to have sufficient documentation and characterisation of the use of nanomaterials in consumer products. Against this background it is recommended including exposure as a selection criterion for toxicological tests. Nanomaterials with high exposure potential should be given priority in this identification and characterisation work.

4.2.1 Consumption of nanomaterials

In order to describe a risk information is needed, for instance, on the scale on which people come into contact with the nanomaterials. If no such information is available, the consumption of nanomaterials can be used as an estimated parameter. In this context the experts were asked to estimate the development of the consumption of various nanomaterials up to 2015:

> *“The global consumption of nanomaterials in 2001 and 2006 is presented in the table below (Haas, K.-H. et al. 2003). How do you see the future development in the product categories listed up to 2015? Please rate the development for 2015 in the drop-down list.”*

Table 22: Global consumption of nanomaterials [according to Haas, *et al*. 2003][2]

Products/materials	2001 in mass (1000 t)	2001 in value ($ million)	2006 in value ($ million)
Metals	1–2	35–70	approx. 200
Al nanocoatings	1.7	193	252
SiO_2 Classical (µm scale) Pure nanostructures	 (540) 370	 (840) 1200	 (930) 1600
Metal oxides (Al, Zr, Zn, Ti, Fe) Pyrolytic Wet-chemical	 4.5 190	 100 1300	 >200 1850
Effect pigments	15	400	500
Nanotones/layered silicates Polymer nanocomposites	0.2 4	1.5 15	25 300
Carbon: Fullerenes, nanotubes. nanofibres	 <0.1	 approx. 5	 25–70
Organic materials: Dendrimeric, highly branched polymers POSS*	<<	<1	5–15
Total	**> 580**	**> 3100**	**> 4400**

Comments:
* **POSS** = **P**olyhedral **O**ligomeric **S**il **S**esquioxane -
The values in () are not included in the aggregate value "total" as the nanoproperty of the respective nanomaterial can no longer be detected in the end product. The product characteristics no longer depend on specific nanoquality and can be achieved without any nanomaterial.

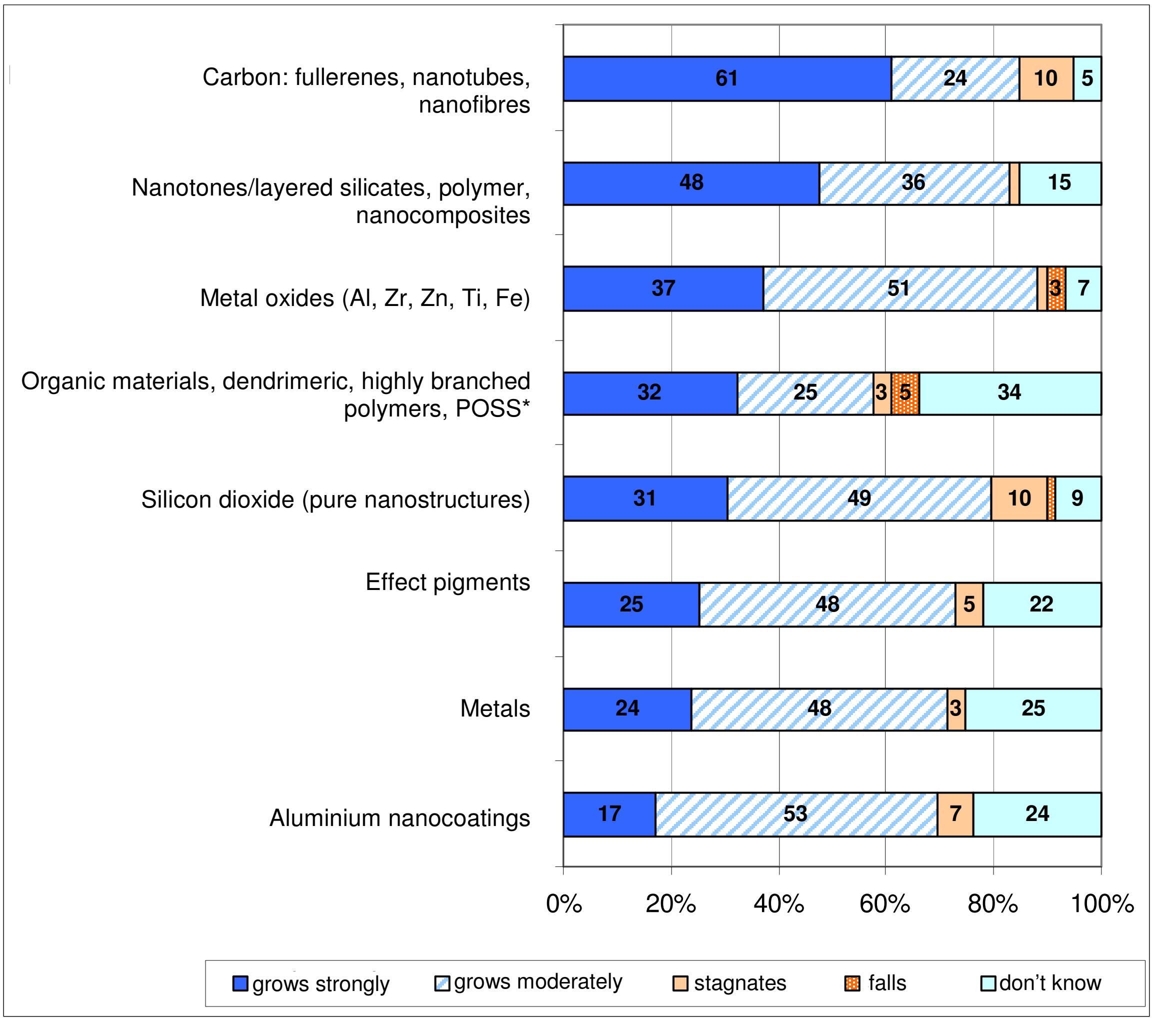
The goal of this question was to establish for which nanomaterials experts expect particularly high consumption. Based on the current consumption figures the first estimation can be made about the possible exposure of consumers to nanomaterials.

The majority of the experts forecast a moderate to major increase in consumption for all nanomaterials (see Fig. 10).

Carbons (fullerenes, nanotubes, nanofibres, nanotones/layered silicates, metal oxides) are seen as the materials which are likely to chalk up the highest increase in consumption. The lowest growth rate is expected for metals, aluminium, nanocoatings and dye pigments. This estimation can only be interpreted as an approximation. In their comments the experts point out the lack of a database and the problems involved in classifying individual applications in the groups covered. Regarding the rating of carbons as the material with the highest expected growth rate, it should be borne in mind that the volumes currently produced in Germany are too low according to comments by a few experts. Hence they should be treated with caution particularly as the carbon compounds in the further course of the Delphi study rank amongst the materials viewed critically.

[2] Haas, K.-H.; Hutter, F.; Warnke, P.; Wengel, J.: (2003)Produktion von und mit Nanopartikeln – Untersuchung des Forschungs- und Handlungsbedarfes für die industrielle Produktion. Gefördert durch BMBF Förderkennzeichen: 02PH 2107, Projektträger PTF. Würzburg July 2003.

Fig. 10: Estimated consumption of nanomaterials in the world (n= 59 responses)



Explanation: percentages rounded up

4.2.2 Exposure pathway

In principle, there may be exposure to nanomaterials via the dermal, oral and inhalation pathways. Dermal exposure is possible to cosmetics or correspondingly treated textiles. Nanomaterials in cosmetic formulations may also influence the penetration of other ingredients. The use of nanoscale titanium dioxide and nanoscale zinc oxide as UV filters in sunscreens has been common knowledge for some time now. Not enough information is available at the present time about other nanomaterials in cosmetics or other articles of daily use that come into contact with the skin or the mucosa. Oral exposure could result in the consumption of foods containing nanomaterials. It may, however, also occur when nanomaterials migrate from packaging material to food. In this context, beside the need for information about food and packaging materials of this kind, there is a need for research on the question of absorption in the intestinal tract, the related systemic availability, possible accumulation in specific compartments of organs and the migration behaviour of various nanomaterials from food packaging. Inhalational exposure occurs, for instance, when aerosols are used in the home. Just how unreliable information on exposure can be was shown by the case of a "nano" sealing spray whose use led to severe lung diseases. In the end it turned out that the "nanoproduct" did not, in fact, contain any nanomaterials (BfR 2006).

This section, therefore, aims to examine the importance attributed to the various exposure pathways by experts for negative health effects. The aim here was to obtain some indication whether specific nanomaterials could be expected to have a negative effect on health in general or only via certain exposure pathways. The experts were asked to choose between the categories “no importance”, “minor importance”, “average importance” and “high importance”. The selection of the two last categories was seen as an indication that the experts attribute negative health effects to this exposure pathway in the case of a concrete nanomaterial.

Table 13 gives the number of mentions in descending order. To improve transparency of the findings the values indicating “average” or “high” importance of the ingestion pathway for negative health effects have been added together and listed for the respected exposure pathway.

The result was that high values were obtained for the inhalation exposure pathway. The oral or dermal exposure pathway only seems to be relevant for a few nanomaterials like, for instance, chromium(III)-oxide or nickel oxide. However, this has less to do with the fact that experts think that these substances will have negative health effects from exposure to nanoparticles. It is far more the case that chromium(III)-oxide and nickel oxide are substances with high inherent toxicity irrespective of the exposure pathway or particle size.

The responses on exposure pathways were supplemented with comments by 54% of the respondents. They mainly pointed out that, in many cases, inhalational exposure to nanomaterials is only possible during processing. Corresponding health and safety measures had already been taken according to industry. Various stakeholders pointed out that exposure did not automatically mean “adverse effects”. In this context it was also explained that agglomerates frequently occur instead of nanoparticles. Furthermore, it was noted that in the case of nanoscale organic dye pigments toxicity is dependent on the respective individual substances. It was likewise confirmed that inorganic dye pigments, chromates and cadmium pigments are expected to have negative health effects for all exposure pathways. The comment was also made that the toxicity of most of the materials listed here is currently being examined in research projects with standardised measurement methods.

Substances which were attributed negative health effects in the first survey round by at least one-third of experts for the inhalational, oral and dermal pathways, were reviewed once again in Round 2. The second round of questions with exactly the same questions is a typical methodological component of Delphi surveys aiming to test the robustness of the evaluations. Table 24 from Round 2 shows that the stakeholder assessments for all substances tend to go in the same direction as in Round 1. The result is that the inhalation of nanomaterials is seen as the exposure pathway which is expected to have the biggest health effects.

Table 23: Attribution of negative health effects to various exposure pathways in Round 1. The percentages in the columns refer to the number of experts (n) who expect negative health effects from nanomaterials for the respective exposure pathway

Substances with negative health impact/exposure pathway				
Nanomaterials	n	oral (%)	dermal (%)	inhalational (%)
Silicon dioxide	46	12.5	4.2	79.2
Titanium dioxide	45	17.8	24.4	82.8
Carbon nanotubes	45	33.3	22.2	88.9
Zinc oxide	44	20.5	25.0	79.5
Fullerenes	41	36.6	43.9	78.0
Aluminium oxide	40	17.5	15.0	70.0
Iron oxide	38	15.8	2.6	76.3
Silver	36	36.1	27.8	63.9
Vitamins	36	47.2	16.7	30.6
Nickel oxide	35	60.0	48.6	65.7
Inorganic dye pigments	34	20.6	32.4	70.6
Nanocomposites	34	11.8	11.8	52.9
Degradable materials (lipid compounds, biopolymers)	34	35.3	20.6	26.5
Chromium(III)-oxide	33	51.5	39.4	84.8
Silicates	32	9.4	6.3	75.0
Organic dye pigments	31	32.3	41.9	77.4
Nanotones/layered silicates	30	16.7	10.0	53.3
Polymers	29	17.2	17.2	58.6

Explanation: percentages rounded up

Table 24: Attribution of negative health effects to various exposure pathways in Round 2. The percentages in the columns refer to the number of experts (n) who expect negative health effects from nanomaterials for the respective exposure pathway.

Substances with negative health impact/exposure pathway				
Nanomaterials	n	oral (%)	dermal (%)	inhalational (%)
Carbon nanotubes	37	40.5	35.1	91.9
Fullerenes	31	51.6	51.6	96.8
Silver	33	36.4	39.4	63.6
Vitamins	33	36.4	15.2	18.2
Nickel oxide	31	51.6	80.6	71.0
Degradable materials (lipid compounds, biopolymers)	32	28.1	18.8	28.1
Chromium(III)-oxide	30	60.0	50.0	80.0
Organic dye pigments	23	34.8	43.5	60.9

Explanation: percentages rounded up

The individual exposure pathways are examined in more detail below in the sequence oral, dermal and inhalational on the basis of selected comments.

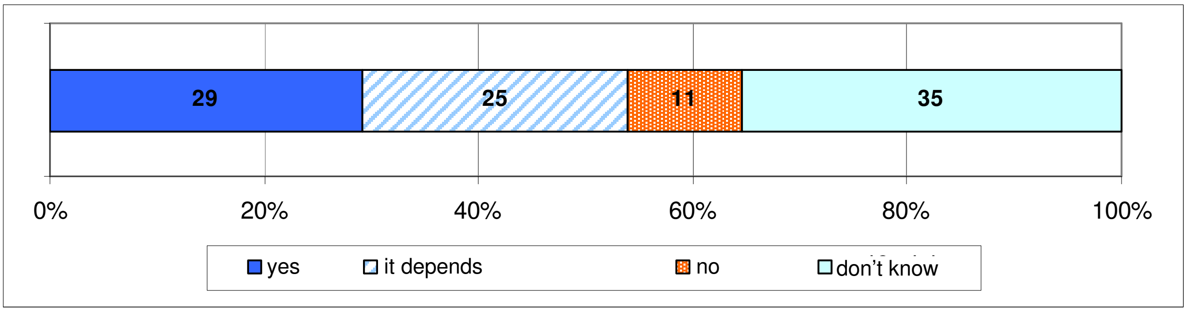
4.2.3 Oral exposure pathway

This section and the following one contain statements on the various exposure pathways that were submitted to the experts for assessment. The response categories were "yes", "no", "it depends" and don't know". In Round 1 the statements were commented on in detail by all stakeholder groups. Based on these comments the questions from the first survey round were in some cases adjusted and resubmitted in Round 2.

A first theory concerned the question whether the oral intake of nanoparticles leads to systemic exposure of the organism. Just under one-third of the respondents agreed with this theory, 11% rejected it (Fig. 11). What is noticeable is the high proportion of respondents who chose the categories "it depends" or "don't know". Hence there is no clear assessment trend on this statement.

In the opinion of the experts the intake of nanoparticles via the intestines leads to systemic exposure of the organism. However this did not apply to the oral intake of nanoscale vitamins or carotinoid formulations. Furthermore, substance, size, surface chemistry, material and coating, charge and solubility would have to be included in the evaluation of systemic exposure. Other experts point out that the intake threshold of nanoparticles was higher in the case of oral exposure than for inhalation.

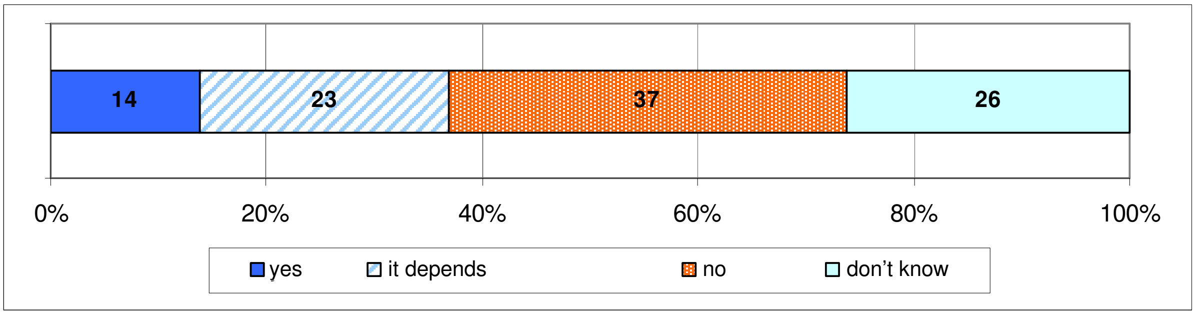
Fig. 11: Evaluation of the theory: the oral intake of nanoparticles leads to systemic exposure of the organism (n= 65 responses)



Explanation: percentages rounded up

The next theory "Metallic nanoparticles are not ingested by the body via the gastrointestinal tract" was rejected by more than one-third of experts. Only 13.8% of the respondents supported the theory (Fig. 12). The experts referred to the specific properties of nanomaterials and the fact that general statements were again difficult. It depended far more on surface chemistry, charge and solubility. Some experts added that it was unlikely that metallic nanoparticles would not be absorbed at all and that this depended far more on the dose which was determined, in turn, by the properties of the nanoparticles. Furthermore, it was noted that if the nanoparticles are soluble in gastric acid, these substances could reach other areas too. In the case of insoluble nanoparticles intake was – similar to that in the lungs – a question of the condition of the membranes. The active role of the intestinal walls would have to be taken into account as for instance Hg^{2+}, Ag^{+}, Cd^{2+} would be absorbed.

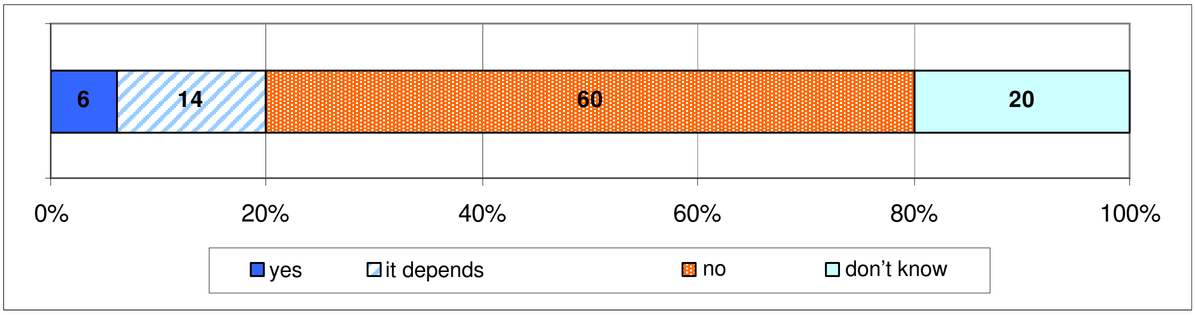
Fig. 12: Assessment of the statement: Metallic nanoparticles are not ingested via the gastrointestinal tract (n= 65 responses)



Explanation: percentages rounded up

A third theory that nanoparticles need specific receptors in order to be ingested at all was rejected by almost two-thirds of the experts (Fig. 13). For instance, nanoscale vitamins and carotinoid formulations didn't need specific receptors in order to be ingested. Nanoparticles could also form complexes with other biomolecules that assume a vehicle function. In principle, no general statements were possible here as the potential intake pathways of nanoparticles in cells had not been sufficiently elucidated.

Fig. 13: Evaluation of the theory: Nanoparticles need specific receptors in order to be ingested at all (n= 65 responses)

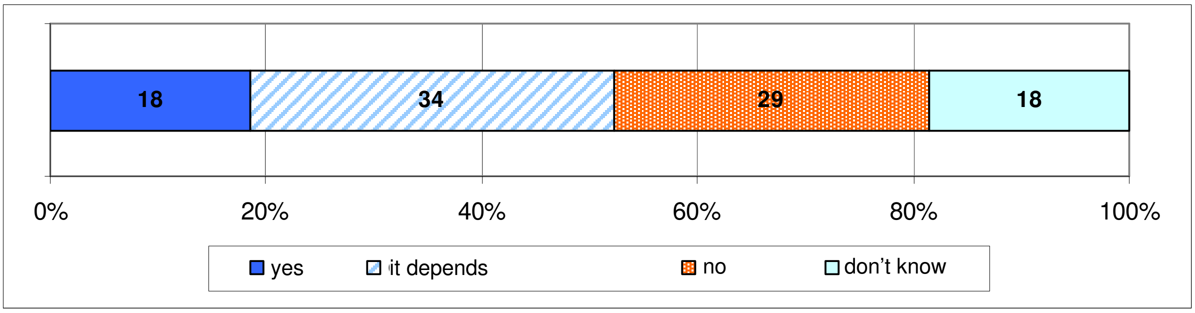


Explanation: percentages rounded up

4.2.4 Dermal exposure pathway

The experts did not make any clear comments on the first theory from the section on dermal exposure that nanoparticles can cross through the skin and cause systemic exposure of the organism. 29% of the respondents rejected this theory but 34% felt that this required specific consideration (Fig. 14). On the one hand it was pointed out that scientific studies with nanoscale titanium dioxide and zinc oxide confirm that nanoparticles do not penetrate the skin. However, attention was also drawn to the cavities in the skin layers, hair roots and perspiration glands where systemic exposure was possible. Furthermore, very small TiO_2 particles were similar in size to biomolecules and proteins that can penetrate the skin. Hence it was important to examine this theory from the scientific angle.

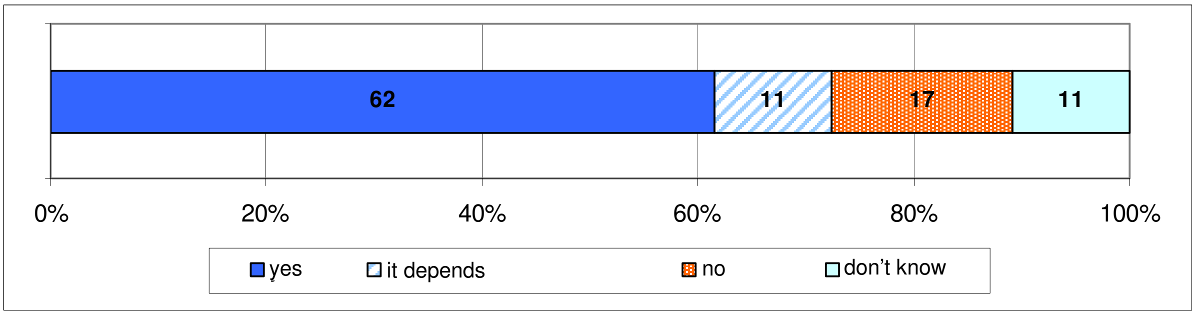
Fig. 14: Evaluation of the theory: Nanoparticles can cross through the skin and cause systemic exposure of the organism (n= 65 responses)



Explanation: percentages rounded up

This unclear result was addressed in more detail in the next theories. The theory "The skin is mainly impermeable to nanoparticles if it can assume its protective function and is free from damage or strong mechanical strain" was confirmed by almost two-thirds of the experts (Fig. 15). Some comments by the respondents did, however, point out that the possibility of skin penetration by nanoparticles was dependent on their size, chemical composition and surface condition, that allergic reactions were possible, and that further contributory factors like perspiration glands should be taken into account. Furthermore, it was stated that so far there was no evidence that "damaged" skin was more easily penetrated by nanoparticles than healthy skin. This comment was confirmed at the expert workshop. Moreover, it was stated that nanoparticles could bind to specific skin-permeable biomolecules and/or proteins with whose help they could then penetrate the skin.

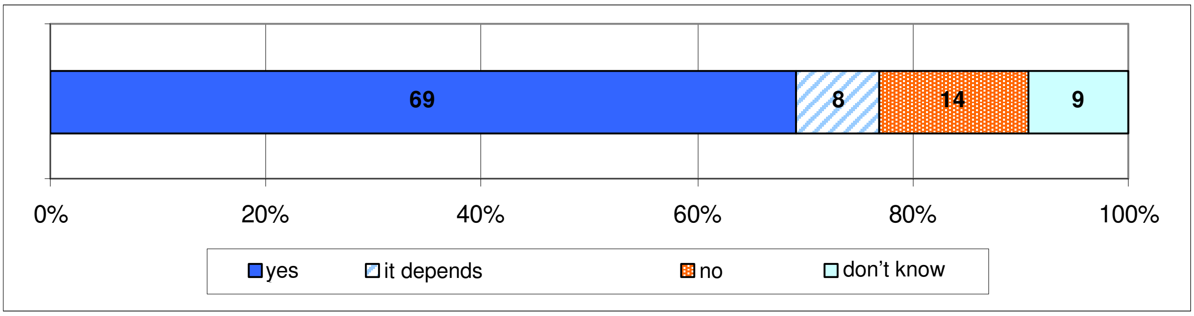
Fig. 15: Evaluation of the theory: The skin is largely impenetrable for nanoparticles when it can assume its protective function and is free of damage or strong mechanical strain (n= 65 responses)



Explanation: percentages rounded up

A second theory contained a counter-claim. The theory was "The protective function is probably impaired in the case of skin injuries, strong mechanical strain and very small nanoparticles" (< 5–10 nm). Once again almost two-thirds of the experts agreed with this theory (Fig. 16). Although, at the present time, no robust scientific findings are available on this topic, a clear majority of the respondents believe that when the protective function of the skin is no longer intact, nanoparticles could also reach the organism.

Fig. 16: Evaluation of the theory: The protective function is probably impaired in the case of skin injuries, strong mechanical strain and very small nanoparticles (< 5–10 nm) (n=65 responses)



Explanation: percentages rounded up

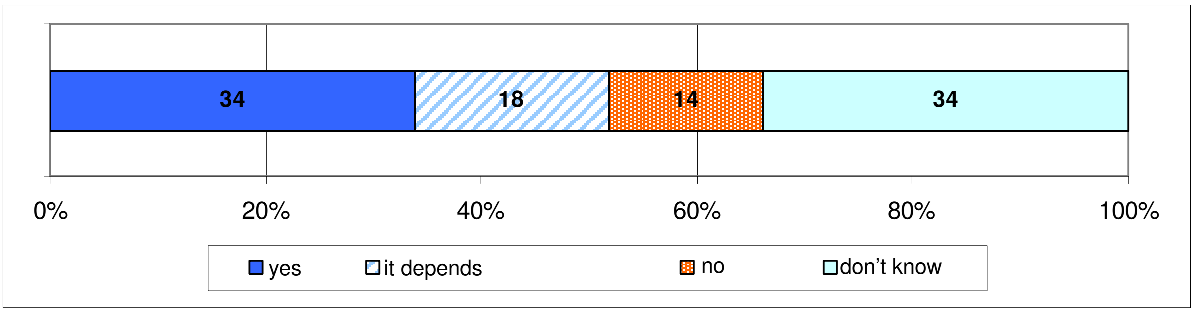
Some comments pointed out that the formulation of this theory was not clear. For the second round of the Delphi survey two new theories were, therefore, developed:

a) Do you expect contact between nanomaterials and stressed skin to have a negative health effect which can be attributed to the nanoscale of the substances?

b) Do you expect contact between very small nanoparticles (<5–10 nm) and healthy skin to have negative health effects?

The responses to the first new theory merely indicate a trend. Only one-third of the experts expect negative health effects to result from contact between stressed skin and nanomaterials and these effects to be linked to the nanoscale of the substances (Fig. 17). In the comments it was pointed out that no increase in skin permeability was to be expected as long as the horny layer is intact. Nanoscale titanium dioxide and zinc oxide were also deemed to be unproblematic in the case of UV-stressed skin. However, it was pointed out that if systemically available nanomaterials show a negative health effect, the probability that these effects could be observed after skin contact with these nanomaterials was higher. This is because damaged skin is more permeable than intact skin. Referring to the results of the European research project "NanoDerm", it was pointed out that "nanoparticles can also reach deeper layers of the skin when the vital dermis is injured". General statements on negative health effect were not, however, possible as the nanoscale alone cannot be deemed to be the cause of a negative effect.

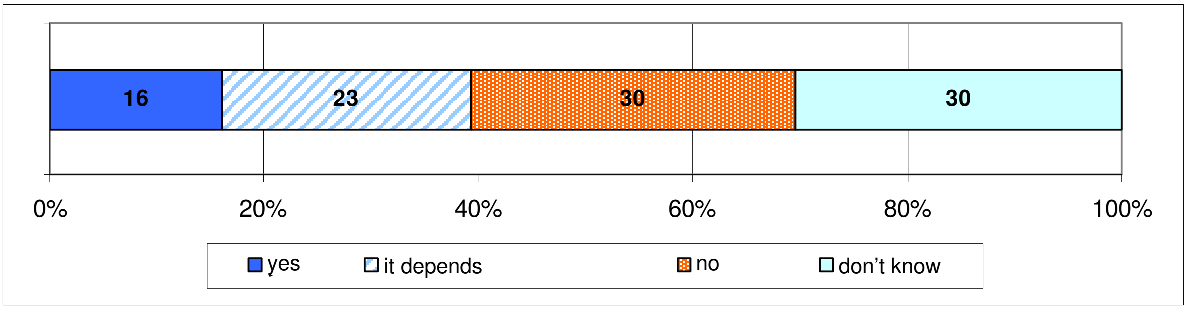
Fig. 17: Evaluation of the theory: Do you expect negative health effects from contact between nanomaterials and stressed skin which can be attributed to the nanoscale of the substance? (n=56 responses)



Explanation: percentages were rounded up

Regarding the assessment of the negative health effects of contact with very small nanoparticles on the skin, the majority pointed out that negative health effects are rather dependent on substance and particle size. One-third of the respondents rejected the theory, "Do you expect negative health effects from contact between very small nanoparticles (<5-10 nm) and healthy skin?" (Fig. 18). One expert did, however, comment that the smaller the nanoparticles were, the more easily they could pass through the membrane barriers. Furthermore, it should be borne in mind that the surface modification of nanoparticles can change skin permeability.

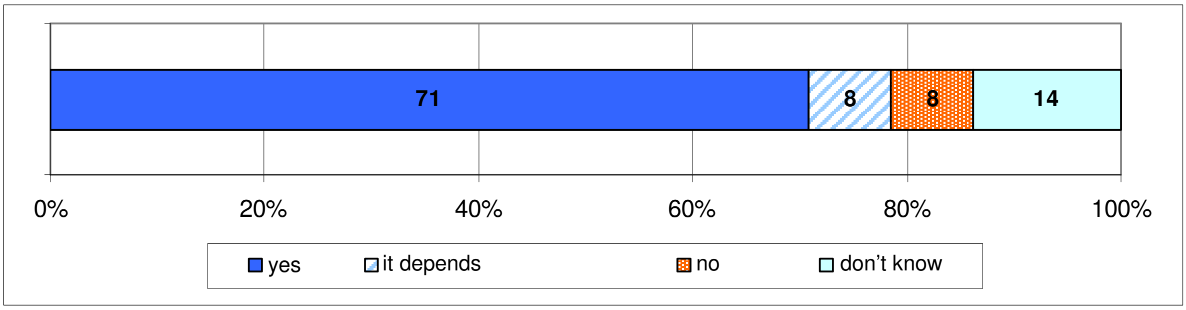
Fig. 18: Evaluation of the theory: Do you expect negative health effects from contact between very small nanoparticles (<5-10 nm) and healthy skin? (n=56 responses)



Explanation: percentages rounded up

Another theory on dermal exposure was clearly supported. More than two-thirds of the experts were of the opinion that manual activities involving dust-shaped or suspended particles can lead to dermal exposure and that dermal exposure remains low when the nanoparticles are embedded in a solid matrix (Fig. 19). However the comment was made that this question could only be answered by means of long-term trials. So far very few findings were available on the migration of nanoparticles. It was also pointed out that the decisive factor was how strongly the particles are embedded in the matrix and that the duration of exposure was relevant too.

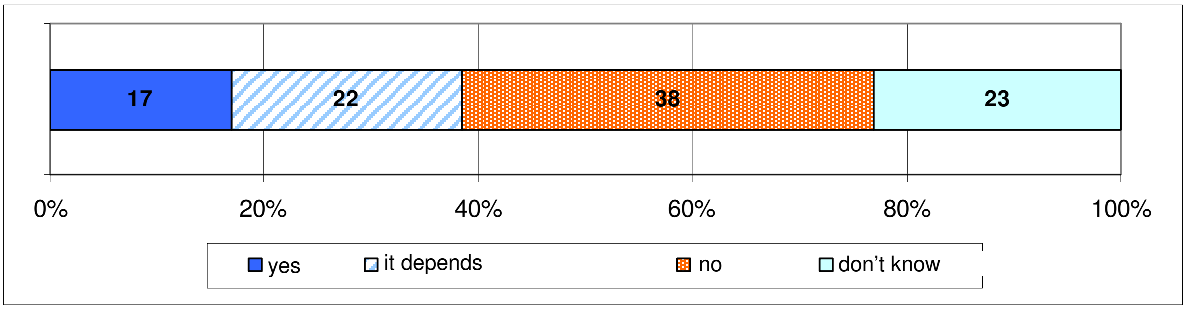
Fig. 19: Evaluation of the theory: Dermal exposure results, amongst other things, from manual activities involving dust-shaped or suspended particles. If the nanoparticles are embedded in a solid matrix, skin exposure is low (n=65 responses)



Explanation: percentages rounded up

The next theory presented to the experts was, “Liposomes cannot pass the intact horny layer nor can they improve the intake of active ingredients”. This theory was rejected by 38.5% of the respondents (Fig.20). Various experts commented that the composition of liposomal preparations could indeed influence the penetration behaviour of active substances. In the opinion of the experts liposomes improve the intake of active ingredients but do not pass the horny layer; they merely serve as a transport vehicle for active ingredients.

Fig. 20: Evaluation of the theory: Liposomes cannot pass the intact horny layer nor can they improve the intake of active ingredients (n=65 responses)



Explanation: percentages rounded up

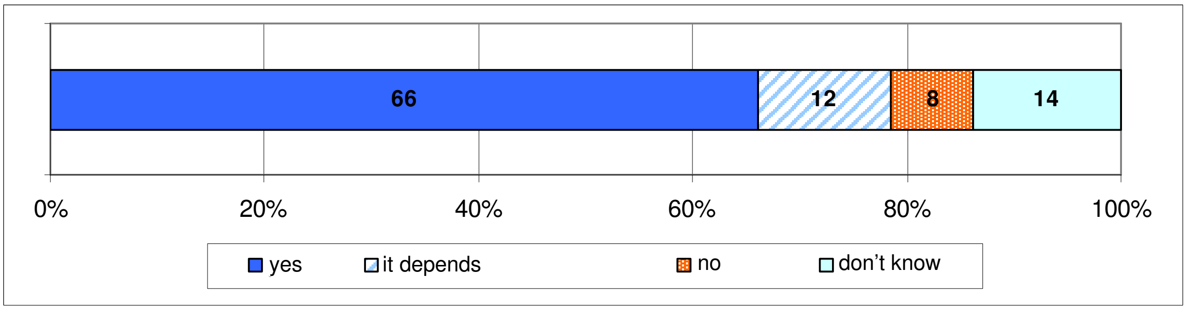
As the liposome theory was not clearly formulated, it was broken down into two parts and resubmitted in the second Delphi round. The two new theories were:

a) Can liposomes pass the intact horny layer?
b) Do they improve the intake of active ingredients?

The new wording did not produce any additional findings. In Round 2 most of the experts said that they had no knowledge of this topic. 58.9% for theory a) and 57.1% for theory b) selected the option "don't know" (n=56).

The next theory, "Nanoscale TiO_2 protects the skin from genotoxic and carcinogenic effects of UV light" was supported by two-thirds of the experts (Fig. 21). Nanoscale titanium dioxide in sunscreen formulations increases light protection and has, therefore, an anti-carcinogenic effect. A genotoxic effect of UV light as suggested in this theory, is however, deemed to be unlikely by the experts. There were also comments which indicate that UV absorption through nanomaterials did take place but that on the other hand TiO_2 itself had a genotoxic and carcinogenic impact.

Fig. 21: Evaluation of the theory: Nanoscale TiO_2 protects the skin from genotoxic and carcinogenic effects of UV light (n= 65 responses)



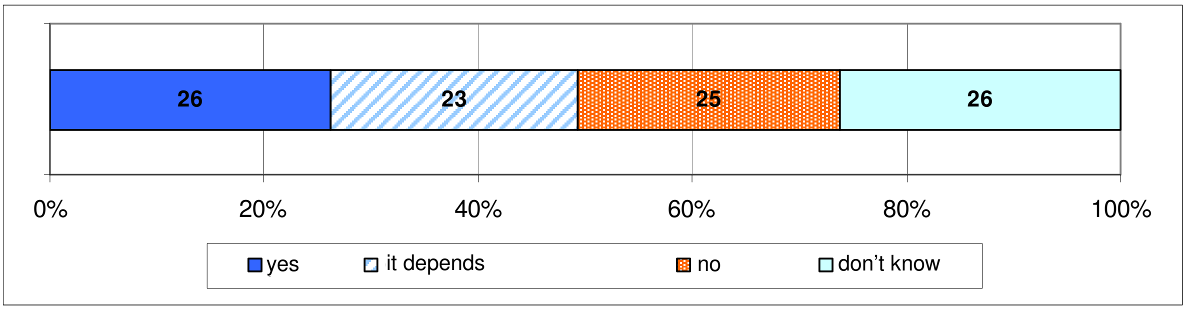
Explanation: percentages rounded up

4.2.5 Inhalational exposure pathway

In the section on the assessment of various exposure pathways, the inhalational exposure pathway was identified as the one for which most experts expected negative effects on human health. This result is discussed below in more detail in conjunction with two further theories.

The first theory was, "Inhaled nanoparticles are systemically ingested and influence the cardiovascular system and the brain". One-quarter of respondents confirmed but one-quarter rejected the theory (Fig. 22). As it depends on the substance and type of coating of the nanoparticles, no general statements can be made according to the experts. Considerations would have to be undertaken on a case-by-case basis. This theory would then have to be examined for each individual material and size category. First studies do, however, indicate that inhaled nanoparticles were systemically ingested and influenced the cardiovascular system and the brain (Li *et al* 2007; Kwon *et al* 2008).

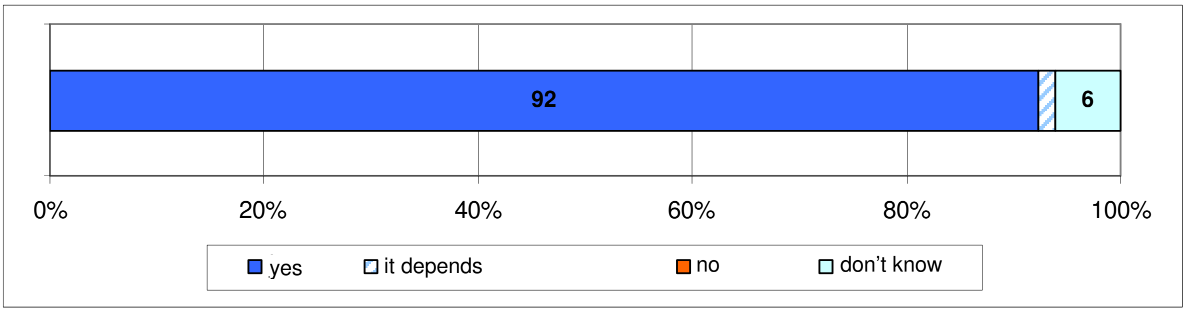
Fig. 22: Evaluation of the theory: Inhaled nanoparticles are systemically ingested and influence the cardiovascular system and the brain (n= 65 responses)



Explanation: percentages rounded up

In contrast, there was major agreement amongst the experts about the second theory regarding the inhalational exposure pathway. 92 % of respondents agreed with the theory that inhalational exposure could be considerably reduced when nanoparticles were embedded in a solid matrix or in a liquid suspension (Fig. 23). In the opinion of some experts, however, the life cycle of nanomaterials would have to be taken into account as through aging and degradation processes nanoparticles could possibly leach out from the matrix.

Fig. 23: Evaluation of the theory: The use of particles in a non-dust form or in a liquid suspension (solid in liquid) that is not sprayed as well as the embedding of particles in a solid matrix (solid in solid) can considerably reduce inhalational exposure (n=65 responses)



Explanation: percentages rounded up

4.2.6 Recommendations for health and safety at work

The exposure chapter has clearly shown that inhalational exposure should be avoided for precautionary reasons. Here the main emphasis is on exposure avoidance strategies and concrete protection measures. This also applies to dermal and oral exposure. At the expert workshop concrete instructions were elaborated for health and safety at work. The experts formulated the following recommendations:

Avoidance of inhalational exposure

- The reduction of inhalational exposure to the level of background exposure is recommended if adequate toxicological data are not available.
- Closed systems should be used for flame processes in order to avoid any exposure in principle. Where appropriate, local aspiration is to be provided.
- System limits in the case of closed systems are to undergo critical examination (question of indoor ventilation): exposure to nanoparticles is possible when filters are changed. Here a case-by-case examination is recommended in order to establish which protective measures are needed.
- Filter systems are normally surface filters: because of the high diffuseness nanoparticles can easily separate. First studies on NaCl are available which demonstrate that filters can effectively separate nanoparticles. These studies must now be conducted for the common nanoparticles. Separation rates and standing times should be examined.

Avoidance of dermal exposure

- If precipitation reactions in solutions are used, dermal exposure through gloves is to be avoided. If solvents do not penetrate the gloves, then it can be assumed that dispersed/suspended nanoparticles in the solvent will not penetrate either.

Further measures

- At all events a workplace area analysis is to be conducted to establish any necessary local protective arrangements and personal protection measures (dust mask down to full body suit).
- Protection concepts are intended for technical facilities which work with toxic materials and gases.

Measurements

- A targeted workplace area analysis is dependent on measurements of exposure. The measurement technology for nanomaterials is currently being developed. The question is how long work can continue using standard measures or whether protective measures must be taken in line with the precautionary principle. The experts urgently recommend the continuation of the dialogues that have been initiated.
- Measurement methods for nanomaterials must be harmonised and standardised on the international level. This process should be stepped up.
- Stationary measurements depending on use are deemed to be advisable.

Limit values

- New limit values may have to be elaborated for handling nanomaterials – normally the general dust limit values apply. There is a need to re-examine this; the experts see a need for research on this topic.

Communication

- The communication between suppliers and processors concerning the possibilities of workplace assessment and, where appropriate, the necessary protective measures should be improved.

- What is seen as problematic is above all dealing with the lack of knowledge amongst employers and employees. This is where experts see a major need for information and for a coordinated communication strategy between companies, associations, trade unions, employers' liability insurance associations and public authorities.
- The findings from research and science should be passed on in a more targeted manor to the stakeholders. Events for the exchange of knowledge between the stakeholders should definitely be continued.

4.3 Conclusion on the risks of nanomaterials

Hazard

- The assessment by the experts of the toxicity of nanomaterials did not supply a clear picture. At the current time no meaningful risk assessment is possible on the basis of critical, easily identifiable factors like for instance size, shape or solubility.
- For each application context a specific database must be established before a coherent description of toxicity potentials and mechanisms of action can be given. To this end 18 factors were elaborated which must be used to assess nanomaterials in the concrete application context.
- Based on the results there is a clear tendency for airborne nanomaterials to be assigned high toxic potential far more frequently than in all other aggregate states.
- Oxidative stress, inflammation processes and genotoxic effects were described as the most important mechanisms of action for the toxic effects of nanomaterials.
- The possible carcinogenicity of nanomaterials is linked above all to surface reactivity, the type of nanosubstance, its potential to produce free radicals and the persistence of nanomaterials.

Exposure

- Experts expect to see a moderate to major increase in the consumption of nanomaterials which means that, in future, employees and consumers are likely to be exposed more to nanomaterials. The market for carbon-based nanomaterials and nanocomposites is seen as being particularly dynamic.
- In the opinion of experts the inhalational exposure pathway is the most critical one. This is where negative health effects resulting from exposure to nanomaterials are most likely. However, employees are the most probable group who will be affected by inhalational exposure. Here corresponding health and safety measures need to be taken.
- In the case of the oral intake of nanoparticles at least some of the experts assume that there was systemic exposure of the organism. The theory that metal nanoparticles can be ingested by the organisation is not rejected either. Far more it is assumed that no specific receptors were necessary in order for nanoparticles to be ingested via the gastrointestinal tract.
- The protective function of healthy skin against exposure to nanoparticles is confirmed by the majority. Even in the case of very small nanoparticles a majority of the experts feel that nanoparticles cannot reach the organism through the skin. A majority of the experts likewise believe that injured skin has an impaired protective function. If nanomaterials are embedded in a solid matrix, most of the experts expect low skin exposure.
- Overall the experts warn against general statements and advocate case-by-case consideration.

5 Nanoproducts

New findings from nanotechnology are increasingly being used to optimise existing products but also to open up completely new product segments. In the area of the environment nanotechnological developments can lead, for instance, to more careful use of resources, to improvements in the efficiency of energy production systems and more high performance filter systems for air, water and soil purification. In the area of medicine new diagnosis and therapy methods are appearing on the horizon. It is expected that diagnosis will be possible at an earlier stage, prevention and treatment methods used in a more targeted manor and methods rendered more patient-friendly. Furthermore, nanotechnology has already entered our daily lives. Nanotechnology plays a role in a large number of new product ideas whether they are self-cleansing ceramic surfaces or nano-impregnated clothing which offers effective UV protection. At the present time around 600 products are available on the market that contain nanomaterials (cf. Woodrow Wilson International Centre for Scholars 2007) and others are currently in the development phase. Market forecasts estimate sales revenues of between US$ 700 to 800 billion a year (Hullmann 2006; VDI Technologiezentrum 2004).

This chapter looks at the concrete applications of nanotechnology in the areas of surfaces, textiles, cosmetics and food. The first part of this chapter examines the economic importance of nanoproducts. The second looks at possible negative health effects which may be caused by nanoproducts and the third examines consumer acceptance of nanoproducts. Moreover, questions are asked about other elements which should be used to assess the risks of nanoproducts. The application examples were compiled on the basis of the BfR Expert Meeting “Nanotechnologies – Use, Trends and Risks”, a review of scientific and general interest journals and several expert interviews. The selection was made on the basis of an equal number of current and future applications. Examples of applications which are already on the market were generalised and formulated without mentioning any company or product names.

5.1 Economic importance of nanotechnologies

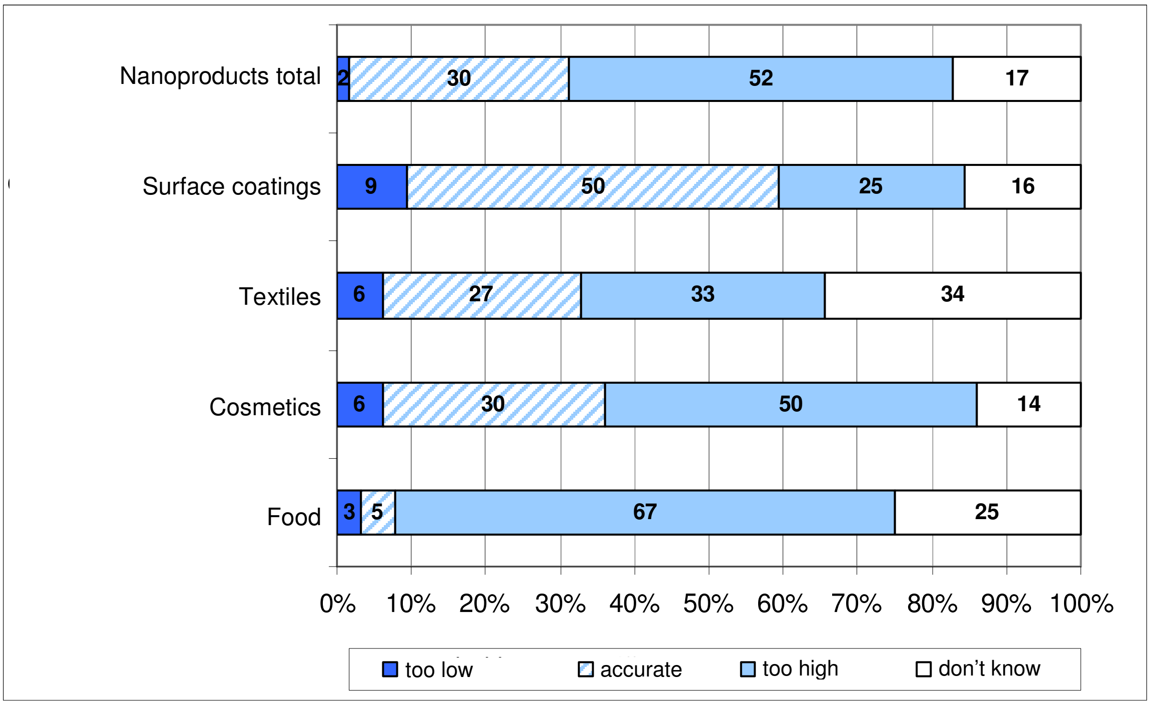
5.1.1 Total sales revenues with nanoproducts

In order to be able to assess the economic importance of nanoproducts, experts were asked to estimate the growth potential of various nanotechnology applications. The question was:

> “At the present time annual sales revenues of approximately US$ 52 billion are generated around the world. According to a study by Lux Research, the market of all nanotechnology products will grow by 70% every year which means that total sales revenues would already amount to US$ 1400 billion by 2012. Do you think that this growth forecast of 70% is accurate?”

64 out of the 71 experts who took part in the first survey round gave their estimation of the development of total sales revenues with nanoproducts. The experts felt that the growth forecast of 70% annual sales revenues with nanoproducts around the world was too high (52%). Nonetheless, 30% of the respondents felt that the growth forecast was accurate and only 2% felt that it was to low (see Fig. 24).

Fig. 24: Estimation of the growth forecast of 70% for global sales revenues with nanoproducts (n=64)



Explanation: percentages rounded up

Experts expect the biggest growth potential for nanoproducts in the area of surface coatings. In this context 50% of the respondents were of the opinion that the sales revenues with nanoproducts will increase every year by 70% around the world. A further 9% of the respondents felt that even this growth forecast was too low. In the area of textiles experts were divided. 33% believe that the growth forecast of 70% is accurate or too low. A further 33% of the respondents feel that the sales revenue forecast is too high. In the areas food and cosmetics the experts were of the opinion that the envisaged growth forecast for sales revenues with nanoproducts was unrealistic. In the case of cosmetics 50% of the respondents and for food as much as 67% felt that the annual sales revenue increases of 70% were too high. Particularly for food the experts do not seem to expect any major market development for nanoproducts in the near future.

The estimation of sales revenue development for nanoproducts was accompanied by major uncertainties at least in some areas. For textiles one-third of the respondents and for food one-quarter of respondents selected the “don't know” option. A glance at the comments of the experts shows that this uncertainty is founded above all on the three following elements:

- The growth forecast of 70% is seen as questionable by several respondents as no reliable figures are available for a forecast.
- The growth potential of nanotechnology depends on the image, acceptance and perception of the topic amongst the population at large and their representatives. In this context the importance of open, competent, credible and responsible communication is stressed.
- A reliable estimation is not currently possible because there is no clear definition, at the moment, about which products count as “nanoproducts”. Mention is made of the distinction between “old nanoproducts” which have been produced for many years now using nanotechnology methods but had not been covered by this designation up to now and “new nanoproducts”. The later possess novel properties which are based on synthetic nanomaterials or the use of a new nanomethod. Here is a typical quotation:

"Every year around 15 billion m² of foil materials are produced which are vacuum coated with a 40nm thin barrier layer made of aluminium. Depending on whether one only includes this vacuum coating step and the related intermediate products or also the end products produced from these intermediates, this leads to annual sales revenues of between US$ 0.7 billion and US$ 10 billion just for this small segment. (The estimations from the following table for the "value" are weakened by this very point. I would estimate a figure which is between 3 and 15 times higher). The same applies to food technology in which very varied colloidal and disperse systems are manufactured. The term "nanoproducts" is already so unclear in terms of the definition that one can assume here, too, far higher total sales revenues today. In contrast it can however be said that the corresponding products are far more established than one would assume and therefore no extreme growth rates are likely."

As almost all the stakeholder groups represented in the survey called for a more precise definition, questions were asked in the second Delphi round about how one could distinguish between "new" and "old" nanomaterials. Although various demarcation criteria were mentioned, there was no agreement amongst experts about the actual content of the criteria. Hence this question was examined in more depth at the expert workshop. The participants in the workshop developed factors that indicate how a definition could be elaborated that would permit classification in "old" and "new" nanomaterials:

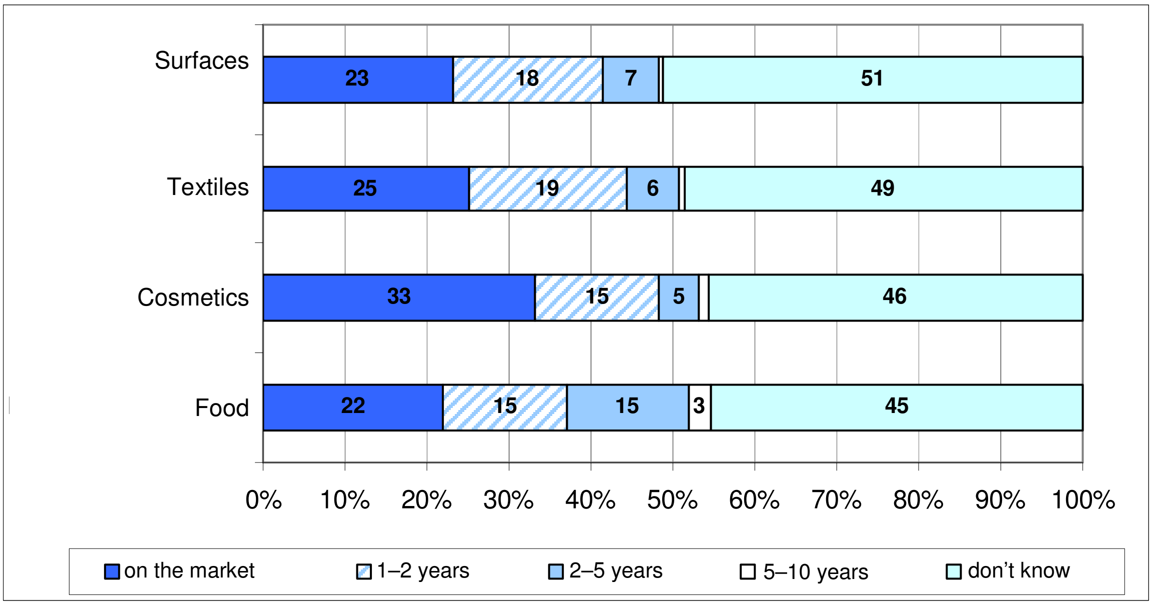
- Volume/tonnage (relevant for regulation)
- A link between volume and exposure
- Properties (new/old)/expert assessment (toxicity)
- Regulatory classification
- Time (of patent application and market launch)

5.1.2 Market maturity of nanoproducts

In this part of the survey experts were confronted with various nanoapplications in the areas surfaces, textiles, cosmetics and food. The applications were described on the basis of theories and the experts were asked to estimate when the applications would actually enter consumer markets. The following categories were given: "on the market", "market maturity in 1–2 years", "market maturity in 2–5 years", "market maturity in 5–10 years" and "don't know". The experts were given thirty application examples in total. Fig. 25 contains the experts' estimations for the respective applications across all examples.

Nanoproducts from the area of cosmetics were deemed to have the greatest market maturity. Here a total of 33% of experts believe that products are already available on the market and a further 15% estimate that nanocosmetics will be available for purchase in 1- 2 years. In the opinion of the experts nanoproducts in the area of food have the lowest market maturity. Nonetheless here, too, 22 % of the respondents are of the opinion that nanotechnology applications could already be purchased in the food sector. It is noticeable that the estimation is accompanied by major uncertainty. In all product areas around half of the respondents select the category "don't know".

Fig. 25: Estimation of the time when nanoproducts will be placed on the market by Delphi experts. "n" is the sum of mentions for the individual applications covered for the four areas surfaces (8 single applications), textiles (8 single applications), cosmetics (7 single applications) and food (7 single applications)



Explanation: percentages rounded up

A closer look reveals, however, that this overview merely reflects a rough trend. In all applications the estimation of market maturity of concrete examples varies considerably. Hence a more detailed look is now taken at nanoapplications in the areas surface coatings, textiles, cosmetics and food.

5.1.3 Market maturity of nanoproducts in the area of surfaces

The use of nanomaterials for the surface coating of consumer products is very varied. Nanomaterials are used for instance for food packaging, kitchen appliances, paints and varnishes. They are also used in products for the sealing or cleaning of surfaces and as polishing agents. For the packaging industry what is interesting is the use of nanoparticles which adhere as coatings to polymer surfaces (foils and containers). In food packaging nanoparticles prevent gases passing through the packaging or humidity exiting the packaging. They can likewise be used to improve the mechanical and thermal properties of food packaging and protect food against UV light. For instance, in the future, intelligent packaging materials will be developed for food using nanotechnology that indicate whether the refrigeration chain has been interrupted or the sell-by date exceeded.

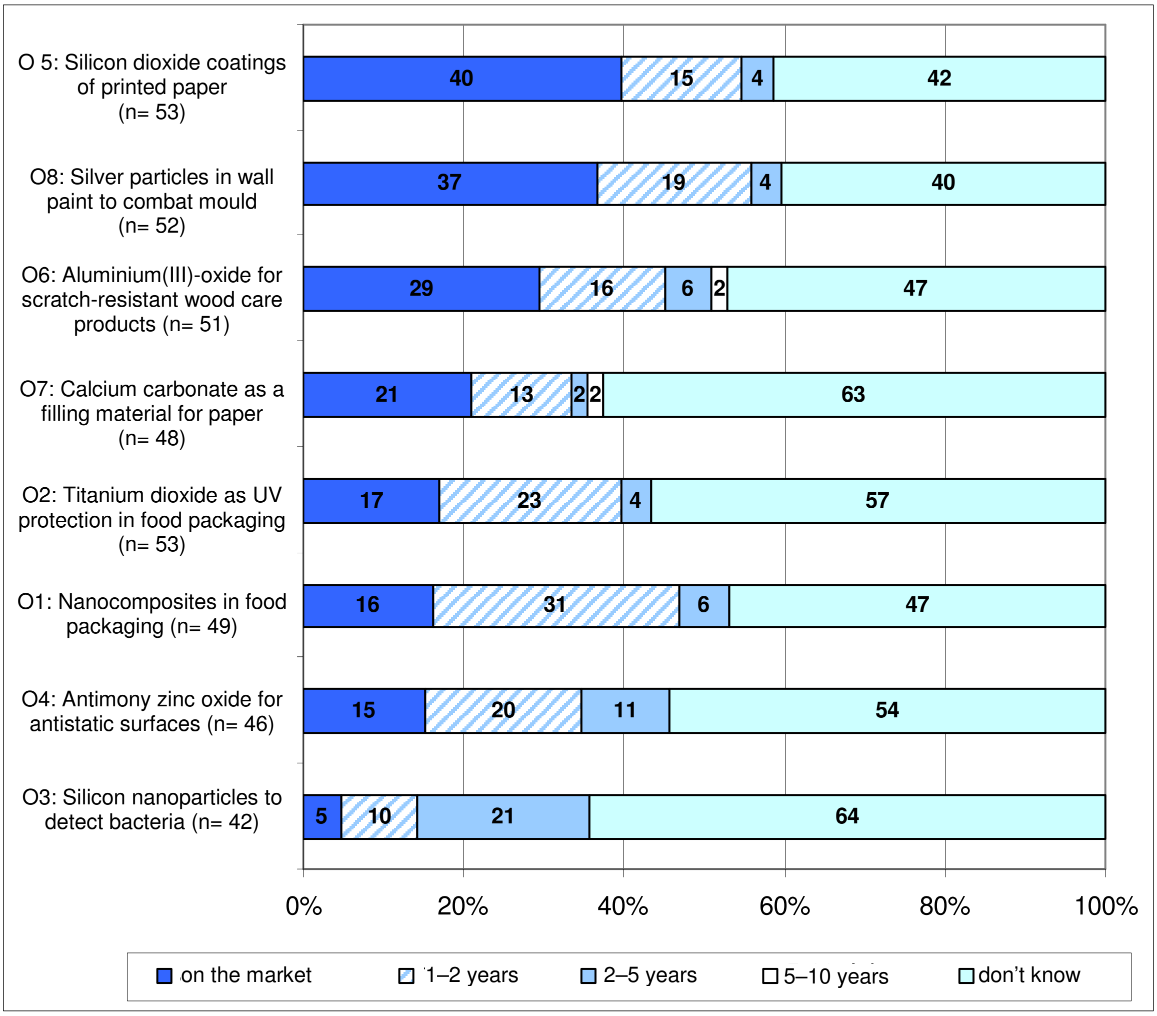
In the area of surface coatings experts were asked about their estimation of the market maturity of eight different nanoapplications (see Fig. 25).

Table 25: Potential applications of nanotechnology in the area of surfaces

Applications in the area of surfaces
O 1: The use of nanostructured materials (nanocomposites made from modified aluminium layer silicate + one polymer) in food packaging can considerably extend the shelf life of processed food by means of improved barriers to oxygen, carbon dioxide and humidity.
O 2: Plastic foils into which particles of titanium oxide (diameter 10- 20 nm) have been incorporated, block UV rays and, in this way, prevent chemical processes in food. The packaged product still looks appetizing several days later.
O 3: Silicon nanoparticles which contain fluorescent dye molecules and antibodies help to detect bacteria. When the antibodies dock onto the antigens of a bacterium, this can be indicated by the fluorescent illumination of the nanoparticles.
O 4: Antimony zinc oxide (Sb:Sn ratio= 1:9, purity 99.5+%, particle size 30 nm) is admixed to coatings in order to improve the antistatic properties of surfaces.
O 5: Ink jet paper and films which are coated with amorphous nanoparticles of salicylic acid or mixed oxides (e.g. silicon dioxide and aluminium oxide) adhere well and rapidly absorb the ink droplets.
O 6: A 30% dispersion of aluminium (Al2O3) nanoparticles (particle size 45 nm) is used to improve the scratch resistance of parquet and furniture varnishes.
O 7: Nanoscale CaCO3 (particle size approx. 50 nm) is used as a functional filler for paper and coatings in order to improve rigidity and stability.
O 8: A wall paint in which nanometre size silver particles are evenly distributed, prevents mould formation in indoor areas and algae growth on facades. The particles release silver ions that block the nutrient- transporting enzymes, destroy important proteins, dock onto hereditary material and intervene in cell wall synthesis.

More than half of the respondents believe that coatings of printed paper with silicon dioxide nanoparticles and wall paints with silver particles to combat mould are already on the market or are about the reach the market (Fig. 26). The use of aluminium (Al_2O_3) nanoparticles in parquet and furniture varnishes to improve scratch resistance is likewise, according to around one-third of the experts, a nanoapplication that is already available on the market. The most distant, in terms of time, application in the opinion of experts is the use of silicon nanoparticles which are equipped with fluorescent dye molecules and antibodies in order to detect bacteria. Here 21% of respondents believe that this application will only be available in 2- 5 years. This application is, at the same time, the example with the highest percentage of “don’t know” votes (64%).

Fig. 26: Estimation in number of years when nanoproducts from the area of surfaces will reach the market by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

In the second survey round experts were given the results of the first survey and asked to undertake a second assessment (Table 26).

Table 26: Estimation in number of years when nanoproducts from the area surfaces will reach the market by Delphi experts (comparison survey Round 1 with survey Round 2)

	Survey round (number of responses)	Already on the market (%)	in 1–2 years (%)	in 2–5 years (%)	in 5–10 years (%)	Don't know (%)
O 3: Silicon nanoparticles to detect bacteria	R1 (n=42)	5	10	21	0	64
	R2 (n=37)	19	41	0	0	41
O 4: Antimony zinc oxide for anti-static surfaces	R1 (n=46)	15	20	11	0	54
	R2 (n=37)	19	41	5	0	35
O 6: Aluminium (Al_2O_3) for scratch-resistant wood care products	R1 (n=51)	29	16	6	2	47
	R2 (n=39)	56	10	5	0	28
O 8: Silver particles in wall paint to combat mould	R1 (n=52)	37	19	4	0	40
	R2 (n=40)	65	8	0	0	28

Explanation: percentages rounded up

For all examples the proportion of "don't know" was considerably reduced. For two examples (silver nanoparticles in wall paints to combat mould and Al_2O_3 for scratch-resistant varnish surfaces) a majority of the experts were even of the opinion that these products were already on the market (65% and 56%).

5.1.4 Market maturity of nanoproducts in the area of textiles

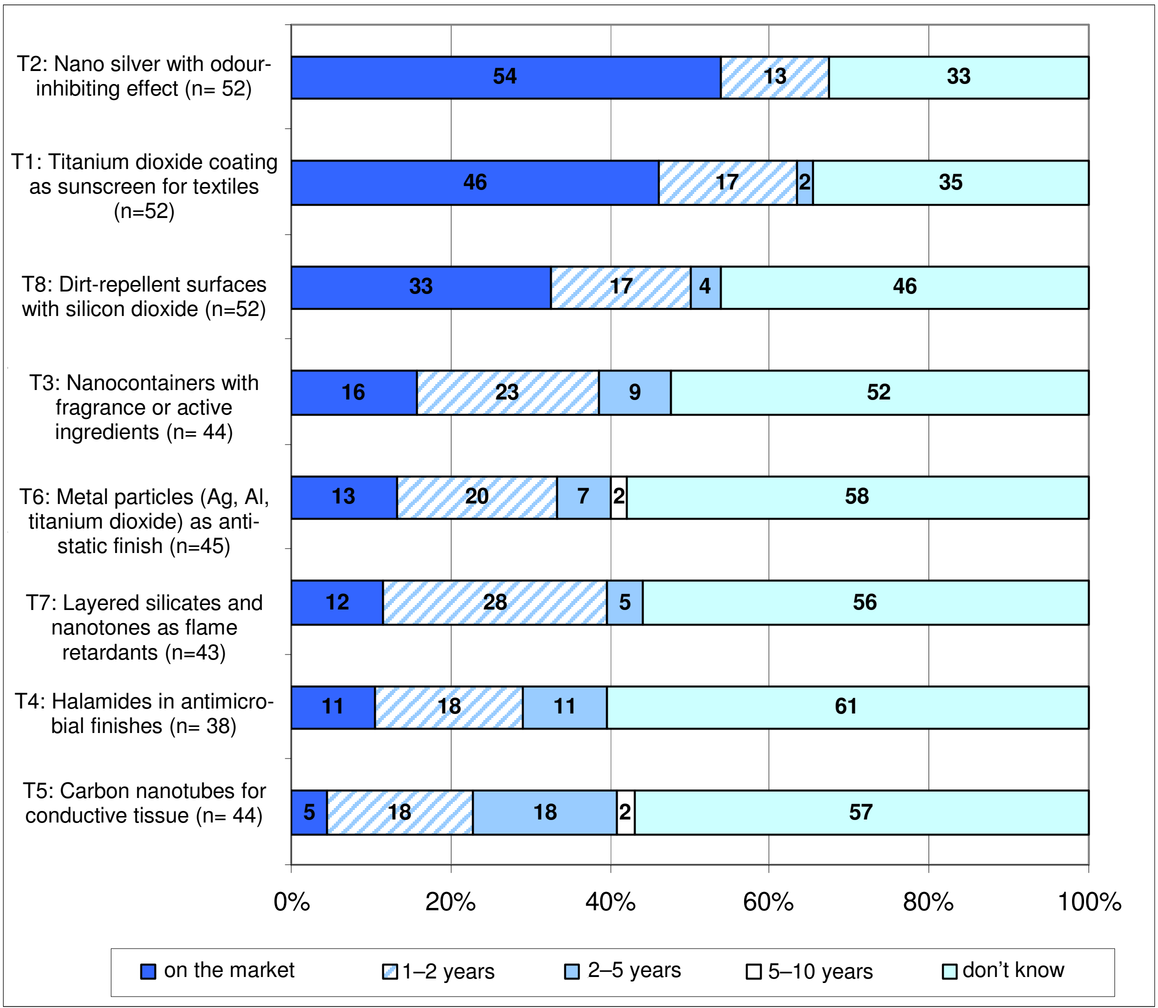
In the area of textiles special functional textiles are being developed which are to offer for instance extremely insulating thermal insulation clothing or self-cleaning textile surfaces. The application of nanostructured polymer layers to textile surfaces will give them new properties in future and protect against UV rays or act as a water barrier. Antimicrobial silver nanoparticles are already used in shoes, arch supports and some clothing textiles. Table 27 gives eight nanotechnology applications in the area of textiles that were assessed by the experts.

Table 27: Potential applications of nanotechnology in the area of textiles

Application in the area of textiles
T 1: Titanium dioxide is used as an UV-absorbing nanolayer in textiles. The small size of the pigment particles of around 20 nm ensures high absorption potential coupled with a low level of light scattering. This means that the particle layer is transparent and the sun protection is invisible.
T 2: A new anti-odour technology embeds millions of silver nanoparticles (diameter 15nm) in the fibres of socks, shoes and cloths. The silver particles kill odour-forming bacteria or inhibit their growth.
T 3: Nanocontainers with fragrances and active ingredients are integrated into textiles (clothing as well as carpets and settees). The capsules form when the fragrance isocyanine oil droplets (from 100nm in size) are incorporated into an aqueous polyamine solution and the isocyanine molecules react on the surface of the oil droplets with the surrounding polyamines in water. In this way they encapsulate the fragrance. Capsules with a porous shell continue to release even amounts of the substance over a period of months.
T 4: Halamides (polymer molecules) are used to coat textiles. Materials are formed which trap and kill viruses and bacteria. The antimicrobial materials are used to protect medical personnel and farmers who work with pesticides.
T 5: Single-walled and multi-walled carbon nanotubes are used to improve the electrical and thermal conductivity of fibres.
T 6: Fibres acquire antistatic properties by coating them with Ag, Al or Ti nanoparticles.
T 7: The integration of layered silicates (e.g. Montmorillonit) and nanotones into bicomponent fibres improves temperature stability and the flame-retardant properties of textiles.
T 8: Nanoparticles made of SiO2 are used to form nanostructured surfaces on fibres. This gives the textiles dirt-repellent properties.

The use of nanosilver in socks, shoes and cloths to avoid unpleasant odours, the coating of textiles with titanium dioxide nanoparticles for improved UV protection and the use of silicon dioxide in order to equip textiles with dirt-repellent properties are the three examples where a majority of the experts assumes that these products are already available on the market (Fig. 27). The experts are of the opinion that the use of carbon nanotubes to improve the electrical and thermal conductivity of fibres is the furthest away in terms of time. Here 18 % of experts assume that this application will only take on market relevance in 2 to 5 years time and a further 2 % believe that this will be even further in the future.

Fig. 27: Estimation of when nanoproducts from the area of textiles will be placed on the market by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

In the second survey round the proportion of "don't knows" was markedly lower in some cases for all application examples (Table 28). In the case of silver and silicon dioxide applications almost all the experts agreed that products are already on the market (80 % and 71 %). When it comes to the integration of nanofragrance containers into textiles and the use of halamides for the antimicrobial finish of occupational clothing, the experts could not agree on any clear time for implementation even after the second round.

Table 28: Estimation of when nanoproducts from the area of textiles will reach the market by Delphi experts (comparison survey Round 1 with survey Round 2)

	Survey round (number of responses)	Already on the market (%)	in 1–2 years (%)	in 2–5 years (%)	in 5–10 years (%)	Don't know (%)
T 2: Nanosilver with odour-inhibiting effect	R1 (n=52)	54	13	0	0	33
	R2 (n=41)	80	5	0	0	15
T 3: Nanocontainers with fragrances or active ingredients	R1 (n=44)	16	23	9	0	52
	R2 (n=36)	14	33	17	0	36
T 4: Halamides in antimicrobial finishes	R1 (n=38)	11	18	11	0	61
	R2 (n=32)	22	19	25	0	34
T 8: Dirt-repellent surfaces with silicon dioxide	R1 (n=52)	33	17	4	0	46
	R2 (n=38)	71	13	0	0	16

Explanation: percentages rounded up

5.1.5 Market maturity of nanoproducts in the area of cosmetics

Nanoparticles like titanium dioxide and zinc oxide are the most widespread products which are used as UV filters in sunscreen. Nanoparticles are very effective and protect the skin against UV rays. Nanotechnologically produced materials (so-called biocomposites) in toothpaste support the natural tooth repair mechanism of saliva. In skin care products nanocapsules are intended to protect the skin, transport active ingredients and improve care. Fullerenes (football-shaped cage molecules made of carbon atoms) are also used in the first cosmetic products to this end. Research is currently being undertaken to examine the improvements to the physical properties (e.g. transparency) of cosmetic finished products through nanomaterials.

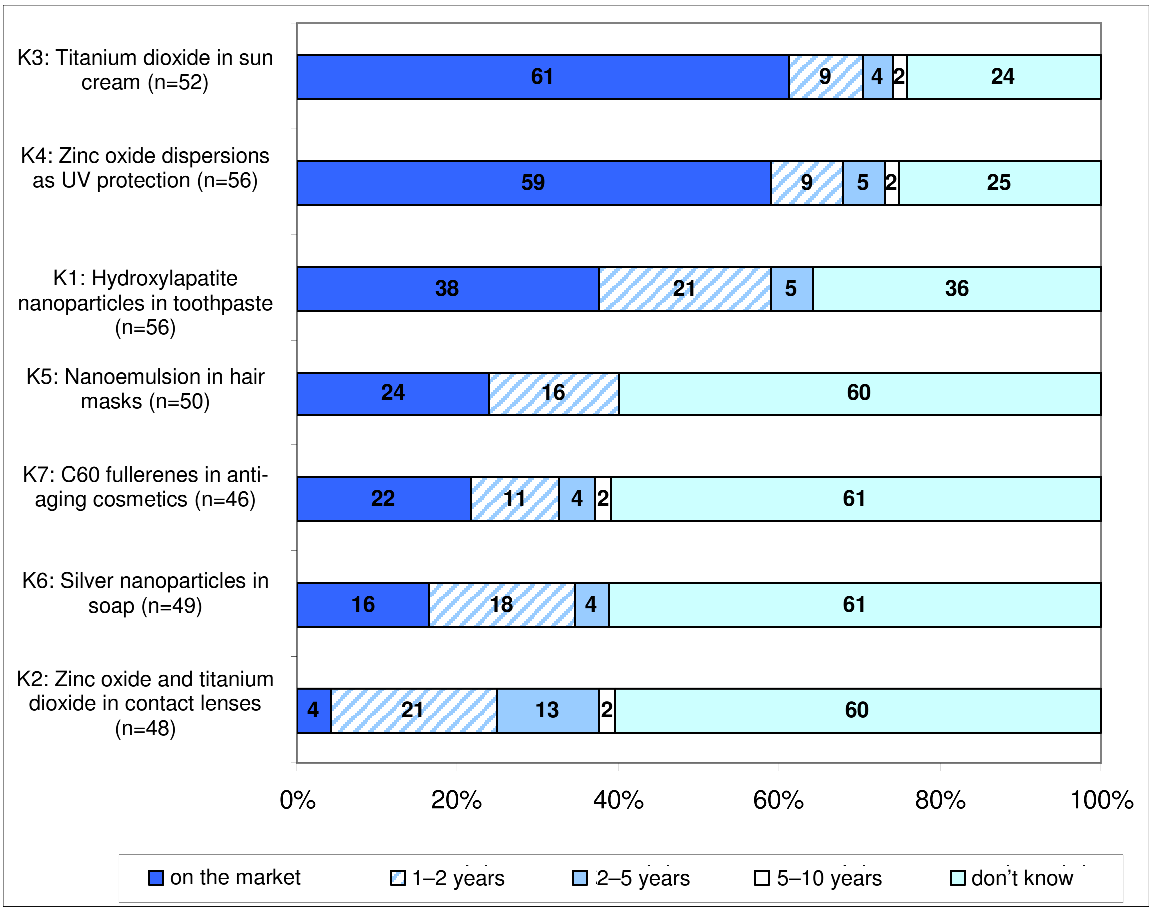
The seven potential or existing applications of nanomaterials in cosmetics, which were assessed by the experts, are compiled in Table 29.

Table 29: Potential applications of nanotechnology in cosmetics

Applications in the area of cosmetics
K 1: With the help of hydroxylapatite nanoparticles the weakened dental enamel can be restored whilst brushing teeth. The chemical structure of the material is identical to that of the dental enamel. After application the particles form a thin film which covers the gaps.
K 2: Nanoparticles (zinc oxide and titanium dioxide) are used to produce the new generation of contact lenses. The lenses are not completely coloured but have an interrupted pattern with various pigments. In this way the nanoparticles create a natural-looking eye colour.
K 3: Sunscreens contain materials made from titanium dioxide particles with a diameter of 15- 20 nm as UV filters. The smaller the particles are, the more closely they are aligned on the skin and the better they are said to protect the skin from UV light.
K 4: Hydrophilic or hydrophobic dispersions of ZnO (particle size 100nm) ensure transparent cosmetic UV protection.
K 5: Nanoemulsions with avocado oil, jojoba oil are used in hair masks. The drops in this emulsion are 100 times finer than in a normal emulsion and make the hair more combable and shiny after just a few seconds.
K 6: Silver nanoparticles (diameter approx. 7nm) are used in soap to clean and disinfect the skin. This prevents the onset of acne and skin cells are activated.
K 7: C60 fullerenes are used as anti-oxidants in creams. Fullerenes are able to neutralise dangerous free radicals and in this way prevent premature aging of the skin.

When it comes to the use of titanium dioxide and zinc oxide nanoparticles in sunscreens the experts all more or less agree that products are already on the market (Fig. 28). 61% and 59% of the respondents assume market availability. In the case of toothpaste with hydroxylapatite nanoparticles, a majority of the experts are still of the opinion that products are already available on the market. The experts believe that the use of zinc oxide and titanium dioxide nanoparticles to produce the latest generation of contact lenses is the most distant application in terms of time.

Fig. 28: Estimation of when nanoproducts from the area of cosmetics will be on the market by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

The renewed survey of experts led to the result that far more of the respondents believe that soap with silver nanoparticles and creams with fullerenes are already on or about to appear on the market (Table 30).

Table 30: Estimation of when nanoproducts from the area of cosmetics will reach the market by Delphi experts (comparison of survey Round 1 one with survey Round 2)

	Survey round (number of responses)	Already on the market (%)	in 1-2 years (%)	in 2-5 years (%)	in 5-10 years (%)	Don't know (%)
K6: Silver nanoparticles in soap	R1 (n=47)	16	18	4	0	62
	R2 (n=42)	33	36	0	0	31
K7: C60 fullerenes in anti-aging cosmetics	R1 (n=46)	22	11	4	2	61
	R2 (n=41)	54	17	2	0	27

Explanation: percentages rounded up

5.1.6 Market maturity of nanoproducts in food

Nanoproducts are supposedly already being used in food as auxiliaries and additives. For instance salicylic acid and other silicon-containing compounds are used as trickling or thickening agents. This can prevent, for instance, the baking together of sodium chloride crystals and powdered food and ketchup has improved flow properties. Salicylic acid is also used as a flocculent in the production of wine and fruit juice. At the present time it is not clear whether nanoparticles are actually used or whether free nanoparticles occur in the food. Nanomaterials are also said to be used specifically as food supplements. There are reports of the use of silicon dioxide, colloidal silver, calcium and magnesium in nanoparticle form. Whether the substances are indeed present in food as nanoparticles or in agglomerated form is unclear. The food industry is currently developing functional foods in which vitamins, omega 3 fatty acids, phytosterols and aromas are incorporated into nanocapsules and then released in a targeted manner in the body.

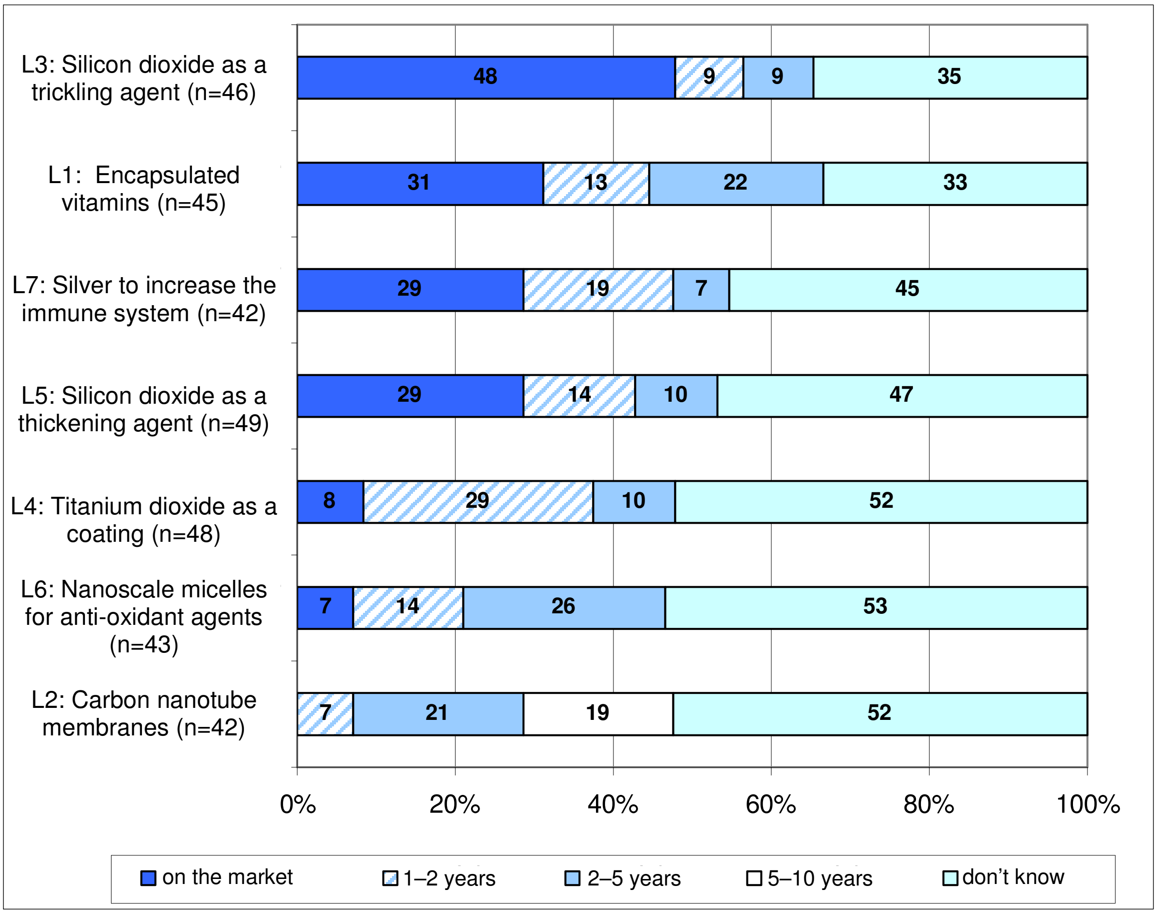
The assessment of the market maturity of various applications of nanotechnology in the food industry was examined in the BfR expert Delphi procedure. The categories were: “on the market”, “market maturity 1–2 years”, “market maturity in 2–5 years”, “market maturity in 5–10 years” and “don’t know”. The following seven potential applications of nanotechnology were assessed (Table 31).

Table 31: Potential applications of nanotechnology in food

Applications in the area of food
L 1: Vitamins or amino acids are encapsulated in nanocontainers (e.g. liposomes). These capsules, measuring between 10 and 100 nm, are more soluble, more mobile and more robust than conventional food additives in microdroplet form.
L 2: Membranes from (multi-walled) carbon nanotubes are used to separate biomolecules with functional value (e.g. proteins, peptides, vitamins and minerals). They can be used to fortify food or to produce dietetic additives or medicines.
L 3: Colloidal salicylic acid or silicon dioxide is used as a trickling agent or carrier material because of its high absorption capacity in order to prevent the baking together of sodium chloride crystals and food.
L 4: There are plans to coat chocolate bars with a titanium dioxide layer that is only a few nm thick and is neutral in taste to ensure that they still look attractive even if they have been lying around for some time.
L 5: Highly disperse salicylic acid is used in ketchup as an efficient thickening agent. The nanoparticles have a diameter of between 5 and 30nm.
L 6: Nanotechnology anti-oxidant systems help food to stay fresh longer. Nanoscale micelles are used as carriers for anti-oxidants.
L 7: Silver particles dissolved in pure water (diameter: 0.8nm, concentration 10ppm) are available as food supplements. The charge of silver and its nanoscale formulation are said to increase a feeling of wellbeing and boost the immune system.

Although there is no clear proof of the use of nanomaterials in food, 48 % of experts nonetheless assume that nanoparticulate silicon dioxide is already used as a trickling agent in food (Fig. 29) and just under one-third of the respondents believe that nanoencapsulated vitamins and silicon dioxide nanoparticles are used today as thickening agents in food and silver nanoparticles in food supplements. The experts believe that the use of carbon nanotubes to separate biomolecules with functional value is an application that will reach the market at a later stage in the future.

Fig. 29: Estimation of when nanoproducts in the area of food will reach the market by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

Four examples of applications from the area of food were presented to the experts in survey Round 2 for a second assessment. The experts agreed that nanoparticulate silicon dioxide is already used as a trickling agent in food (77% of respondents) (table 32). When it comes to the use of silver nanoparticles to increase the defence system, 50% of experts also now believe that a product of this kind is already available on the market. For the two other application examples the trend was confirmed when experts expect to see this happen: for the titanium dioxide coating of chocolate bars 1-2 years and for the use of nanoscale micelles as anti-oxidants 2-5 years.

Table 32: Estimation of when nanoproducts from the area of food will be placed on the market by Delphi experts (comparison survey Round 1 with survey Round 1)

	Survey round (number of responses)	Already on the market (%)	in 1–2 years (%)	in 2–5 years (%)	in 5–10 years (%)	Don't know (%)
L3: Silicon dioxide as a trickling agent	R1 (n=46)	48	9	9	0	35
	R2 (n=39)	77	5	0	0	18
L4: Titanium dioxide as a coating	R1 (n=48)	8	29	10	0	52
	R2 (n=38)	13	37	8	0	42
L6: Nanoscale micelles for anti-oxidant agents	R1 (n=43)	7	14	26	0	53
	R2 (n=37)	11	22	30	5	32
L7: Silver to boost the immune system	R1 (n=42)	29	19	7	0	45
	R2 (n=36)	50	19	6	0	25

Explanation: percentages rounded up

5.2 Potential harmful effects of nanoproducts

In order to estimate whether nanoproducts entail specific health risks it is important to know whether the nanomaterials used are embedded in a matrix or are present in unbound form in the product. In particular free nanoparticles, nanotubes or nanofibres could lead to health risks because of their size, shape, high mobility and higher reactivity. So far, however, most nanoproducts have been made of structures in which nanoparticles are embedded in a matrix or a liquid suspension. Furthermore, nanoparticles tend to join forces in larger unions which then as a rule are larger than 100nm. The toxic effects of nanoparticles, which are based on their small size and higher reactivity, are then no longer relevant.

In the previous section it was shown that the experts in the BfR Delphi survey believe that some nanoapplications are already ready for the market. This section examines whether this could entail health risks for consumers.

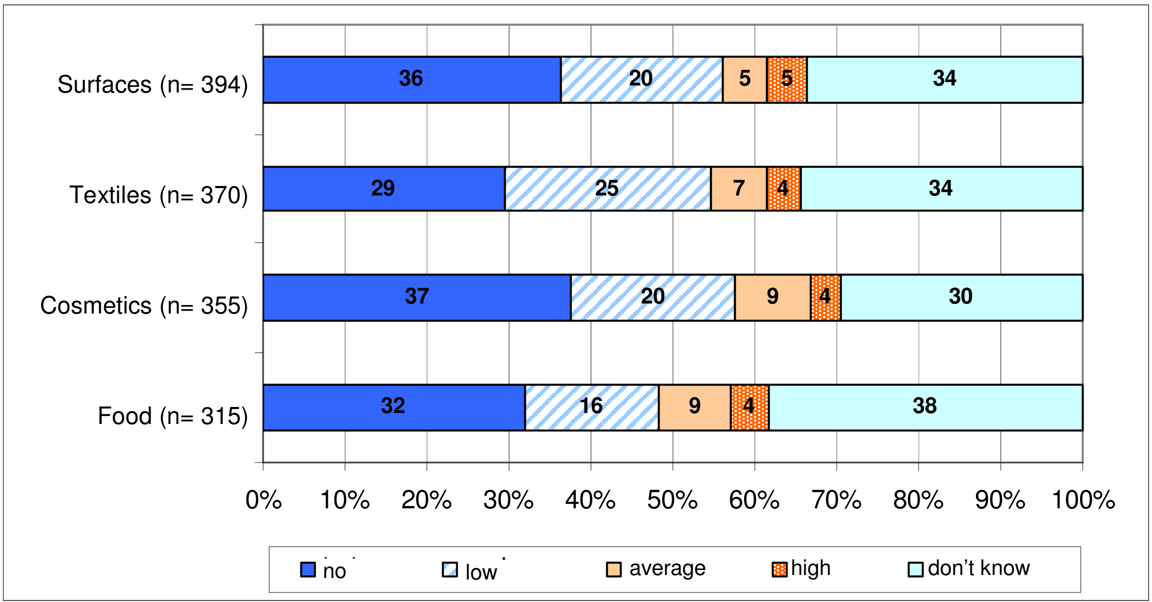
5.2.1 Estimation of potential harmful effects of nanoproducts overall

For the estimation of the potential harmful effects of nanoproducts, experts were again presented with the 30 application examples from the areas surface coatings, textiles, cosmetics and food which they had already been asked to assess in respect of their market maturity. The assessment categories for potential harmful effects given to the experts were: “no effects”, “minor effects”, “average effects”, “high effects” and “don’t know”. In the second survey round only those applications were examined which had low, average or high toxicity in Round 1.

Before presenting the results for the individual applications, an overview is given of the four applications of nanotechnology. To this end, the votes per category were methodologically combined for all examples within one application.

The analysis shows that the estimation of the four applications by experts only differs to a minor degree (Fig. 30). More than 50 % of experts are of the opinion that nanoproducts from the areas surfaces, textiles and cosmetics do not have any or at most minor negative effects on consumer health. Even in the case of nanotechnology applications in the area of food 48% of respondents believe that nanoproducts have none or only minor negative effects. The food sector is, nonetheless, also the area in which uncertainty amongst experts is greatest. 38% of them selected the category “don’t know”.

Fig. 30: Estimation of potential health effects of nanoproducts by Delphi experts. The "n" in brackets is the sum of mentions from the individual applications covered for the four areas surfaces (8 single applications), textiles (8 single applications), cosmetics (7 single applications) and food (7 single applications)



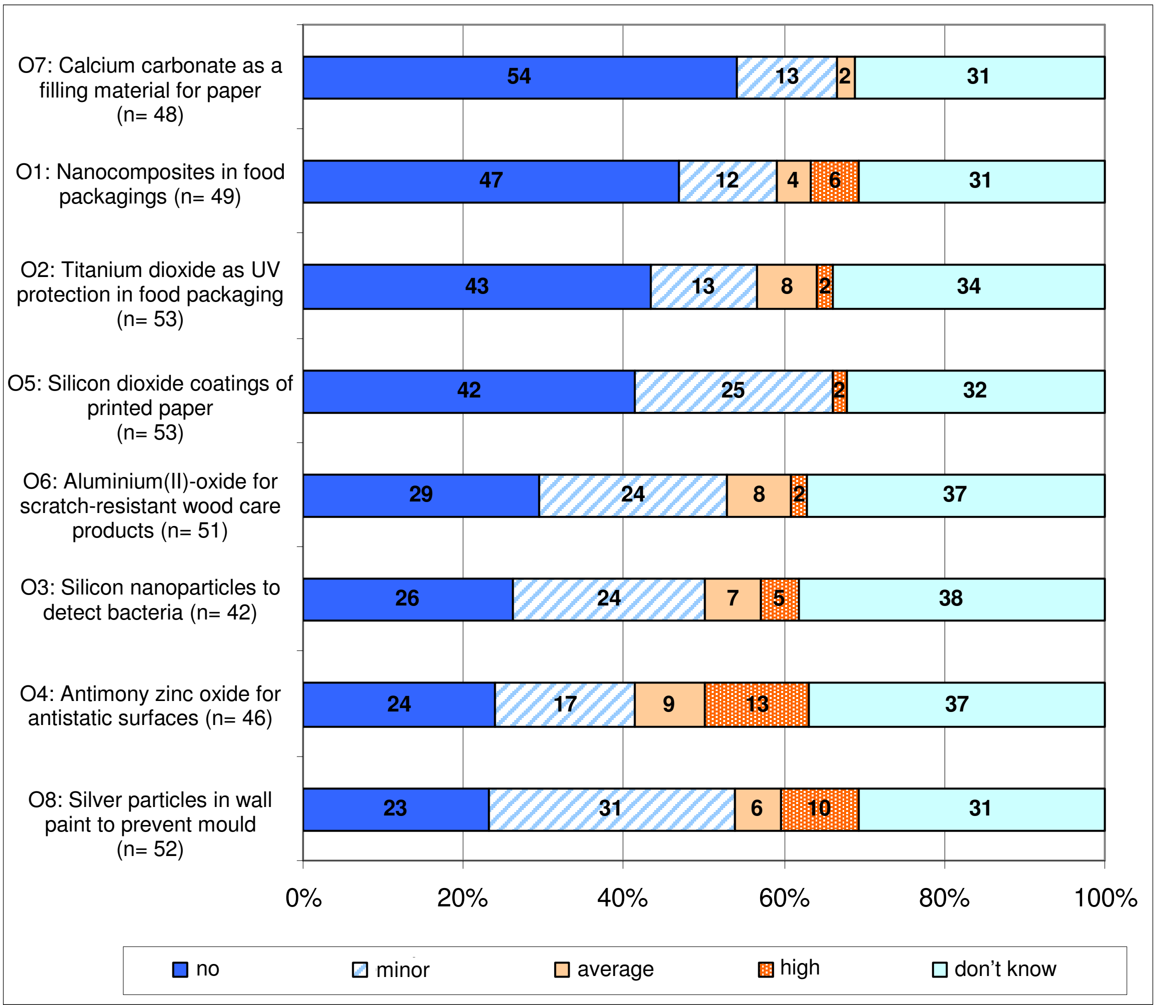
Explanation: percentages rounded up

As there were, in some cases, major differences in the estimation of the potential harmful effects of individual applications in the four application areas, the following section takes a closer look at this. In addition the experts were presented with theories which throw greater light on individual aspects of potential health risks.

5.2.2 Estimation of potential harmful effects of nanotechnology applications in the area of surfaces

For the area surface coatings almost all applications are deemed to be safe, even those where there could be direct contact with food (Fig. 31). In the case of applications with silver – here for instance to avoid mould formation on walls – the experts see a low toxic potential although they did add that silver is used specifically because of its antimicrobial properties.

Fig. 31: Estimation of potential harmful effects of nanoproducts from the area of surfaces by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

The second survey round confirmed the trend that almost all application examples in the area of surface coatings are deemed to be safe (Table 33). The experts to continue to see a low toxic potential when it comes to the use of silver nanoparticles in paint dyes to prevent mould.

Table 33: Assessment of potential harmful effects of nanoproducts from the area of surfaces by Delphi experts (comparisons survey Round 1 with survey Round 2)

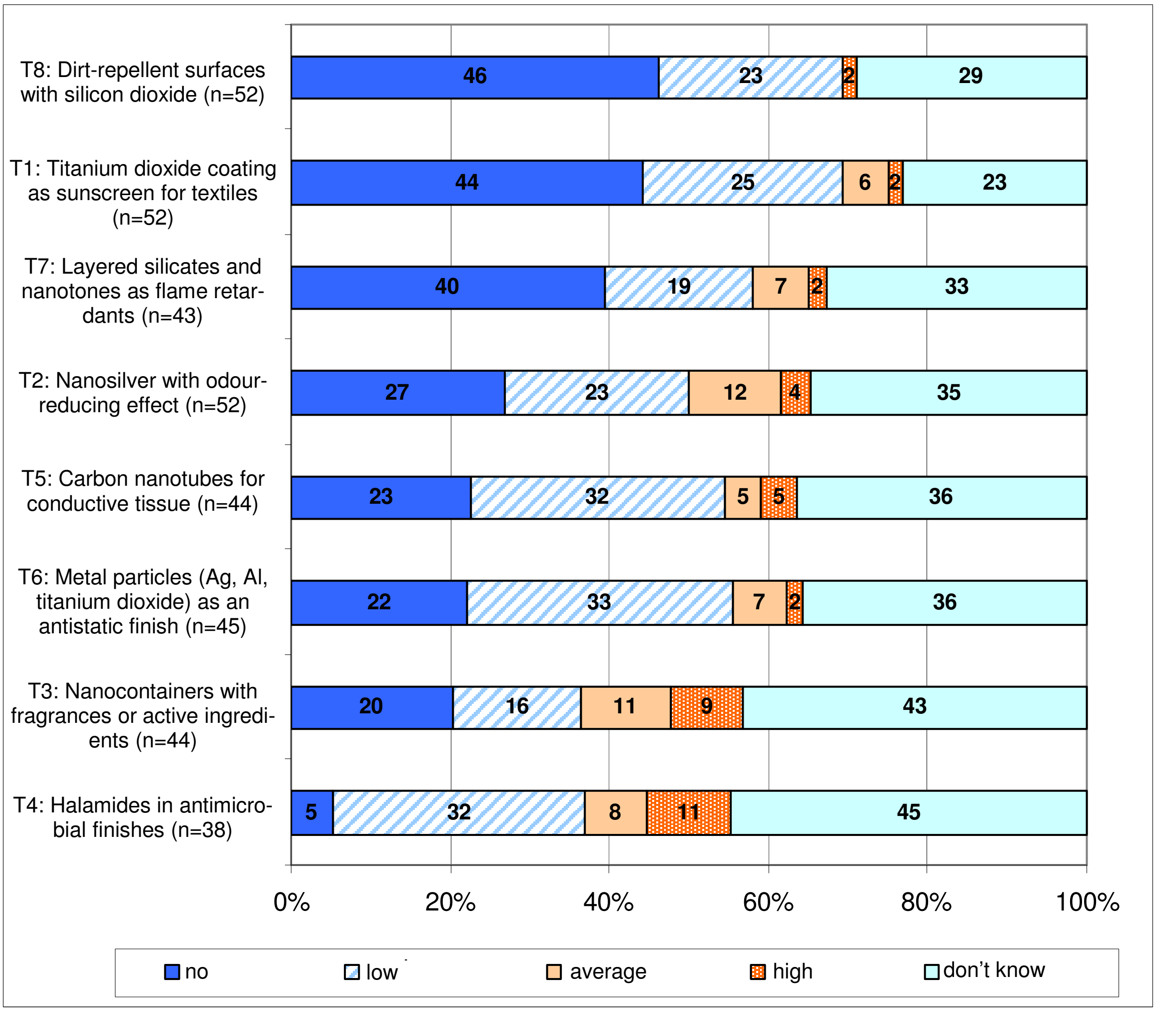
	Survey round (number of responses)	None (%)	Low (%)	Medium (%)	High (%)	Don't know (%)
O3: Silicon nanoparticles to detect bacteria	R1 (n=42)	26	24	7	5	38
	R2 (n=37)	35	22	0	3	40
O4: Antimony zinc oxide for antistatic surfaces	R1 (n=46)	24	17	9	13	37
	R2 (n=37)	35	22	5	14	24
O6: Aluminium (Al203) for scratch-resistant wood care products	R1 (n=51)	29	24	8	2	37
	R2 (n=39)	49	23	5	3	21
O8: Silver particles in wall paint to prevent mould	R1 (n=52)	23	31	6	10	31
	R2 (n=40)	28	30	10	3	29

Explanation: percentages rounded up

5.2.3 Estimation of potential harmful effects of nanotechnology applications in the area of textiles

In the area of textiles the majority of experts do not expect any harmful effects from nanoproducts (Fig. 32). For instance the majority of experts sound the all clear for the use of silicon dioxide nanoparticles to equip fibres with dirt-repellent properties or the use of titanium dioxide nanoparticles to implement UV-absorbing layers. Most of the experts do not have any health concerns about use of nanosilver coatings with odour-reducing effect either. The experts only see a minor toxic potential when carbon nanotubes are used to produce conductive tissue, when metal particles (Ag, Al or TiO_2 nanoparticles) are used for anti-static coatings and when halamides are used to give an anti-microbial finish to occupational clothing.

Fig. 32: Estimation of potential health harmful effects of nanoproducts from the area of textiles by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

Four examples from the area of textiles were once again presented to the experts for assessment. The trend was confirmed whereby the experts do not expect any harmful effects in particular for the nanosilver application and the dirt-repellent surfaces with nanoparticulate silicon dioxide (Table 34). In contrast, the trend was heightened whereby the use of halamides to give an antimicrobial finish to occupational clothing is seen as having low negative health effects.

Table 34: Estimation of potential harmful effects of nanoproducts from the area of textiles by Delphi experts (comparison survey Round 1 with survey Round 2)

	Survey round (number of responses)	None (%)	Low (%)	Medium (%)	High (%)	Don't know (%)
T2: Nanosilver with odour-reducing effect	R1 (n=52)	27	23	12	4	35
	R2 (n=41)	41	29	0	2	28
T3: Nanocontainers with fragrances or active ingredients	R1 (n=44)	20	16	11	9	43
	R2 (n=36)	28	19	3	11	39
T4: Halamides in antimicrobial finishes	R1 (n=38)	5	32	8	11	45
	R2 (n=32)	9	41	3	6	41
T8: Dirt-repellent surfaces with silicon dioxide	R1 (n=52)	46	23	0	2	29
	R2 (n=38)	68	13	3	3	13

Explanation: percentages rounded up

5.2.4 Exposure to nanomaterials from surface coatings and textiles

In the chapter on exposure the inhalational exposure pathway was identified as the one which is most likely to lead to potential harmful effects of nanomaterials. The various possibilities of consumer exposure to nanoproducts are examined below. As, in the case of nanoapplications in the area of textiles, these are normally also surface coatings, the data on exposure possibilities are dealt with jointly in the area of surface coatings and textiles.

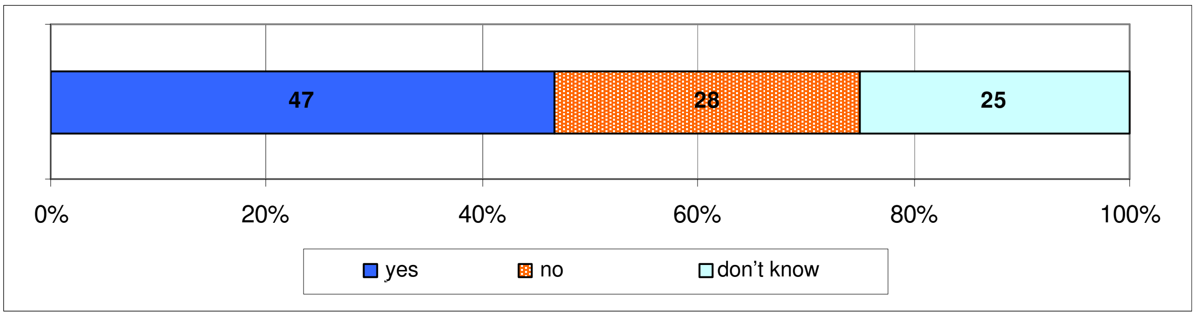
In the survey the experts were presented with general theories concerning the potential exposure of consumers in order to identify critical areas of consumer protection. The presentation of general theories is one of the standard methods in Delphi surveys in order to identify generally applicable assessment trends. The response behaviour of the experts was shaped by very high proportions of "don't know" and corresponding qualitative comments. This shows that the respondents only make general statements in the area of nanotechnologies with major reservations.

One first theory which was presented in this section was:

> *"In your opinion are consumers exposed to nanomaterials through abrasion in the case of textiles or surface coatings? If so, what effects do you expect? Can you attribute specific effects to specific materials?"*

The responses show that 46.7 % of experts expect abrasion and 28.3 % no abrasion (see Fig. 33).

Fig. 33: Estimation of potential exposure of consumers to nanomaterials through the abrasion of textiles or surface coatings (n= 60 responses)



Explanation: percentages rounded up

Comprehensive comments on the special effects triggered by the abrasion of textiles or surface coatings were made by 34% of the respondents. Table 35 provides a detailed compilation of comments that were made particularly frequently:

Table 35: Exposure of consumers to abrasion of surface coatings and textiles (qualitative comments)

Industry	"For exposure a case-by-case consideration is necessary/general statements are not possible" "No effect" "Measurements of the release of nanoparticles show that for various products from different applications that there is only a low level of release" "The question cannot be answered in a general way. There are a number of nanomaterials which create a bond with the substrate (e.g. cotton) and hence do not constitute a hazard (any more). On the other hand some nanomaterials release respirable nanoparticles as a consequence of abrasion. Depending on the chemical composition, corresponding exposure may lead to irritation/inflammation of the respiratory tract."
Science	"Every textile has always released nanoparticles in conjunction with abrasion" "In the case of many surface coatings – e.g. metals – an additional layer of varnish is necessary, in particular as protection against corrosion. This dramatically reduces the likelihood of exposure" "Abrasion is feasible in individual cases, however, rapid aggregation is expected; very low levels" "In particular in the case of mechanical abrasion nanomaterials can be released which can be ingested via the inhalational and dermal pathways. In addition nanomaterials can be released from surface coatings exposed to thermal strain and elevated weathering processes."
NGO/trade union	"Allergies, accumulation, autoimmune processes, in particular in conjunction with dermal exposure" "Rather low exposure, possibly in conjunction with broken skin" "Depending on the substance and level of exposure, dermal effects, possibly inhalational effects"
Public authority/politics	"Mechanical abrasion normally leads to larger particles in the micrometer range" "Allergies"
Networks	"Inhalation of the finest dust particles cannot be ruled out"
Insurers	"In principle depending on how firmly the nanoparticles are embedded a certain exposure may occur. We do not have the necessary knowledge to comment on effects."

In the second survey round responses to the questions about the abrasion of surface coatings and textiles were recorded separately and the question was asked whether, in principle, there can be any abrasion and whether this is likely to be in the nanoscale or rather in the micrometer range and thus no longer contain any nanoproperties. Generally speaking, the abrasion of nanomaterials and also nanoscale abrasion from surface coatings are deemed to be feasible under certain circumstances (see Table 36).

Table 36: Estimation of potential exposure of consumers to abrasion from surfaces (n=56 responses)

	yes (%)	no (%)	it depends (%)	don't know (%)
There may be abrasion of nanomaterials from surface coatings	55.4	7.1	14.3	23.2
This abrasion from surface coatings maybe nanoscale	32.1	10.7	30.4	26.8
This abrasion from surface coatings is in the micrometer range and does not show any nanospecific effects	16.1	7.1	41.1	35.7

Explanation: percentages rounded up

Highly differentiated comments on the assessment of the abrasion of surfaces were made by all stakeholder groups. Firstly, it was repeatedly pointed out that nanoparticles are very firmly embedded in the surface matrix and hence release is unlikely. Furthermore, it depends on whether the nanomaterial is part of the surface coating or is located in deeper material layers of the product. Overall nanoscale abrasion cannot be ruled out particularly in conjunction with mechanical strain. One respondent from industry pointed out that nanoscale particles were released in some measurements under mechanical strain (rubbing/grinding). Moreover, several comments pointed out that the effects of aging processes and weathering on the products should be taken into account.

Similar to the situation with surface coatings the experts believe that in the case of surface coated textiles nanoscale abrasion is also possible. The expert survey produced the following results (see Table 37):

Table 37: Estimation of potential exposure of consumers to abrasion from textiles (n= 56 responses)

	yes (%)	no (%)	it depends (%)	don't know (%)
There may be abrasion of nanomaterials from textiles	53.6	1.8	17.8	26.8
This abrasion from textiles maybe nanoscale	32.1	3.6	30.4	33.9
The abrasion from textiles is in the micrometer range and does not show any nanospecific effects	7.1	7.1	41.1	44.7

Explanation: percentages rounded up

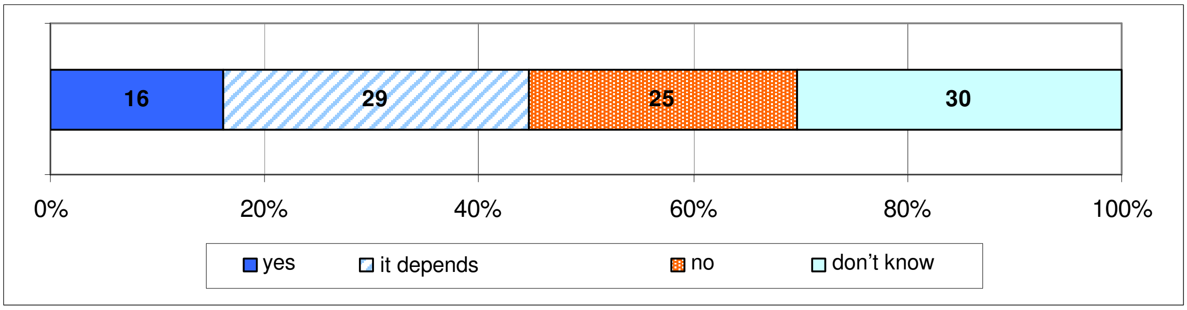
These results were then discussed at an expert workshop. There, the majority of experts recommended a qualification of the abrasion problem in the case of textiles as they would always produce submicrometre-size abrasion, particularly in the case of natural fibres. Generally speaking exposure to nanomaterials could only occur in the case of textile coatings according to the experts. If nanomaterials were embedded in a polymer thread, then they were unlikely to be loosened by abrasion. Hence a distinction between coated and incorporated functional chemical fibres is deemed to be necessary.

The experts confirm that inhalational and dermal exposure are, in principle, possible in the case of coatings as is oral exposure when, for instance, baby clothing is sucked and chewed on. Nonetheless, general abrasion still did not say anything about potential harmful effects as the dose and health condition had to be taken into account too. In the case of normal consumption theoretical exposure could only be assumed when nanoparticles were released at the break points in conjunction with the cracking of submicrometer size coatings. As a rule this abrasion was in the micrometer range. According to the experts abrasion probably occurs mostly during washing which meant that there is probably only very low direct inhalational, oral or dermal exposure to nanomaterials.

At the workshop the experts pointed out that some knowledge is already available on the health effects of abrasion. They referred in particular to the effects of silver particles. Even if they do not become detached, they could trigger sensitisation because of the mechanisms of action. Generally speaking the concern was raised that the bactericidal effect, coupled with frequent use of silver textiles, could lead indirectly to an increase in allergies. Silver textiles were, therefore, only suitable for specific medical applications (reduction of existing inflammations in the case of patients suffering from neurodermatitis) but not for daily use. This was stressed by the experts.

In response to the question whether there is an elevated risk of allergies when nanomaterials come into contact with the skin, the experts in the second Delphi round tended to give deviating answers. As Fig. 34 shows, almost two-thirds of the respondents selected the categories “don't know” or “it depends”:

Fig. 34: Estimation of an allergy risk through contact with nanomaterials (n= 56 responses)



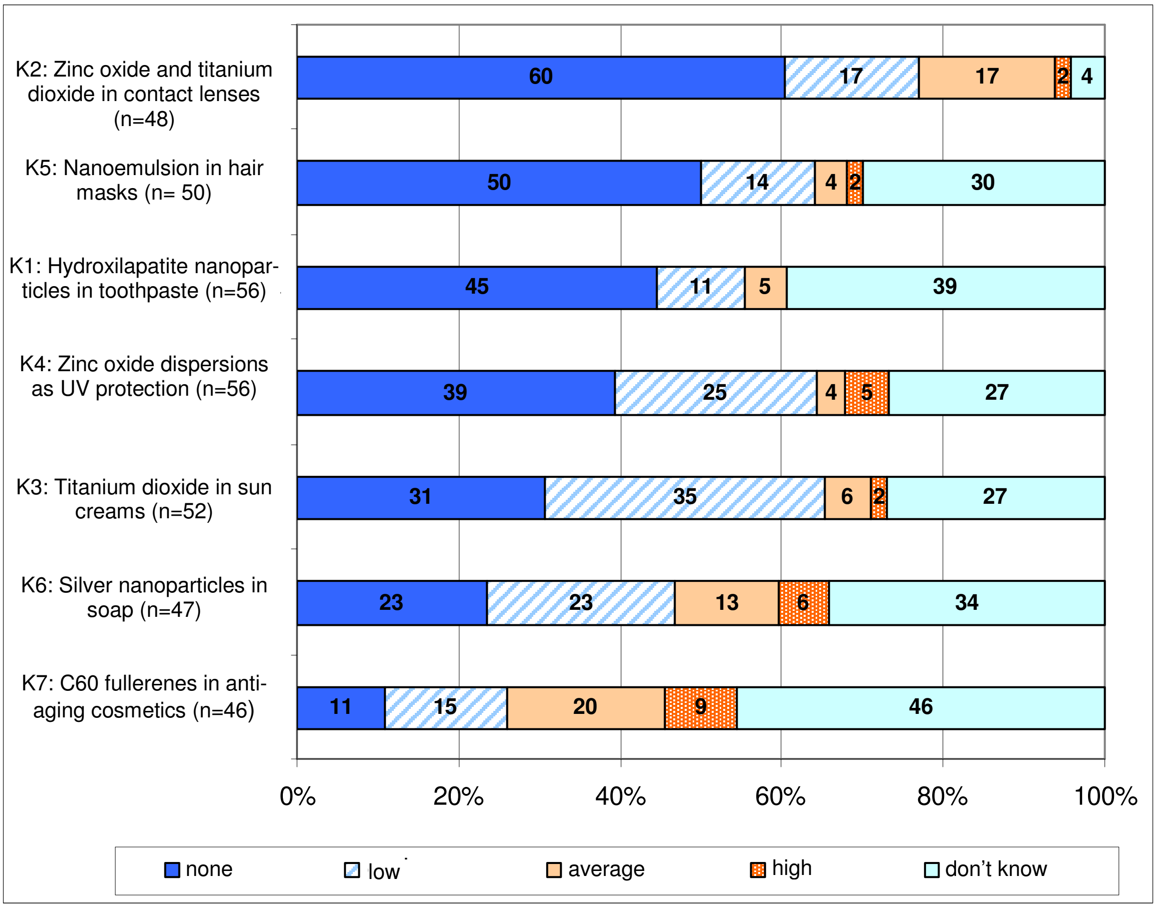
Explanation: percentages rounded up

As in the survey from Delphi Round 2 no clear assessment trend could be identified, the workshop participants took a more in-depth look at the concrete examples. The experts did not expect any negative effects from the dermal application of titanium dioxide-containing formulations. In scientific studies on TiO_2 no sensitising potential was observed for nanoparticles that were larger than 20nm. No sensitising potential could be detected for SiO_2 either. Generally speaking the experts stressed that above the size threshold of 20nm there is no penetration of the horny skin by nanoparticles.

5.2.5 Estimation of potential harmful effects of nanotechnology applications in the area of cosmetics

The experts do not expect any harmful effects from most of the nanotechnological applications in the area of cosmetics (Fig. 35). The exceptions are the use of silver nanoparticles in soap for skin washing and fullerenes as anti-oxidants. Regarding the use of fullerenes in skin creams, if one leaves aside the high proportion of "don't know" for once, then the proportion of experts who expect medium, possible harmful effects is the largest. But what is also surprising is the high proportion of experts who expect at least low harmful effects from the use of zinc and titanium dioxide nanoparticles in sunscreens.

Fig. 35: Estimation of potential harmful effects of nanoproducts in the area of cosmetics by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

The assessments in survey Round 2 in terms of weighting were again consistent with the enhancement effect described above. For silver, low harmful effects are seen (Table 38). 41% of experts now expect medium negative health effects from the use of C60 in creams.

Table 38: Estimation of potential harmful effects of nanoproducts from the area of cosmetics by Delphi experts (comparison survey Round 1 with survey Round 2)

	Survey round (number of responses)	None (%)	Low (%)	Medium (%)	High (%)	Don't know (%)
K6: Silver nanoparticles in soap	R1 (n=47)	23	23	13	6	34
	R2 (n=42)	24	29	14	5	28
K7: C60 fullerenes in anti-aging cosmetics	R1 (n=46)	11	15	20	9	46
	R2 (n=41)	5	10	41	7	37

Explanation: percentages rounded up

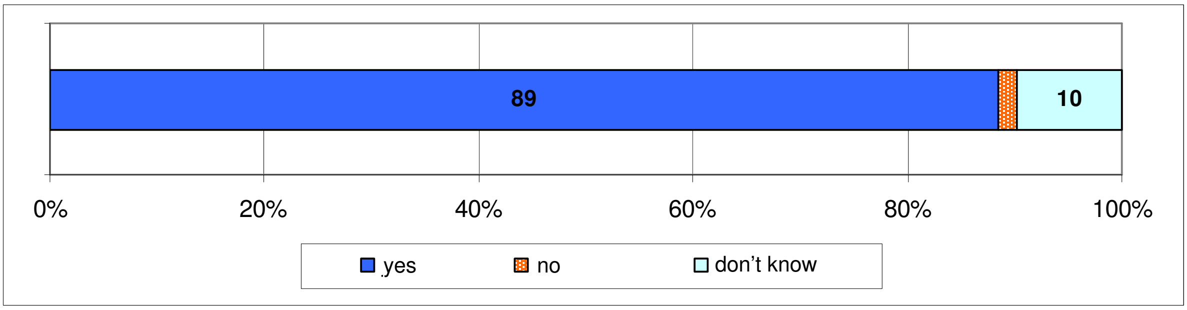
5.2.6 Exposure to nanomaterials in cosmetics and pharmaceutical products

The experts were presented with the following theory concerning potential exposure to nanomaterials in cosmetics and pharmaceutical products:

> *"Do you expect to see consumer exposure to nanomaterials in cosmetics and pharmaceutical products? If so, what effects do you expect? Can you attribute specific effects to specific materials?"*

As this concerns intended exposure from the use of nanomaterials in pharmaceutical products and cosmetics similar to that in food, the responses are clear as expected. 88.5% of experts confirmed that there is exposure (Fig. 36).

Fig. 36: Estimation of consumer exposure to nanomaterials in cosmetics and pharmaceutical products (n= 61 responses)



Explanation: percentages rounded up

In the case of the comments on the effects of cosmetics and pharmaceutical products (Table 39) 52%, just more than half of the respondents from the stakeholder groups, in particular the representatives of industry, made comments. Double mentions were deleted.

From the comments of the group of science and NGOs it can be concluded that the use of fullerenes in cosmetic applications is attributed special status. The comments differ clearly when it comes to applications with and without a systemic effect.

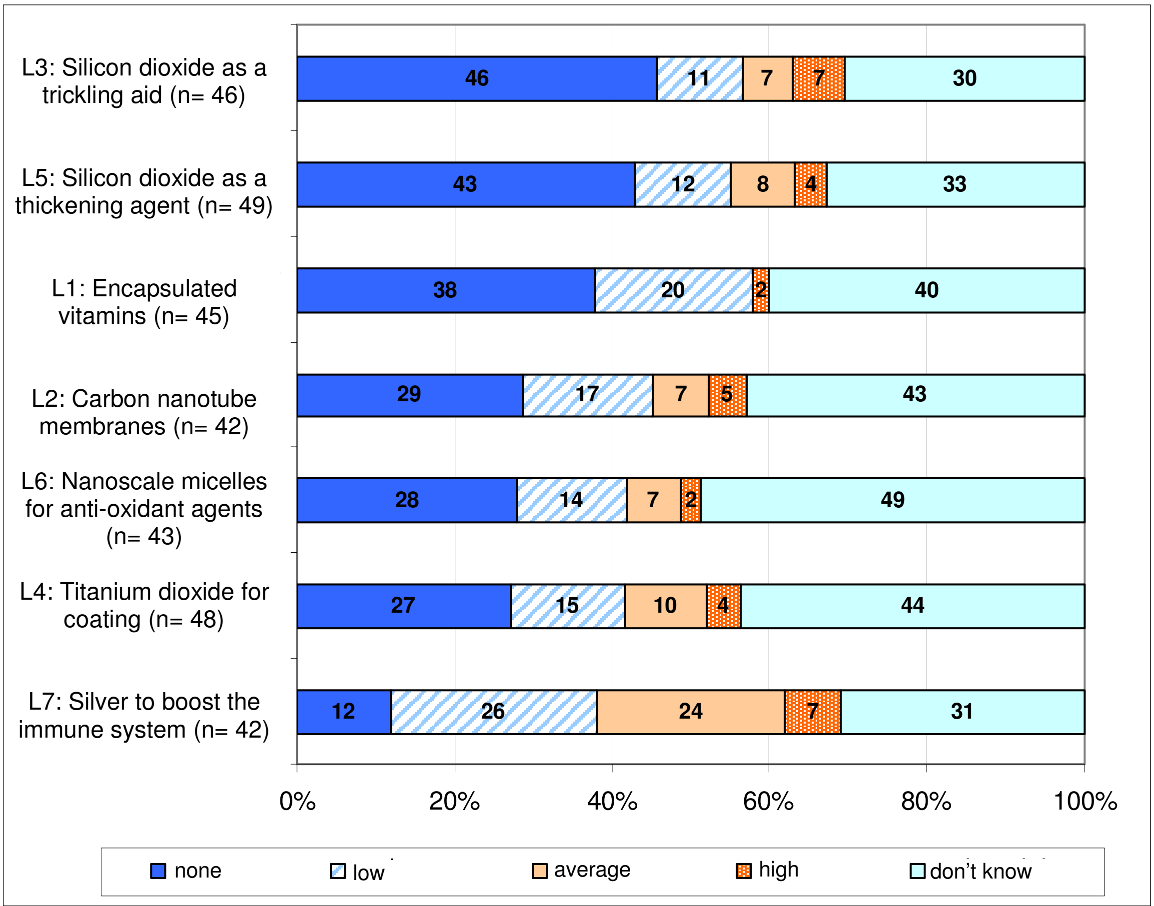
Table 39: Estimation of consumer exposure to nanomaterials in cosmetics and pharmaceutical products

Industry	"There is dermal exposure to light filter pigments, but there is no systemic exposure given the proven non-penetration" "Examination must be done on a substance by substance basis and no comments can be made in general for cosmetics. If there is no penetration, then there cannot be any exposure either (zinc oxide, titanium dioxide)" "Generally speaking the question is trivial: when nanomaterials are contained in cosmetics and pharmaceutical products, then there is also exposure. The fact that there is exposure does not, however, mean that there is also a hazard and, by extension a risk linked to exposure. According to the results of "NanoDerm", nanoparticles do not penetrate healthy skin. Medicinal products are governed by a strict marketing authorisation procedure" "Titanium oxide zinc dioxide intake through skin/hair roots" "Possible effects depend very much on the materials. The nanodelivery systems currently on the market are biodegradable, i.e. they are converted in the skin by enzymes and do not constitute a risk. "
Science	"There are no cosmetics without 'nanoparticles'" "Conventional systems are not a concern as long as the critical particle size is not undercut" "Exposure to the most diverse materials: copper, zinc oxide, silver, titanium dioxide, fullerenes" "If the nanomaterials in cosmetic nanoproducts can penetrate the skin and circulate in blood, then it must be examined whether these nanomaterials - given their special properties - can lead to oxidative stress or to other proinflammatory (allergic) reactions. In the case of pharmaceutical nanoproducts the comprehensive safety requirements to be met by medicinal products should be sufficient. However, here too, the specific properties of nanomaterials and their interaction with biological tissue should be taken into account" "The skin is a good barrier but an internal burden (e.g. fullerenes) can also result from lipophilic substances in creams. The anti-oxidative effect of fullerenes has not been clearly proven"
NGO/trade union	"Autoimmune processes, increase in allergies, inflammations" "Allergies and intolerances" "It depends whether degradable or non-degradable nanomaterials are used. In the case of non-degradable materials (e.g. fullerenes) there is an elevated risk of exposure down to crossing of the blood-brain barrier"
Public authority/ politics	"Extensive absorption of toxic materials"
Networks	"Nanoparticles can – quasi as carriers – promote the passage of specific substances through the skin and thus the "chemical substance risk" takes on a new dimension – it must be assessed at all events for each specific substance"
Insurers	"Passage to cells and long-term accumulation there, toxic effects so far disputed"

5.2.7 Estimation of potential harmful effects of nanotechnology applications in the area of food

The experts are of the opinion that most of the nanotechnology applications in the food area do not constitute any harmful effects (Fig. 37). Particularly when it comes to the use of nanoparticulate silicon dioxide as a trickling aid or as a thickening agent the majority of experts do not see any health problems (46% and 43% of experts). Only the application of silver nanoparticles in food is seen by the majority of experts as having low harmful effects (26%).

Fig. 37: Estimation of potential harmful effects of nanoproducts from the area of food by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

In the second survey round the experts' assessments remained relatively constant in terms of their weighting (Table 40). The values were slightly higher. This effect is found above all for the nanosilver application where 38% of experts now deem it to have a low and 33% an average toxic potential.

Table 40: Estimation of potential harmful effects of nanoproducts from the area of food by Delphi experts (comparison survey Round 1 with survey Round 2)

	Survey round (number of responses)	None (%)	Low (%)	Average (%)	High (%)	Don't know (%)
L3: Silicon dioxide as a trickling aid	R1 (n=46)	46	11	7	7	30
	R2 (n=39)	46	13	3	3	35
L4: Titanium dioxide for coating	R1 (n=48)	27	15	10	4	44
	R2 (n=38)	32	21	5	8	34
L6: Nanoscale micelles for anti-oxidant agents	R1 (n=43)	28	14	7	2	49
	R2 (n=37)	41	16	5	3	35
L7: Silver to boost the immune system	R1 (n=42)	12	26	24	7	31
	R2 (n=36)	11	39	33	3	14

Explanation: percentages rounded up

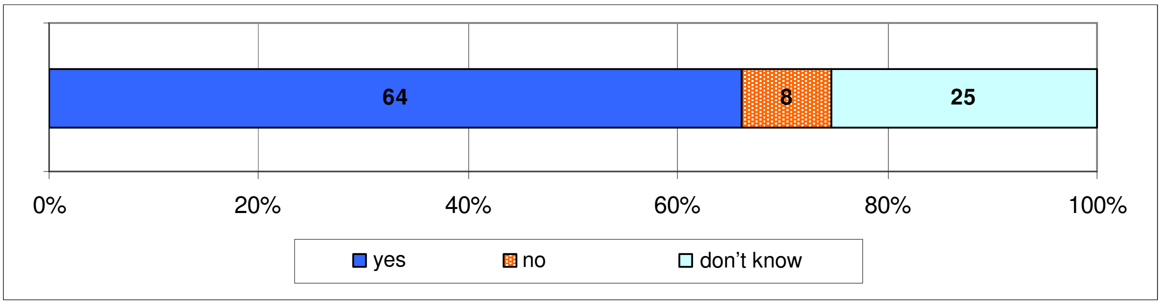
5.2.8 Exposure to nanomaterials in food and food supplements

In conjunction with possible or existing nanotechnology applications in food and food supplements, the experts were presented with the following theory:

> *"Do you expect consumers to be exposed to nanomaterials in food and food supplements? If so, what effects do you expect? Can you attribute specific effects to specific materials?"*

In their responses 64% of respondents confirmed that consumers are exposed to nanomaterials (see Fig. 38). Based on the comments this high percentage mainly results from the fact that exposure is generally intended in this application area.

Fig. 38: Estimation of exposure of consumers to nanomaterials in food and food supplements (n= 61 responses)



Explanation: percentages rounded up

When it comes to the assessment of effects, major differences can be identified between the stakeholders. The comments show that not all the applications are deemed to be safe (Table 41). Whereas none of the comments from industry mentions any negative effects but stress the health-promoting effects, the group of scientists describe potential harmful effects. All of the NGOs assume that negative effects are rather to be expected. Here, a selection of highly detailed comments contain a great deal of information or were made several times over.

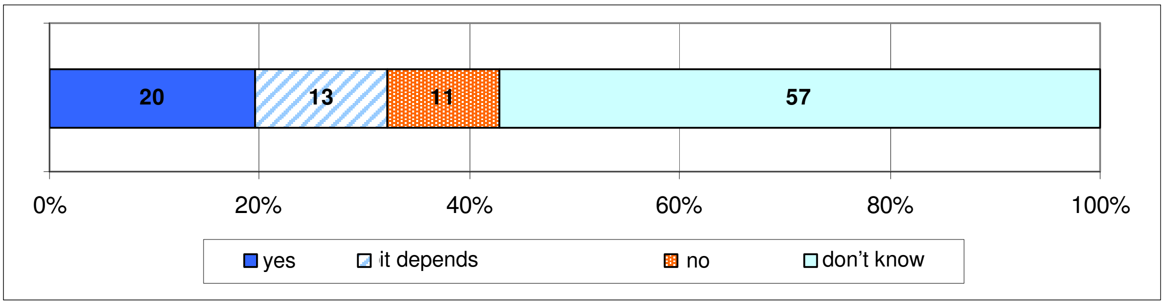
Table 41: Estimation of consumer exposure to nanomaterials in food and food supplements

Industry	“No effect (milk contains nanoparticles)” “In food, in particular functional food, fortified food and food supplements there are bound to be substances with health-promoting effects (health ingredients) like “formulated” vitamins, carotinoids and other substances in order to achieve sufficient stability, easier use in the food and good bioavailability. Formulation means giving the substance a protective sheath which is for instance water soluble. Substances in formulated form are generally present as > 100 nm particles. During digestion the particles are dissolved and the encapsulated substances are ingested as individual molecules, as is customary during digestion by the intestines. No negative health effects are to be expected from formulations nor are there reports of any. Quite the contrary, the formulation improves bioavailability.” “No effects in the case of approved materials” “No negative health effects because of marketing authorisation and safety requirements”
Science	“Consumers have been exposed for a long time (disperse food additives, disperse food systems themselves). Size-specific negative effects have not been identified or attributed as far as I know up to now” “For conventional systems like SiO_2 no concerns; caution in the case of other materials; various risks linked to translocation in various organs” “As nanomaterials - because of the specific properties - can be absorbed in the gastrointestinal tract and circulate in blood, it must be examined whether these nanomaterials can lead because of these special properties to oxidative stress or to other pro-inflammatory (allergic) reactions” “Aerosil has been broken down for a long time in food” “Modulation of bioavailability as well as improvement and reduction are feasible; hypervitaminosis and hypovitaminosis in the case of a poor diet; effects on intestinal flora” “Induction of pro-inflammatory status, interaction with genome, systemic translocation“
NGO/trade union	“Autoimmune processes, allergies, inflammation” “Allergies and intolerances” “Oral intake of nanoparticles: risk of inflammation, perhaps of accumulation in the organs”
Public authority/politics	“Polymers and by-products of packaging material could migrate to food”
Networks	“If inorganic, non-soluble particles are involved which remain in the body” “I would not see any risk that goes beyond the chemistry of the substances – in the case of natural substances too”
Insurers	“ Effects probably rather low”

5.2.9 Nanotechnology applications with fullerenes

Given the references to the potential harmful effects linked to the use of fullerenes in cosmetics from Round 1, this topic was assigned special status in Round 2 and also examined at the expert workshop. The importance of this question is confirmed by the fact that all 56 participants in Round 2 answered this question. What is noticeable in this area is the very high level of non-knowledge (Fig. 39).

Fig. 39: Estimation of systemic exposure to fullerenes in conjunction with dermal contact (n=56 responses)



Explanation: percentages rounded up

One additional question was put and it addressed whether experts expect any possible harmful effects. Despite the high proportion of non-knowledge more than 87% of respondents expect a possible harmful effect, i.e. in this case 49 out of 56 respondents. At the expert workshop the low level of knowledge about fullerenes was critically discussed and the question was asked whether a discussion at this early point in time made sense as risk research was still in the early stages. In the course of the discussion, however, some references to research work were identified. An overview of risk studies already published on the subject of fullerenes can be accessed on the website "Nanotechnology and Risk Resources" of Wisconsin University on: http://www.nsec.wisc.edu/NanoRisks/NS--NanoRisks.php .

5.2.10 Nanotechnology applications with silver

The experts at the workshop confirmed the antibacterial effect of silver applications. As a rule corresponding surface layers are applied galvanically and are mainly located in the micrometer range. However, the same technology can be used in the nanometre range. In the case of textiles silver nanoparticles are mainly glued with pigment binders to the fibres or incorporated into polymer fibres. In the latter case no abrasion is to be expected. However, attention was drawn to the indirect effect of elevated allergic potential through the antimicrobial effect and the possible ensuing increase in sensitisations in conjunction with permanent applications.

The experts expressly pointed out the difference between the use of silver nanoparticles and the electrostatic effects caused by the separation of silver ions e.g. in washing machines. It was stressed that this effect was not a nanoeffect and that no silver nanoparticles can reach the environment via this pathway. Nonetheless, the experts were of the opinion that the modes of action of silver ions in washing water, during processing in waste water treatment plants and the ensuing impact on the environment should be examined more comprehensively.

In conjunction with oral exposure to nanoscale silver from food supplements or abrasion, the experts do not expect any clear antibacterial effects of silver nanoparticles in the human intestines as the level of exposure is probably exceedingly low.

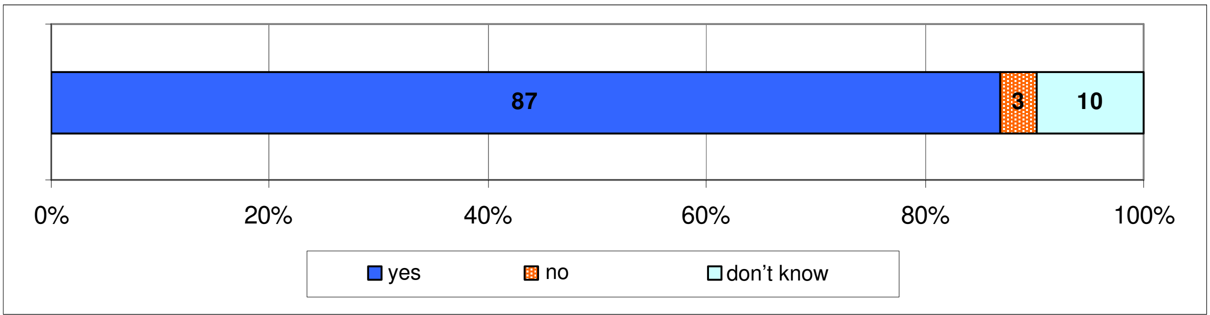
5.2.11 Application of nanomaterials in aerosols

Although the inhalation of nanoparticles is probably more a problem of health and safety at work, there may also be possible situations in which consumers could inhale nanomaterials. In the context of one theory, the experts were therefore asked:

> *“Do you expect consumers to be exposed through the use of nanomaterials in aerosols? If so, what effects do you expect? Can you attribute specific effects to specific materials? “*

86.9 % of experts expect consumer exposure (Fig. 40). What is interesting is that this theory explicitly asked about consumer exposure.

Fig. 40: Estimation of consumer exposure to aerosols (n= 61 responses)



Explanation: percentages rounded up

Concerning the effects from the use of nanomaterials in aerosols, 48% (just under half) of the respondents did not make any further comments (see Table 42).

Table 42: Consumer exposure to aerosols (qualitative comments)

Industry	“Of course there is exposure during spraying, and inhalation is in principle possible” “I do not know whether aerosols contain any nanomaterials. Not all products bearing the wording “nano” also contain “nano”. At all events exposure must be examined on a case-by-case basis. General statements are not possible.” “Irritations, oedema, inflammations, under certain circumstances cancer “
Science	“Nano-impregnating sprays” “Effect of surfactants” “I do not know of any nanomaterials that are actually used in aerosols” “Intake via the lungs, inflammation processes, translocation in other organs” “If nanomaterials in aerosols can be inhaled by humans either during work processes or from the environment it must be examined whether these nanomaterials - because of their special characteristics - lead to oxidative stress or other pro- inflammatory (allergic) reactions” “Toxicological fibre effects of carbon nanotubes, similar to those of asbestos fibres” “Induction of pro-inflammatory status e.g. by means of oxidative stress, systemic translocation“
NGO/trade union	“Respiratory disorders” “Oral intake of nanoparticles: inflammation in the alveoli, transfer to the blood system“
Public authorities/politics	“When used in sprays in pressurised form fine aerosols are formed which can easily be inhaled“
Networks	“(…) amongst other things allergies, disruptions of the immune system etc.” “Particles can cross through the lungs and accumulate in adjacent lymph nodes – cancer risk differs for each substance“
Insurers	“Indeed the situation in which the highest exposure is to be expected is in the private sphere. The basic knowledge required to make statements about effects is not available“

5.3 Consumer acceptance of nanoproducts

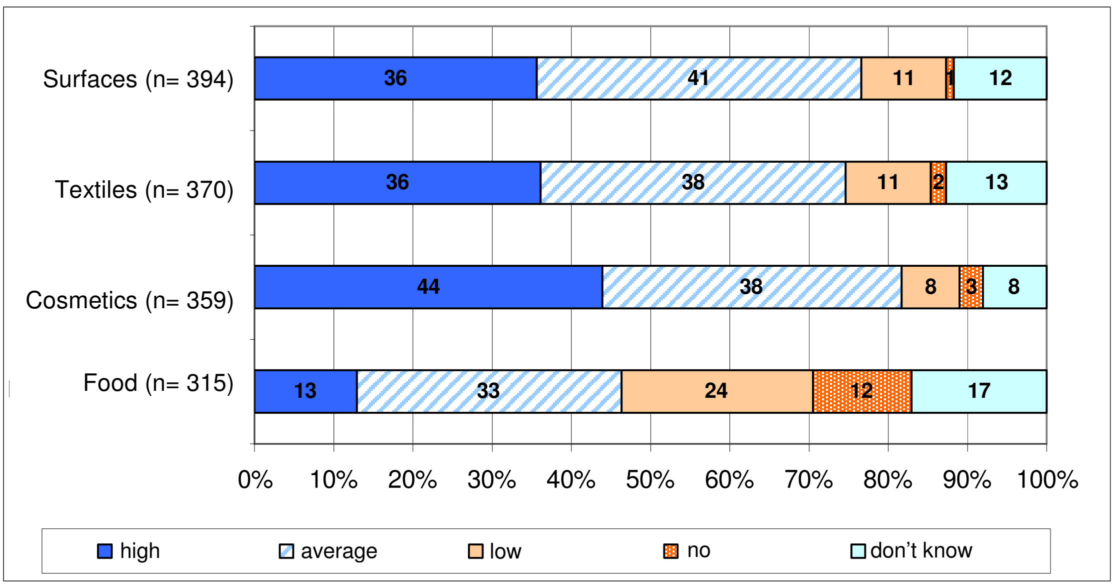
5.3.1 Estimation of consumer acceptance of nanoproducts overall

The rapid development of nanotechnology and the growing importance of this technology for consumers' everyday life have not attracted major attention from the public at large up to now. The social - and for the vast majority of population - also the individual opinion-shaping process on this subject is in its teething stages. Debates on nanotechnology are mainly being conducted at the present time by experts in scientific circles. Politicians and the informed public at large are, nonetheless, aware of the fact that a technology, like nanotechnology, which extends so far into the future and impinges on so many areas of daily life, should be examined in terms of its acceptance by users and consumers.

The 30 application examples were presented once again for assessment to the experts. The estimation of consumer acceptance was to be rated using the criteria "high", "average", "low" and "no" as well as the category "don't know". In a second survey round only those application were examined which had been assigned low to average consumer acceptance in Round 1. Before consumer acceptance for the various applications is examined in detail, it is presented here by way of comparison across the applications. For this analysis the number of ratings like, for instance, "high" or "average" were added together for all the application examples in one area.

For most nanotechnology applications the experts anticipate high consumer acceptance (Fig. 41). Experts expect the highest acceptance for nanocosmetics. Here 82% believe that these products will enjoy average to high acceptance amongst consumers. The expectations are similarly high concerning consumer acceptance for the applications textiles and surface coatings. Here 74% and 77% respectively of the respondents are of the opinion that nanoapplications will enjoy average to high consumer acceptance. In the case of nanotechnology applications in the food area the proportion of sceptical attitudes increases. 46% of experts still expect average to high consumer acceptance for this area. But 36% expect no or low acceptance by consumers of these applications. The sceptical assessment of consumer acceptance in the area of food is 3 times higher than in all other areas.

Fig. 41: Estimation of consumer acceptance of nanoproducts by Delphi experts. The "n" in brackets is the sum of mentions for the individual applications covered for the four areas surfaces (8 individual applications), textiles (8 individual applications), cosmetics (7 individual applications) and food (7 individual applications)



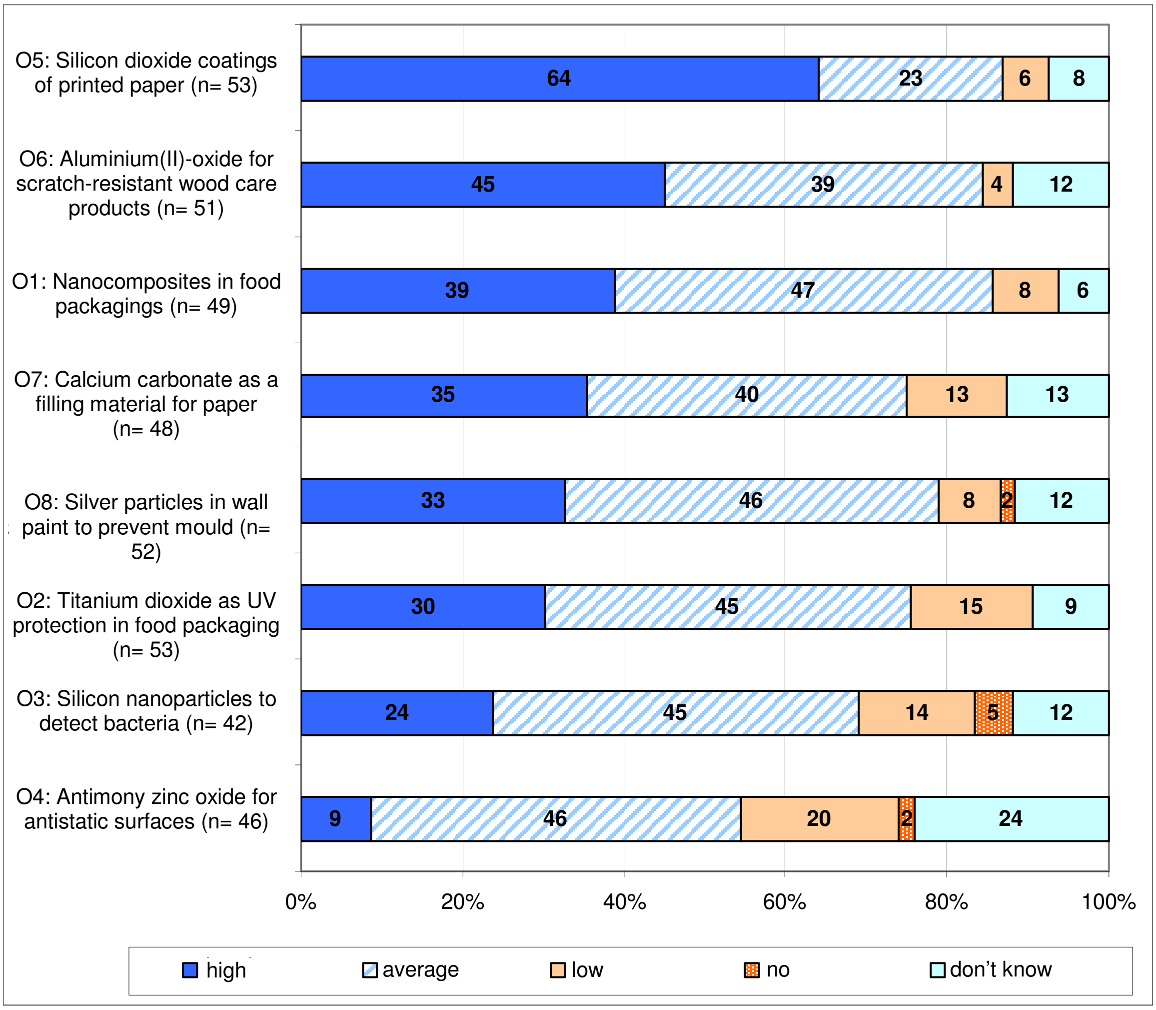
Explanation: percentages rounded up

The acceptance expectations may, however, vary considerably for individual applications within the various areas as shown in the following sections.

5.3.2 Estimation of consumer acceptance of nanoproducts in the area of surfaces

For almost all nanotechnology applications in the area of surface coatings the experts expect average to high acceptance by consumers (Fig. 42). For 6 out of 8 application examples the corresponding values are over 75%. The highest acceptance value is attributed to the silicon dioxide coating of printer paper. Here 87% of experts expect to see average to high consumer acceptance. Experts expect the lowest acceptance rates in the area of surfaces for antimony zinc oxide coatings aiming to give surfaces anti-static properties.

Fig. 42: Estimation of the consumer acceptance of nanoproducts from the area surfaces by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

Four of the eight application examples were presented for a second time to the experts in Delphi Round 2. There was no change in the trend of the results (Table 43). There was, however, a shift towards higher acceptance expectations and the number of "don't know" responses decreased.

Table 43: Estimation of consumer acceptance of nanoproducts from the area of surfaces by Delphi experts (comparison survey Round 1 with survey Round 2)

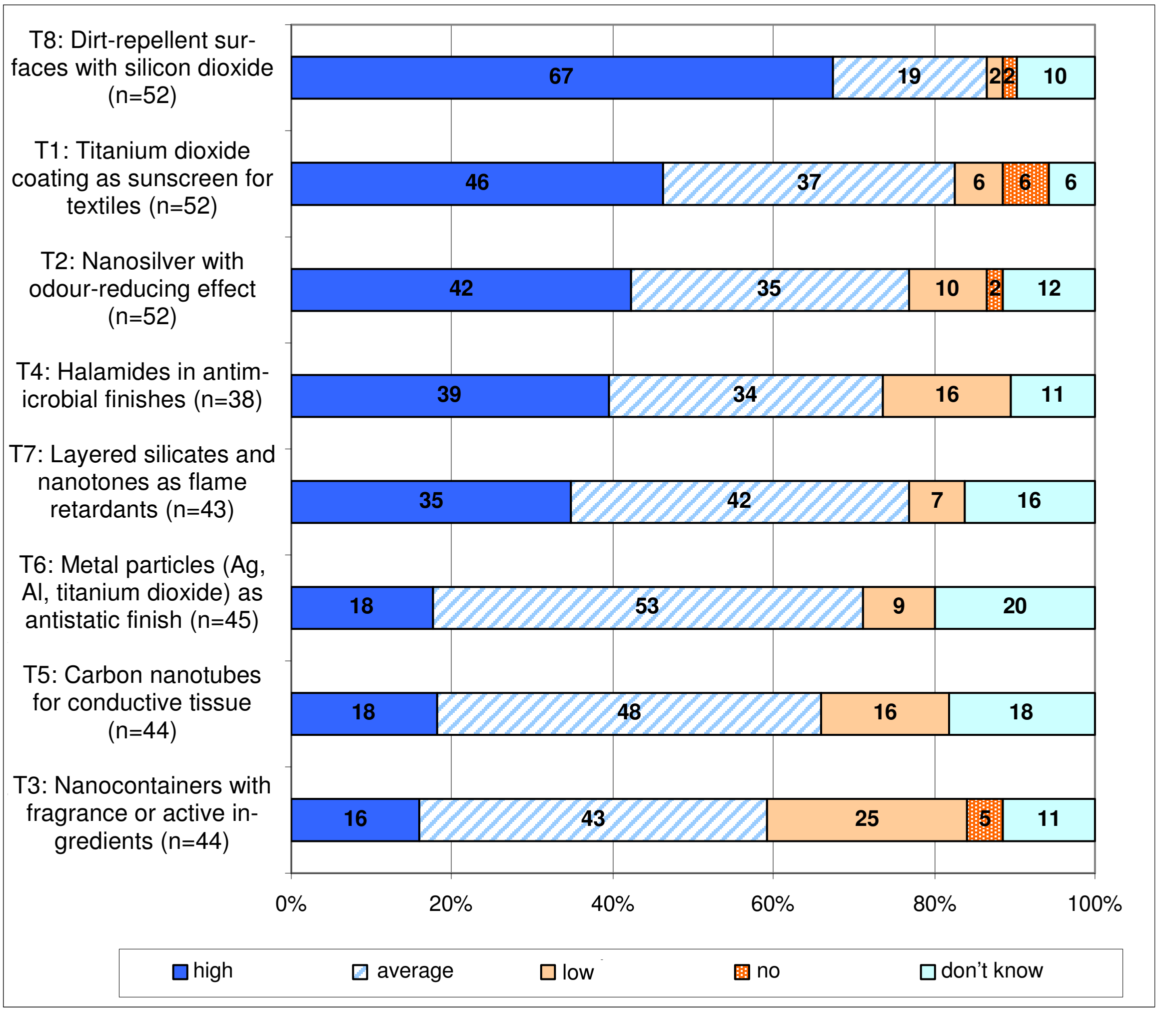
	Survey round (number of responses)	None (%)	Low (%)	Average (%)	High (%)	Don't know (%)
O3: Silicon nanoparticles to detect bacteria	R1 (n=42)	24	45	14	5	12
	R2 (n=37)	30	54	11	3	2
O4: Antimony zinc oxide for antistatic surfaces	R1 (n=46)	9	46	20	2	24
	R2 (n=37)	14	57	14	0	15
O6: Aluminium(Al_2O_3) for scratch-resistant wood care products	R1 (n=51)	45	39	4	0	12
	R2 (n=39)	62	33	0	0	5
O8: Silver particles in wall paint to prevent mould	R1 (n=52)	33	46	8	2	12
	R2 (n=40)	43	50	5	0	2

Explanation: percentages rounded up

5.3.3 Estimation of consumer acceptance of nanoproducts in the area of textiles

For nanoapplications in the area of textiles the experts expect similarly high acceptance as for surface applications. For six out of eight applications more than 70% of respondents expect average to high acceptance amongst consumers (Fig. 43). Dirt-repellent textiles and sunscreen textiles fare best. The values for average to high acceptance expectations are 86% and 83% respectively. 77% of experts expect average to high consumer acceptance for the use of nanosilver in the fibres of socks, shoes or cloths in order to suppress unpleasant odours. The respondents expect the lowest acceptance for the use of nanocontainers with fragrances and active ingredients in clothing but also in carpets and settees. Here 30% of experts do not expect any or only low consumer acceptance.

Fig. 43: Estimation of consumer acceptance of nanoproducts from the area textiles by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

In the second survey round the experts were again asked to assess four application examples from the area of textiles. In the case of the nanosilver application to suppress unpleasant odours and the use of silicon dioxide to create dirt-repellent surfaces, the proportion of expectations of high acceptance rose to over 10% (Table 44).

Table 44: Estimation of consumer acceptance of nanoproducts from the area textiles by Delphi experts (comparison survey Round 1 with survey Round 2))

	Survey round (number of responses)	None (%)	Low (%)	Average (%)	High (%)	Don't know (%)
T2: Nanosilver with odour-reducing effect	R1 (n=52)	42	35	10	2	12
	R2 (n=41)	56	34	5	0	5
T3: Nanocontainers with fragrance or active ingredients	R1 (n=44)	16	43	25	5	11
	R2 (n=36)	6	56	31	0	7
T4: Halamides in antimicrobial finishes	R1 (n=38)	39	34	16	0	11
	R2 (n=32)	38	56	0	0	6
T8: Dirt-repellent surfaces with silicon dioxide	R1 (n=52)	67	19	2	2	10
	R2 (n=38)	79	21	0	0	0

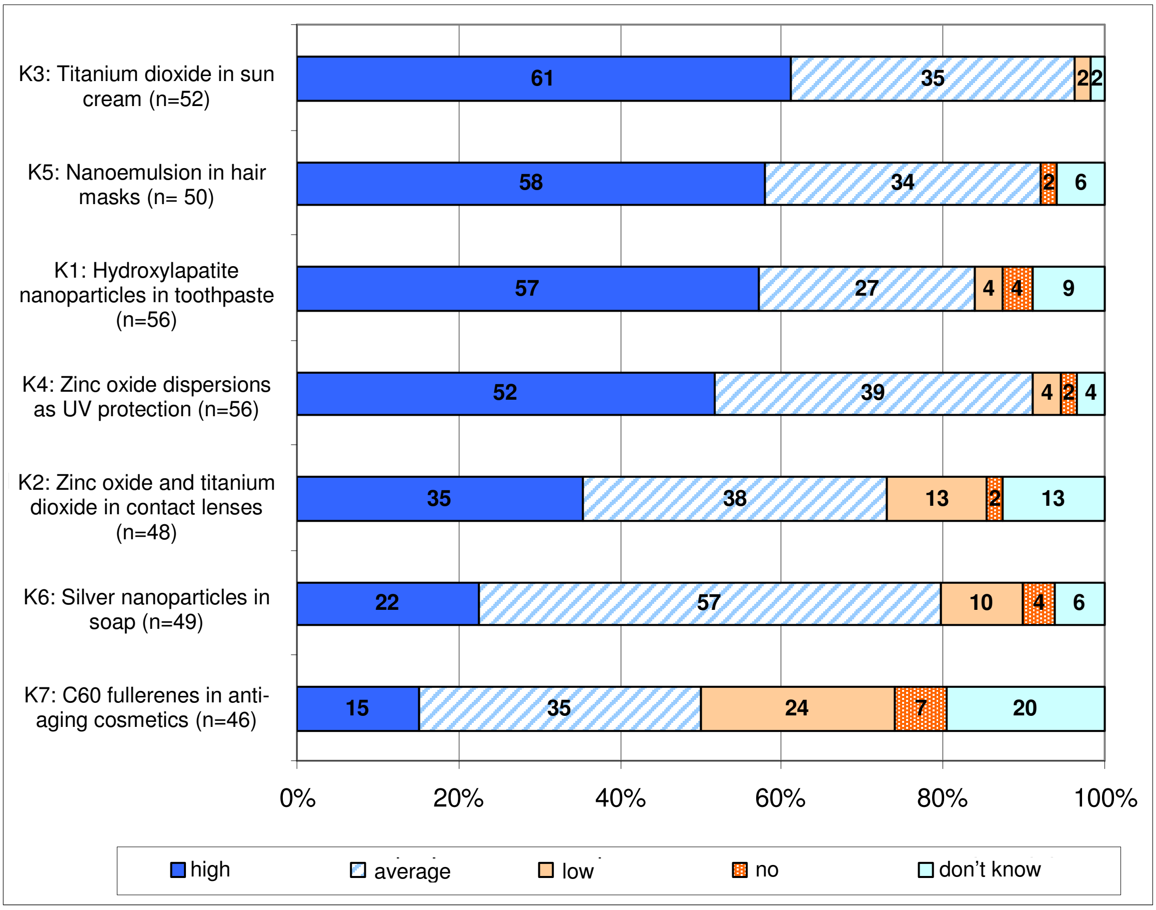
Explanation: percentages rounded up

The proportion of experts who expect high acceptance amongst consumers fell in the case of the use of nanocontainers to integrate fragrances and active ingredients into textiles and the use of halamides to coat occupational clothing for medical staff or farmers.

5.3.4 Estimation of consumer acceptance of nanoproducts in the area of cosmetics

In the area of cosmetic applications the experts assume average to high acceptance (Fig. 44). The expectations are particularly high when it comes to the use of titanium dioxide and zinc nanoparticles for UV protection (96% and 91% respectively of experts expect average to high consumer acceptance). Regarding the use of silver nanoparticles in soap for cleaning and disinfecting the skin, the proportion of experts who assume a high consumer acceptance fell to 22% but a further 57% of experts assume at least average acceptance. The lowest acceptance values in this group are assigned to an application where C60 fullerenes are used as anti-oxidants in creams.

Fig. 44: Estimation of consumer acceptance of nanoproducts from the area of cosmetics by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

The silver and the C60 examples were presented again to the experts in Round 2. There were scarcely any changes in acceptance expectations (Table 45).

Table 45: Estimation of consumer acceptance of nanoproducts from the area of cosmetics by Delphi experts (comparison survey Round 1 with survey Round 2)

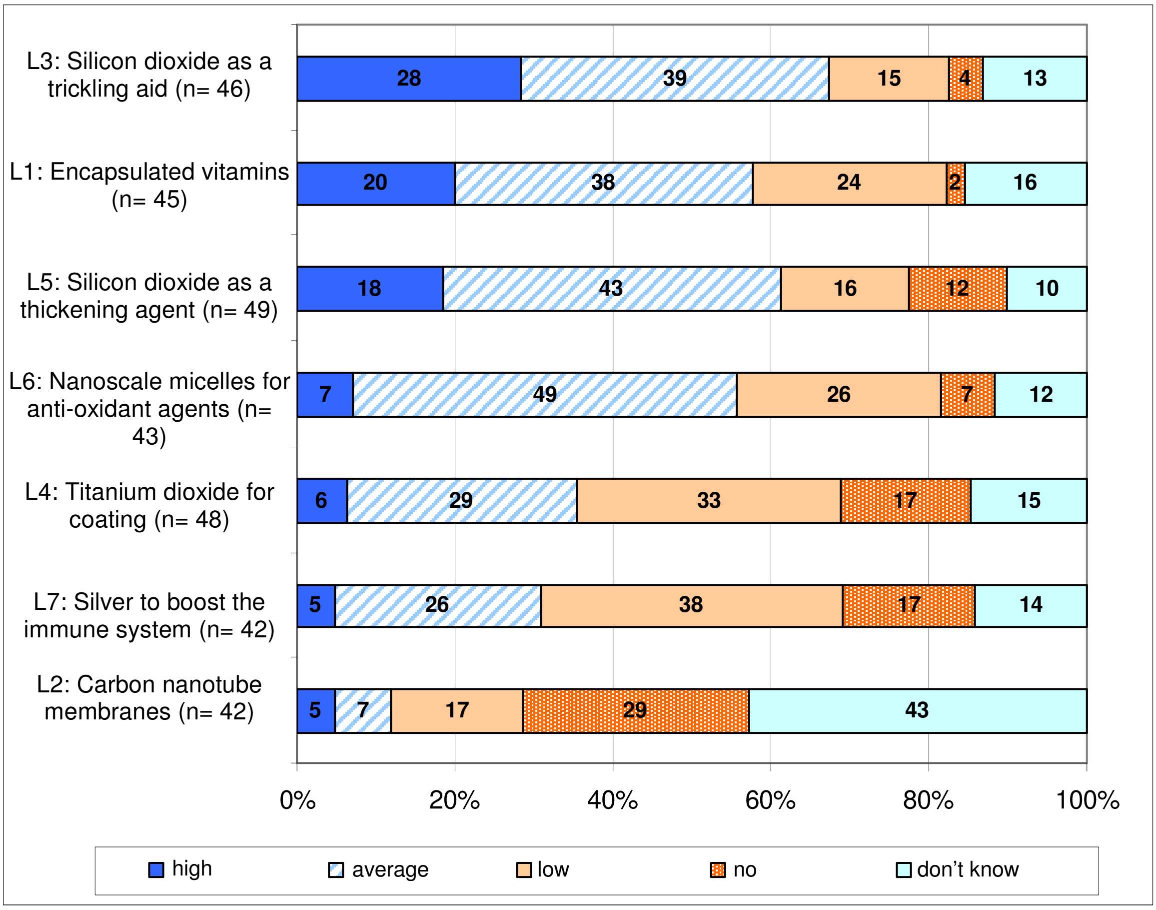
	Survey round (number of responses)	None (%)	Low (%)	Average (%)	High (%)	Don't know (%)
K6: Silver nanoparticles in soap	R1 (n=47)	22	57	10	4	6
	R2 (n=42)	26	55	12	0	7
K7: C60 fullerenes in anti-aging cosmetics	R1 (n=46)	15	35	24	7	20
	R2 (n=41)	10	39	37	0	14

Explanation: percentages rounded up

5.3.5 Estimation of consumer acceptance of nanoproducts in the area of food

The expectations of average to high consumer acceptance by the experts fall considerably in the area of food. For nanoapplications in the areas of surfaces, textiles and cosmetics at best 80% and more of the experts expect average to high consumer acceptance. In the case of the food applications with the most positive ratings (nanoparticulate silicon dioxide as a trickling aid) only 67% of experts anticipate average to high consumer acceptance (Fig. 45). Experts expect that consumers will tend to reject three applications: the use of titanium dioxide to coat chocolate bars, the use of silver nanoparticles dissolved in pure water to boost the immune system and the food technology use of carbon nanotubes to separate biomolecules with functional value. Overall the experts do not, however, predict any general rejection of products in the area of food.

Fig. 45: Estimation of consumer acceptance of products in the area of food by Delphi experts (number of responses in brackets)



Explanation: percentages rounded up

Once again in the second Delphi round four application examples were submitted to the experts for renewed assessment. In the case of the examples "silicon dioxide as a trickling agent", "nanoscale micelles for anti-oxidant agents in order to keep food fresh for longer" and "silver to boost the immune system", the proportion of experts who assume average consumer acceptance rose in some cases markedly (Table 46). When it comes to the use of titanium dioxide to coat chocolate bars, the majority of experts still only assumed low consumer acceptance.

Table 46: Estimation of consumer acceptance of nanoproducts from the food area by Delphi experts (comparison survey Round 1 with survey Round 2)

	Survey round (number of responses)	None (%)	Low (%)	Average (%)	High (%)	Don't know (%)
L3: Silicon dioxide as a trickling aid	R1 (n=46)	28	39	15	4	13
	R2 (n=39)	33	44	10	3	10
L4: Titanium dioxide for coating	R1 (n=48)	6	29	33	17	15
	R2 (n=38)	5	37	47	3	8
L6: Nanoscale micelles for anti-oxidant agents	R1 (n=43)	7	49	26	7	12
	R2 (n=37)	5	70	19	0	6
L7: Silver to strengthen immune	R1 (n=42)	5	26	38	17	14
	R2 (n=36)	0	39	42	6	13

Explanation: percentages rounded up

5.4 Other assessment elements to characterise risks

To assess complex and/or uncertain risks, the Scientific Advisory Committee of the federal government Global Environmental Changes (WBGU) in its annual report 1998 "World in Change: Action strategies to tackle global environmental risks" proposed a more comprehensive concept in which eight criteria for the analysis of environmental risks are explicitly mentioned:

- Scale of damage: quantitative scale of damage (deaths, injuries, costs)
- Probability of occurrence: first occurrence of damage, incidence/frequency of occurrence of damage, chronic damage
- Ubiquity: spatial distribution of potential damage
- Persistence: temporal spread of potential damage
- Reversibility: recreation of state prior to first occurrence of damage
- Delaying effect: latency between incident and occurrence of damage
- Uncertainty: total indicator for various uncertainty components: lack of knowledge (gaps in knowledge about possible consequences of damage and probability of occurrence), uncertainty (difficulty in the case of largely known scale of damage of making reliable statements about the probable occurrence of damage)
- Globalisation potential: potential for social conflicts and psychological reactions as a consequence of the infringement of individual, social or cultural interests in values

In the BfR expert Delphi procedure on nanotechnology, several of these criteria were included in the survey:

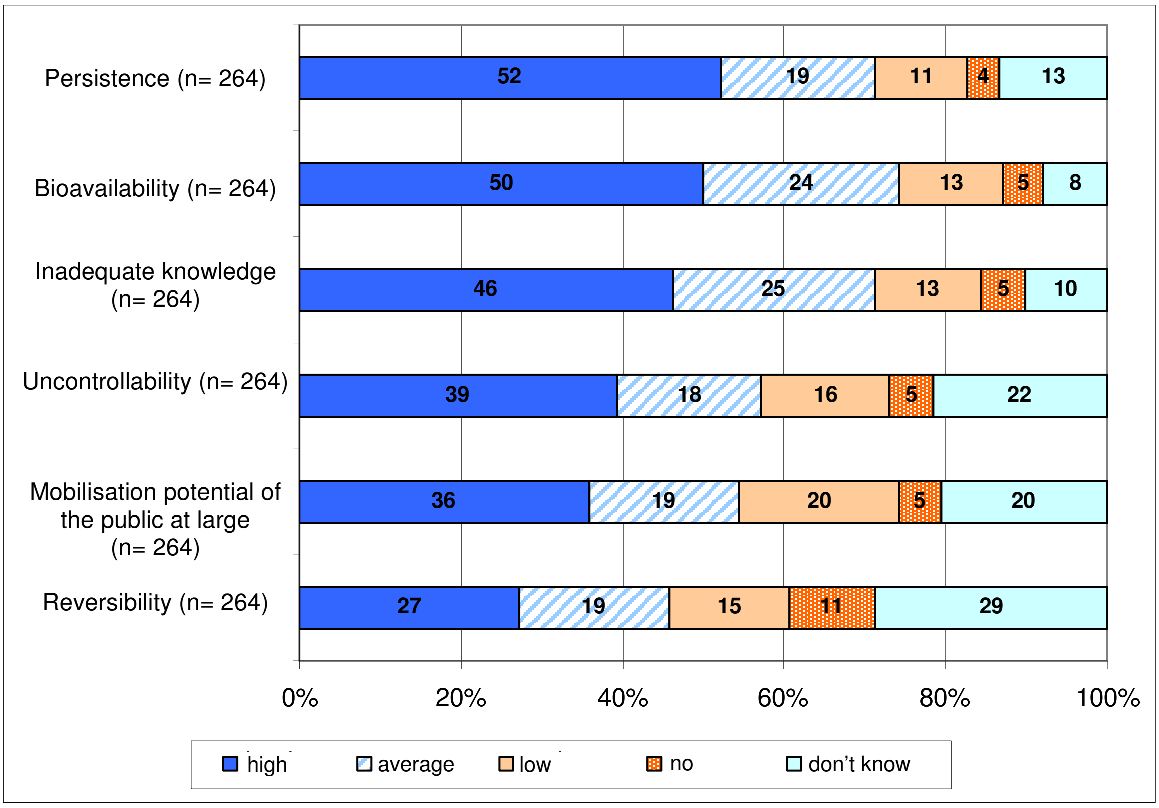
- Persistence
- Reversibility
- Inadequate knowledge
- Mobilisation potential of the public at large

Furthermore, questions were asked about risk controllability. Controllability is reflected in the above-mentioned methodology firstly in the criteria of ubiquity and persistence from the physical angle and in the criterion of mobilisation from its social side. Finally, questions were asked about bioavailability which can be used as a marker for inner exposure to nanoparticles.

5.4.1 Importance of other risk assessment elements of nanoproducts

In one section the experts were asked to indicate the importance of various other elements for the risk assessment of nanotechnology applications in the areas food, cosmetics, textiles and surfaces. Fig. 48 sums up the responses across all 30 nanoapplications covered and shows that a majority of the experts do indeed attribute major importance to these aspects. The assessments mainly achieve values in the range of between 40% and 50%. In particular "persistence" and "bioavailability" were elements which, in the opinion of the experts, should definitely be included in risk assessments. The experts attribute the lowest importance to the aspect "reversibility" when it comes to risk characterisation.

Fig. 46: Importance of other assessment elements for the characterisation of risks across all applications (Round 1). The "n" in brackets indicates the sum of mentions from the individual applications covered for the four areas surfaces (8 individual applications), textiles (8 individual applications), cosmetics (7 individual applications) and food (7 individual applications)



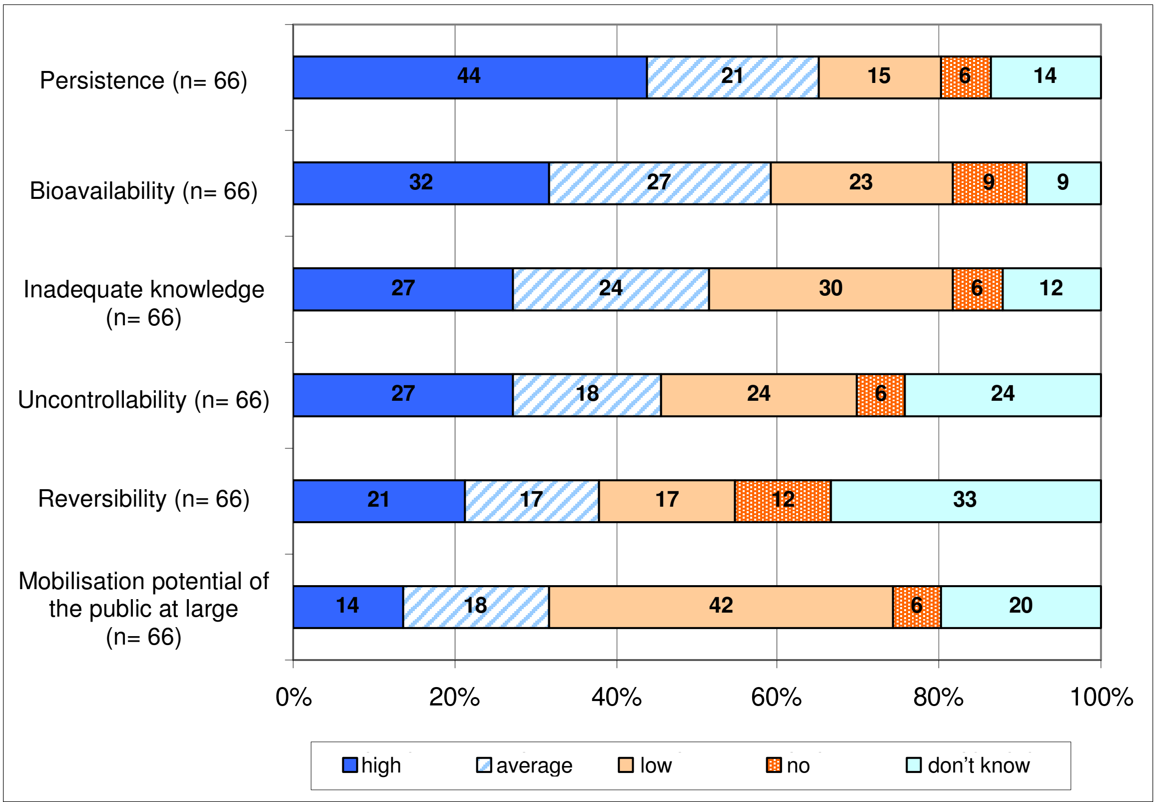
Explanation: percentages rounded up

A glance at the individual applications in the following chapters reveals that despite the generally positive attitude the assessment elements per application are weighted differently. These elements seem to have greater importance for some applications than for others.

5.4.2 Importance of other risk assessment elements for nanoproducts in the area of surfaces

Out of the additional criteria covered in the survey, “persistence” is the most important one in the opinion of the experts which should be used for the risk assessment of surface applications (Fig. 47). Overall 65% of respondents estimate the importance of this criterion to be between average and high. For the criteria “bioavailability” and “inadequate knowledge” more than 50% of experts are still of the opinion that these criteria are of average to high importance for risk assessment in this application area. The “mobilisation potential of the public at large” has the lowest importance for the risk assessment of nanoproducts in the area of surface coatings in the opinion of the experts.

Fig. 47: Importance of other assessment elements for the characterisation of risks of nanoapplications in the area of surfaces (Round 1) (number of responses in brackets)

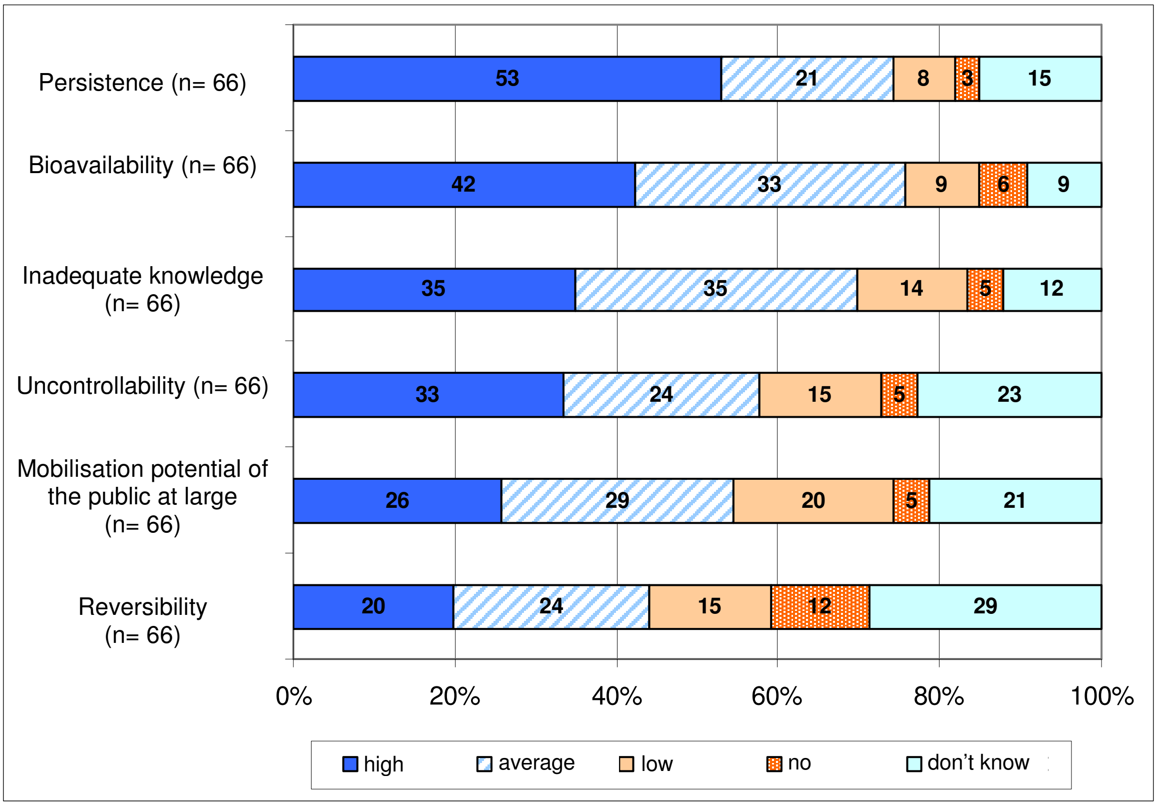


Explanation: percentages rounded up

5.4.3 Importance of other risk assessment elements for nanoproducts in the area of textiles

Similar to the situation for nanotechnology applications in the area of surface coatings, the greatest importance is attributed in the area of textiles to the criteria “persistence”, “bioavailability” and “inadequate knowledge” (Fig. 48). 70% and more of the respondents are of the opinion that these criteria should also be included in a risk assessment. In the case of nanoapplications in the area of textiles the criterion “reversibility” has the lowest importance for risk assessment. The criterion “mobilisation potential” compared with surface coatings has increased by one place. In the case of nanotextiles 55% of the respondents are of the opinion that this criterion has average to high importance for risk assessment.

Fig. 48: Importance of other assessment elements for the characterisation of risks of nanoapplications in the area of textiles (Round 1) (number of responses in brackets)



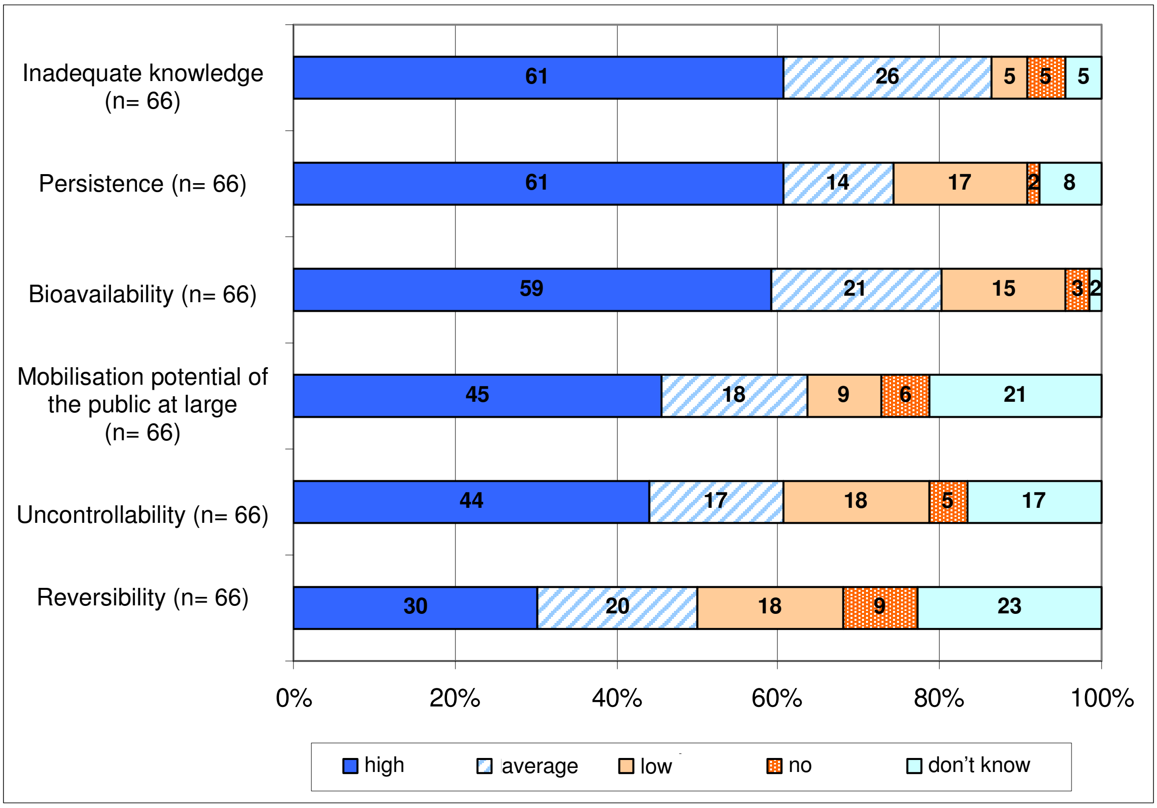
Explanation: percentages rounded up

5.4.4 Importance of other risk assessment elements for nanoproducts in the area of cosmetic applications

Likewise for nanoapplications in the area of cosmetics the greatest importance is again attributed to the three criteria “persistence”, “bioavailability” and “inadequate knowledge” (Fig. 49). But this time the sequence is different. 87% of experts are of the opinion that the additional criterion “inadequate knowledge” has average to high importance for risk assessment in this area. The criteria “persistence” and “bioavailability” follow in second and third place in the ranking of importance. The criterion “mobilisation potential” follows in fourth place. 63% of experts believe that that this criterion enjoys average to high importance for risk assessment. Once again “reversibility” is attributed the least importance.

The relevance of the criteria covered is rated far higher in the area of cosmetic applications than in the areas textiles and surfaces. The average values for “high importance” across all factors increase in the area of cosmetics to 52% whereas in the area of textiles they only reached 36% and 26% in the area of surfaces.

Fig. 49: Importance of other assessment elements for the characterisation of risks of nanoapplications in the area of cosmetics (Round 1) (number of responses in brackets)

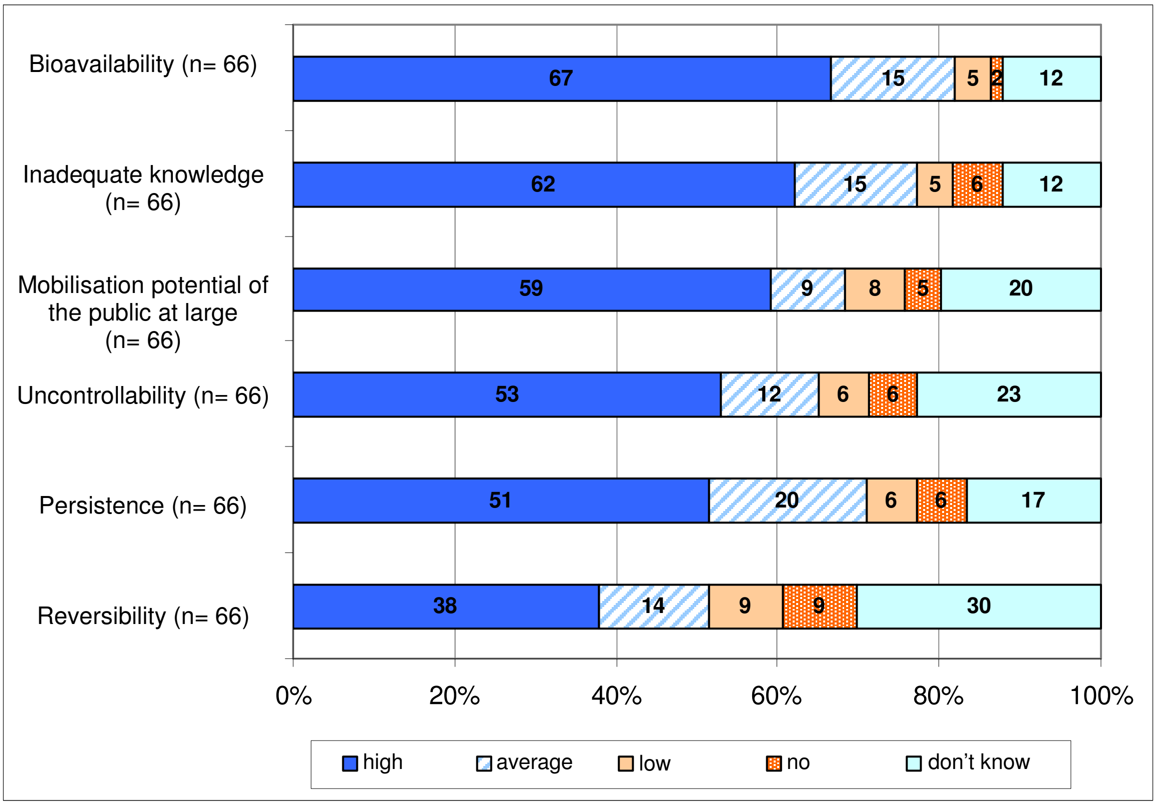


Explanation: percentages rounded up

5.4.5 Importance of other risk assessment elements for nanoproducts in the area of food

There is a major shift in some cases for nanotechnology applications in the area of food when it comes to the importance of other risk assessment criteria (Fig. 50). For the first time the criterion "mobilisation potential of the public at large" ranks amongst the three most important criteria. 68% of respondents are of the opinion that this criterion is of average to high importance for risk assessment. Experts put the criterion "bioavailability" in first place. 82% of them believe that this criterion enjoys average to high importance for risk assessment. The criterion "inadequate knowledge" follows in second place. The criterion "persistence" that was still the most important additional assessment criterion in the applications surfaces and textiles is attributed lower importance in comparison in the area of food. Once again the relevance of the criteria covered for the risk assessment increases in the opinion of the experts and is deemed to be significantly higher than in the areas of textiles and surfaces. The average values for "high importance" across the criteria for surfaces were 26%, for textiles 36% and cosmetics 54%, whereas in the area of food they reach 58%.

Fig. 50: Importance of other assessment elements for the characterisation of risks of nanoapplications in the area of food (Round 1) (number of responses in brackets)



Explanation: percentages rounded up

5.5 Consequences for consumer protection

Although the experts tend to expect risk potential rather for the occupational health and safety area, consequences were also formulated in the ensuing expert workshop for consumer protection:

Basis

- Depending on their relevance for regulatory purposes, a hierarchy of product types should be established for the consumer area.
- Experts only expect minor health effects from nanocoated surfaces.
- Nanoapplications in the body surface area (food and packaging/cosmetics/textiles) should be given the highest priority as the chances of exposure and risk perception are the highest.

Information

- The collection of information on environmentally-related health protection and on the protection of emerging life is deemed to be important.
- Relevant information should be compiled: Which nanoproducts are on the market? What is their purpose? Documentation of safety evidence, mechanisms of action and possible side effects.
- Consumer information should be made available in a centralised manner.
- Labelling should be clear for consumers and there should be exact indications of substances (definition and standardisation/international harmonisation needed).

Substance-related measures for consumer protection

- The experts do not see any need for regulatory measures for nanoparticulate TiO_2, ZnO, or SiO2. The effects of the substances used are well documented and no systemic exposure is expected from with dermal application.
- Nanoproducts that contain fullerenes are seen as problematic by the experts. However, the products are not currently available on the market in Germany. It should be borne in mind that consumers could order cosmetics containing fullerenes on the Internet and this will then require regulatory measures.

5.6 Conclusion

Market relevance

- Experts expect the largest growth potential for nanoproducts in the area of surface coatings. For nanoproducts from the areas of textiles and cosmetics moderate growth is predicted. No major market development is expected for nanoproducts in the area of food.
- In all consumer applications of nanotechnologies the experts believe that products are already on or about to enter the market. Market availability is already seen especially for cosmetic nanoproducts but also for individual products from the area of food. The estimation of market maturity is generally accompanied by major uncertainties.

Possible harmful effects

- The experts do not think that overall harmful effects are to be expected from nanoproducts. 22 out of 30 products covered were classified by the majority as safe. When it comes to the use of nanomaterials in food, degradable or well-documented substances like SiO2 are deemed to be safe.
- Although the majority of experts think that abrasion from surface coatings and coated textiles is theoretically possible in nanoscale form too, no health risk is seen by the majority because of the low dose. Abrasion takes place above all during washing, hence without any direct inhalational, oral or dermal exposure of consumers. The environmental problems, by contrast, have not yet been elucidated.
- Seven out of 30 nanoproducts were attributed minor harmful effects (silver particles in wall paints to combat mould, halamides in antimicrobial finishes, carbon nanotubes for conductive tissue, metal particles as an antistatic finish, TiO_2 in sunscreens, silver nanoparticles in soap, silver nanoparticles in food supplements).
- Applications with silver are intended to have a slight toxic effect and a biocide effect is one of the material properties. Nevertheless, the experts see a need for additional research. The fact that the excessive use of silver in textiles and surfaces could exacerbate sensitisations or that resistances could develop is viewed critically.
- When it comes to the use of C60 fullerenes in anti-aging cosmetics, the experts expect harmful effects although the knowledge base for this estimation is limited.
- Aerosol applications with nanomaterials are viewed critically because elevated exposure is expected. There is no agreement in expert circles about which health effects are triggered by nanomaterials in aerosol sprays and whether nanomaterials are contained in the sprays at all.

Consumer acceptance

- Generally speaking experts expect high consumer acceptance for nanoproducts from the areas surface coatings, textiles and cosmetics. Problems of acceptance are expected for various nanoapplications in the area of food.

- In particular when it comes to the use of new nanomaterials (fullerenes, carbon nanotubes) the experts are sceptical whether consumers will accept them.

Additional risk assessment criteria

- Bioavailability of nanomaterials, their persistence and a generally inadequate knowledge base for these materials are the most important criteria which should be included in an extended risk assessment.
- The importance of the inclusion of additional assessment criteria for nanoproducts increases from surface coatings over textiles, cosmetics down to food.
- The closer the nanoproducts come in their intended use to the human body (surface coatings, textiles, cosmetics, food), the more important it is to include the criterion of “mobilisation potential of the public at large”, in the opinion of the experts, in risk assessment.

6 Risk regulation

Differentiated legislative and sub-legislative regulations are available for adequate risk containment. As the action options for risk containment are oriented towards and derived from the regulations, it is essential for research activities to be oriented towards and adjusted to the statutory framework conditions in order to be able to implement the research findings, if necessary, in concrete measures to protect man and his environment. In the public debate questions are asked about whether the current statutory provisions are sufficient or whether new laws are required. Given that at the present time the advice is to integrate provisions into the existing statutory framework and that no specific nano law is required, there is an even greater need to provide evidence for this by means of corresponding assessments within the framework of the law. It is unclear whether the greater involvement of non-commercial stakeholders or public institutions is necessary and possible in statutory procedures which like REACH are mainly the responsibility of manufacturers. Here there is a need for further clarification.

6.1 Nano-specific regulations

6.1.1 Existing statutory provisions

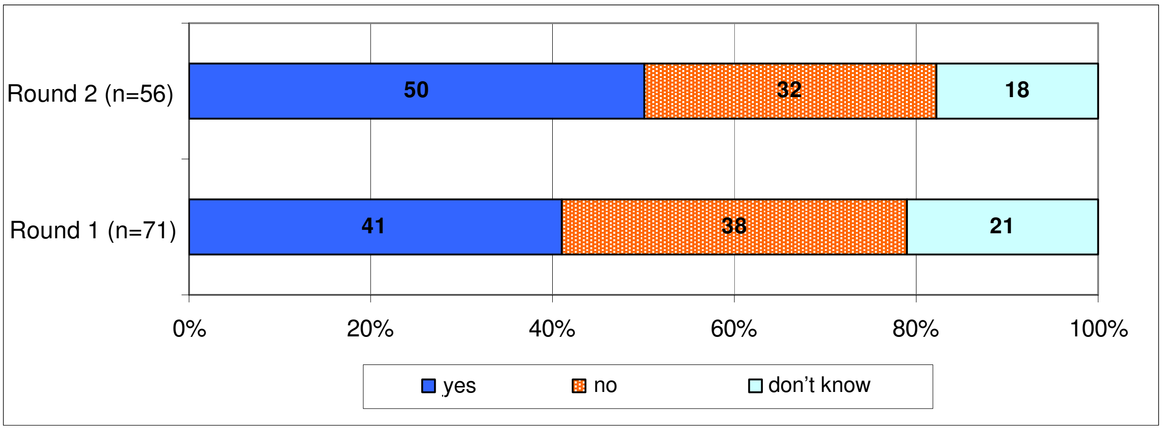
In order to document the need to regulate nanotechnology, questions were put to the experts which could be answered with “Yes”, “No”, or “Don’t know”. For each question the experts were requested to explain or justify their answers.

The first question put to the experts about regulation was: “Are the existing legal provisions (REACH) sufficient?” The formulation “Existing statutory provisions (REACH)” means that the new REACH legislation was already to be included in reflections on the response to this question. The response was comparatively clear: 41% (Round 1) and 50% (Round 2) of the experts believed that the existing statutory provisions are sufficient (Fig. 51). From the qualitative comments in Round 1 it is clear that the majority of respondents do not see any fundamental need for action and are of the opinion that when it comes to the assessment of nanomaterials this does not take place in principle in an “unlegislated area”.

38% (Round 1) and 32% (Round 2) of the respondents do, however, see a clear need for action and believe that the current provisions are not sufficient. 21% and 18% did not provide any details.

Above all experts from industry were of the opinion that the existing statutory provisions are sufficient. They base their arguments on the fact that all the effects discussed in conjunction with nanotechnology up to now can be covered by the existing provisions. According to them, REACH is a reliable information profile and it also covers nanomaterials. In individual cases there are comments recommending additions to REACH or changes to the statutory framework if this is necessary on the basis of new scientific findings. Respondents in the other expert groups state to a far lesser degree that the existing statutory provisions are sufficient. For instance, representatives of the public authorities draw attention to the gaps in the existing provisions on nanomaterials. Furthermore, according to the experts there are no clear statutory definitions. Hence they advocate reassessing the provisions from the angle of the new mechanisms of action of nanomaterials.

Fig. 51: Estimation of the question: Are the existing statutory provisions (REACH) sufficient? (Number of responses in brackets)

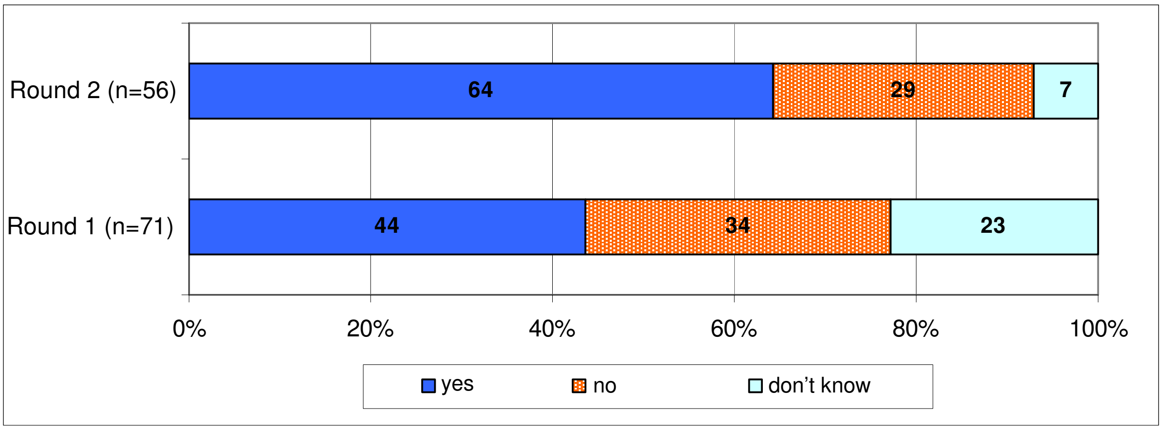


Explanation: percentages rounded up

6.1.2 Adaptation of existing provisions

A second question was: "Is there a need for adjustments to existing statutory provisions for nanomaterials?" The goal of this question was to obtain information on the scale on which existing provisions must be reviewed. 44% of the experts in Round 1 and 64.3% of the experts in Round 2 were of the opinion that the existing statutory provisions should be adapted (Fig. 52). 34% and 28.6% respectively of the respondents were of the opinion that this was not necessary. The proportion of undecided respondents who did not provide any details was 23% in the Round 1 but fell to 7.1% in Round 2.

Fig. 52: Estimation of the question: Is there a need for adjustments to existing statutory provisions for nanomaterials? (Number of responses in brackets)



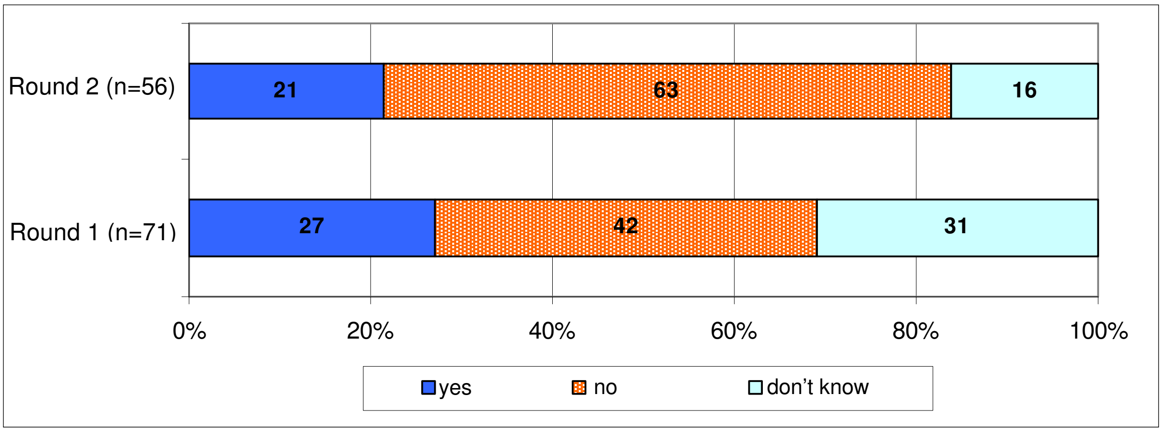
Explanation: percentages rounded up

Experts from industry tended not to be of the opinion that the existing statutory provisions needed to be supplemented by adjustments for nanomaterials. Instead they called for internationally harmonised mandatory labelling for food and cosmetics. Furthermore, the comment was made that nanomaterials should also, where appropriate, be registered as individual chemicals. To this end, a proposal was made for the development of new standardised procedures. Furthermore, attention was drawn to the fact that there are no MAC guidelines for nanoparticle aerosols. The majority of all other groups called for an adjustment to the existing statutory provisions. They justified this on the grounds of the quality of the new effects and new mechanisms of action. The inadequate labelling practise was criticised as it does not take particle size into account. It was suggested that corresponding adjustments should be made in REACH and that the volume thresholds should be lowered.

6.1.3 Need for a new nanoregulation

A third question looks directly at the topic of nanoregulation: “Must new nanoregulations be drawn up?” Only 27% (Round 1) and 21% (Round 2) of the respondents felt that a new “nanoregulation” was necessary. 42% (Round 1) and 62% (Round 2) were of the opinion that no new “nanoregulation” was necessary. The high proportion of undecided respondents in Round 1 (31%) fell considerably, as it did for the other questions, to 16% in Round 2 (Fig. 53).

Fig. 53: Estimation of the question: Do new nanoregulations have to be developed? (Number of responses in brackets)



Explanation: percentages rounded up

In response to this question the majority of experts did not advocate the development of new nanoregulations but supported the supplementation of existing statutory provisions. Frequently, new labelling and a declaration with corresponding mention of the risks were called for.

6.1.4 Information basis for regulations and recommendations

The fourth question was “On the basis of which information can regulatory recommendations be developed?” The question was answered in great detail by respondents in all expert groups. A total of 73% of all respondents in Round 1 commented on this question. All stakeholder groups focus on the fact that validated scientific findings should be the basis for regulatory recommendations which would have to be confirmed by different scientific institutions.

The majority of industry respondents advocated the establishment of limit values as soon as the corresponding measurement methods are available. The development of new regulatory recommendations should, therefore, be based in particular on new scientific findings from toxicological and pharmacological studies. In the comments by industry there was also a call for the consideration of exposure, environmental aspects and benefits. A proposal was also made for regulatory recommendations to be developed on the basis of the Dangerous Substances Regulation and the Technical Rules for Hazardous Substances (TRGS).

Respondents from the sciences gave highly varied answers to the question about the basis for regulatory recommendations. On the one hand, they advocated that comprehensive information and all available knowledge should be included if possible. “*This encompasses not* *only research on the effects of chemicals but also particle research."* There was also a call for a "robust assessment of nanomaterials". But standardised tests would have to be developed first. "*There is no reference material at all in order to be able to undertake comparative studies."* In terms of content the scientists called for regulatory recommendations to be developed on the basis of "*Clear findings from toxicological studies"* and "*knowledge of the level of exposure"*. There were also calls for "*Product studies depending on application and with special consideration of the exposure pathway."* A "hazard assessment along the entire product lifecycle" was likewise proposed. Recommendations were made concerning the urgent need for progress in "eco"toxicity analyses. The various scientists were of the opinion that there were still some uncertainties. "*Today much basic information is missing about the toxicology and environmental behaviour of nanomaterials."* However the comment was made that the lack of knowledge could lead to problems when formulating provisions. Nonetheless, an initial orientation for action which would make sense would involve "*avoiding the release of nanoparticles"*. "*It is unclear which properties of nanomaterials are responsible for their effect and behaviour and how these properties can be determined." "Furthermore there are no detection methods available today in order to track nanomaterials in the environment or check limit values."*

Respondents from NGOs/trade unions suggested the development of regulations on the "*basis of the precautionary principle"*. Furthermore, as with the other expert groups, it was suggested that regulatory recommendations be developed "*only on the basis of in-depth research"* and that "*long-term studies of the impact on man and his environment"* be carried out. A request was made for these studies to be conducted by independent scientists and "*not to introduce any materials until then"*. The aspect of exposure and the specific consideration of nanomaterials beyond REACH were addressed. "*Exposure-related risk assessment would have to be undertaken; REACH is by no means adequate*."

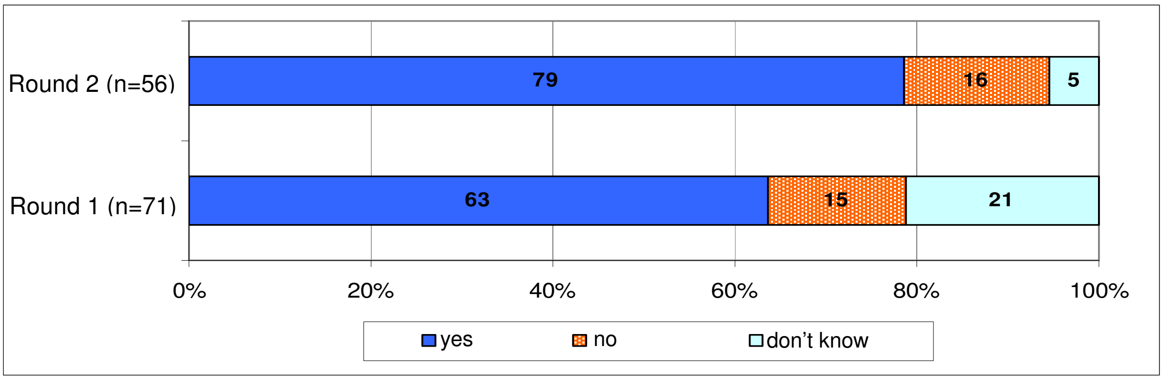
The public authorities argued that the information base for the development of regulation recommendations would have to take into account "*all known research findings, experience and successful work methods"*. A concrete proposal was made: "T*he setting up of a democratically organised, systematic nanodatabase could provide the necessary foundations."* Reference is made here in particular to the importance of toxicology and epidemiology. "*Toxicological research, the generation of further data on exposure and the identification of relevant exposure pathways"* are deemed to be relevant. The decisive factor here is comprehensive toxicological understanding of the "*human organism"* but also of the environment *"accumulation in the food chain".* Furthermore, the respondents were of the opinion that *"a nomenclature should be developed"* and that the *"physical and chemical properties should be recorded in a differentiated manner"*. Furthermore, "*test strategies and test methods had to be laid down in a uniform manner"* and "*reference material proven"*. Reference was likewise made to the precise orientation of regulatory recommendations. "*Regulatory recommendations may only refer to handling during production and not to the finished products."*

Representatives from the area of networks proposed undertaking "*the classification of different nanomaterials along the lines of an ABC analysis (based on the latest scientific findings available) in unproblematic ones and ones with existing up to major potential for concern". "On this basis risk identification along the entire life should be undertaken for substances with a potential for concern in analogy to REACH (in more or less detailed form). This is dependent on corresponding notification obligations for the manufacturers which may have to be stipulated by law. In parallel to this, uniform nomenclature and labelling of nanomaterials are needed".* Furthermore, it was suggested that regulatory recommendations be elaborated "*on the basis of chemico-physical properties, persistence and solubility".* Moreover, reference was also made here to "*toxicity studies with standardised methods and characterisation of the starting materials."*

6.1.5 Voluntary undertakings by companies

In the regulation section experts were asked a fifth question “*Do you think that voluntary undertakings by companies are helpful?”* A clear majority of the respondents answered “Yes” to this question (Fig. 54)

Fig. 54: Estimation of the question: Do you think that voluntary undertakings by companies are helpful? (Number of responses in brackets)



Explanation: percentages rounded up

The experts were of the opinion that voluntary undertakings would increase consumer faith in manufacturers. Voluntary undertakings had proven their worth according to the comments from industry and would help promote compliance with the statutory provisions without requiring any additional red tape for companies. However, the experts felt that voluntary undertakings could only be seen as a first step which would have to be followed by other ones.

6.1.6 Contents of voluntary undertakings

In the next step questions were asked about the elements that should be contained in voluntary undertakings (Table 47). There were clear majorities in favour of all the elements. The experts agreed that in particular “*information for workplace assessment”* and a “*safety assessment of the end product”* should feature in voluntary undertakings.

Table 47: Estimation of various elements which should be contained in voluntary undertakings (number of responses in brackets)

Elements in a voluntary undertaking	yes (%)	no (%)	don't know (%)
Information for workplace assessment (n=71)	87.3	4.2	8.5
Safety assessment of the end product (n=71)	85.9	7.0	7.0
Safety assessments for all individual steps along the production chain (n=71)	67.6	16.9	15.5
Use of the precautionary principle down to adaptation of the regulation(n=71)	62.0	18.3	19.7
Template for detailed nano-specific safety data sheets (n=71)	59.2	28.2	12.7

Explanation: percentages rounded up

Further comments were made in response to the question about voluntary undertakings. Firstly, various experts pointed out that when elaborating guidelines for voluntary undertakings attention should focus on the handling of nanoparticles at the workplace. In contrast, the health aspect of the end products had already been sufficiently covered in the legislation. The comment was, however, made that voluntary undertakings merely serve to minimise the damage but not to prevent it. Hence until the regulations were adapted, the use of the precautionary principle could be a necessary element in voluntary undertakings. Furthermore, there was a call for the aspect of use after consumption to be included in the voluntary undertaking.

Out of the five elements in voluntary undertakings, nano-specific safety data sheets met with the least approval. Here it was the industry representatives in particular who were less in favour. At the expert workshop questions were asked about the reasons. The industry experts stated that information on the safe handling of material already had to be provided in the existing legal framework. This also applied to nanomaterials. In the opinion of industry there was no need for a new nano-specific data sheet. It was merely the case that the existing instructions would have to be complied with more consistently. The public authority representatives commented that there is a need to examine whether new test methods were required and whether this would then lead to new implications. Another critical comment was that when it comes to drawing up safety data sheets manufacturers were free to use their own discretion particularly in the area of new findings.

There was joint discussion of whether consulting in conjunction with statutory provisions should be recommended because of the supposedly limited level of knowledge in small and medium-sized enterprises. "*The start up scene may need specialist advice and support when it comes to implementing statutory regulations"* was the comment from the experts whereby aspects of occupational health and safety, toxicological studies, hazard assessment, preparation of safety data sheets, classification, labelling and exposure scenarios were all touched on.

6.2 Development of action strategies for risk avoidance and risk minimisation

The objective of this part of the project was to develop action strategies together with the experts for the avoidance or minimisation of potential risks. To this end, the experts were given the following action strategies:

- Systematic recording of biological effects
- Life cycle analysis of nanoproducts
- Systematic research into interaction with natural and artificial substances
- Improved networking/communication with information providers (industry, research, public authorities)
- Open, result-oriented dialogue between stakeholders on joint risk assessment
- Stakeholder dialogue on the joint development of voluntary undertakings by industry
- Citizens dialogues/consumer conferences on selected nanotechnology topics

The experts were asked to assess the action strategies using the categories "not useful at all", "not very useful", "useful", "very useful" or "don't know".

The result was that all proposed action strategies received high approval rates and were deemed to be "very useful" and "useful". Table 48 gives the responses for the category "very useful" in declining order. There was a clear drop in the responses in the category "very useful" when questions were asked about citizen dialogues. The values with a dark grey background indicate the highest respective value for each action strategy, the values with the light grey background the second highest value. This shows the shift in the area of dialogues and special citizen dialogues.

Table 48: Estimation of various action strategies for risk avoidance and risk minimisation in Round 1 (n=70 responses)

Action strategy	not useful (%)	not very useful (%)	useful (%)	very useful (%)	don't know (%)
Systematic recording of biological effects	2.8	2.8	35.2	57.7	1.4
Life cycle analysis of nanoproducts	4.2	4.2	38.0	47.9	5.6
Systematic research of interaction with natural and artificial substances	12.7	8.5	29.6	45.1	4.2
Improved networking/cooperation with information providers (industry, research, public authorities)	0.0	1.4	38.0	57.7	2.8
Open, result-oriented dialogues between the stakeholders on joint risk assessment	0.0	5.6	50.7	39.4	4.2
Stakeholder dialogue on the joint development of voluntary undertakings of industry	2.8	12.7	64.8	15.5	4.2
Citizen dialogues/consumer conferences on selected nanotechnology topics	8.5	23.9	46.5	15.5	5.6

Explanation: percentages rounded up

The strategy for recording biological effects was deemed to be useful by all experts. The comment was, however, made that this was very cost-intensive. Furthermore, the research strategy of the senior federal authorities BAuA, UBA and BfR should be taken into account.

The assessment of nanoproducts along the entire life cycle was deemed to be useful or very useful by all experts. In some cases the experts were of the opinion that existing methods of life cycle analysis or methods for assessing eco-efficiency could be used. An individual case assessment had to be undertaken along the entire product life cycle and could be oriented towards the 18 test criteria for the analysis of nanomaterials (p. 22). Particular attention should be paid to the work in research laboratories and in the production phase in order to take due account of aspects of occupational health and safety, and environmental protection. Hence questions about cleaning, maintenance, disposal, input into the environment, agglomeration and deagglomeration were still open and had to be clarified for the purposes of assessment along the life cycle.

The strategy for the systematic study of interaction with natural and artificial substances was also deemed to be very useful by a majority of the experts. Given the large number of nanoproducts (aerosol sprays for cleaning or in cosmetics, creams, medicines, food, abrasion from textiles or surfaces) consumers could be exposed not only to a higher volume of nanomaterials but also to possible interaction between various nanomaterials. One problem that was raised was that, at the present time, no research projects were known which systematically examine interaction.

The strategy for the improved networking of information providers from industry, research and public authorities was welcomed by most of the experts. In their comments they pointed out that the research and dialogue products should be organised on an inter-ministerial and inter-agency basis. The trend in the assessment of stakeholder dialogues towards joint risk assessment by science and industry is very positive. Risk assessment within a dialogue is in the joint interests of all stakeholders and a clear majority of the respondents are convinced of the benefits. A similar pattern emerges for joint dialogues for the elaboration of voluntary undertakings. To this end, new dialogue projects should be launched which cover these issues. When it comes to the question of citizen dialogues opinions differed the most between industry and the other experts. The majority of industry representatives felt that the citizen dialogues were "not useful" or "not very useful". All other experts thought the citizens dialogues were "useful" or "very useful".

Other comments on action strategies dealt with concrete risk avoidance. To this end it is proposed that emissions should be avoided, that work should be conducted in closed loops and that no potentially critical substances or pharmaceutical forms should be used. There was also a call for control of compliance with statutory regulations. Reference was likewise made to the risks of dishonest communication. A loss in confidence was to be avoided by only using the word "nano" when nanoparticles are actually contained in the corresponding product. Furthermore, it was equally important not to conceal the presence of nanoparticles in a product. It should be systematically examined whether the risks of chemical substances known today – inorganic and organic – could be different in nanoparticles. Hence, a correct technology impact assessment was needed.

Based on the results from Round 1, this table was submitted to the experts for a second time. The results show a similar picture with a slight trend towards higher assessments for all factors (Table 49). The gap between the citizen dialogues and the other measures remained.

Table 49: Estimation of various action strategies for risk avoidance and risk minimisation in Round 2 (n=56 responses)

Action strategy	not useful (%)	not very useful (%)	useful (%)	very useful (%)	don't know (%)
Systematic recording of biological effects	1.8	1.8	33.9	58.9	3.6
Life cycle analysis of nanoproducts	0.0	3.6	44.6	44.6	7.1
Systematic recording of interaction with natural and artificial substances	14.3	12.5	14.3	55.4	3.6
Improved networking for better coordination of information providers (industry, research, public authorities)	0.0	0.0	28.6	67.9	3.6
Open, result-oriented dialogues between the stakeholders on joint risk assessment	1.8	5.4	42.9	42.9	7.1
Stakeholder dialogue on the joint development of voluntary undertakings of industry	0.0	10.7	53.6	26.8	8.9
Citizens dialogues/consumer conferences on selected nanotechnology topics	1.8	28.6	37.5	23.2	8.9

Explanation: percentages rounded up

At the expert workshop the differences that occurred in attitudes towards the citizens dialogues were discussed. Some industry representatives had in the mean time adjusted their assessment of citizen dialogues as a consequence of the positive impressions which they had gained during the parallel BfR Consumer Conference on Nanotechnology (Zimmer *et al.* 2007). Another industry representative indicated that he had understood the question about risk avoidance and risk minimisation purely from the technical angle and felt that in this – and only in this – context citizen dialogues were not very useful. Otherwise he stressed the need for stakeholder and citizen dialogues which his company would also support. At the workshop major agreement seemed to emerge in the course of discussions that dialogues were desirable and useful as they could serve the joint generation of knowledge and highlight perspectives and arguments.

6.3 Product labelling and freedom of choice

Besides risk assessment, another of the core tasks of the Federal Institute for Risk Assessment (BfR) is to enable consumers by means of appropriate risk communication to take independent and informed decisions. Bedsides dialogue-based risk communication, the provision of information in the form of the labelling of food, chemicals and consumer products is an important pillar when it comes to achieving the objective of informed consumers. Already now a number of labels are available in consumer areas which give the consumer information about corresponding products, food or chemicals.

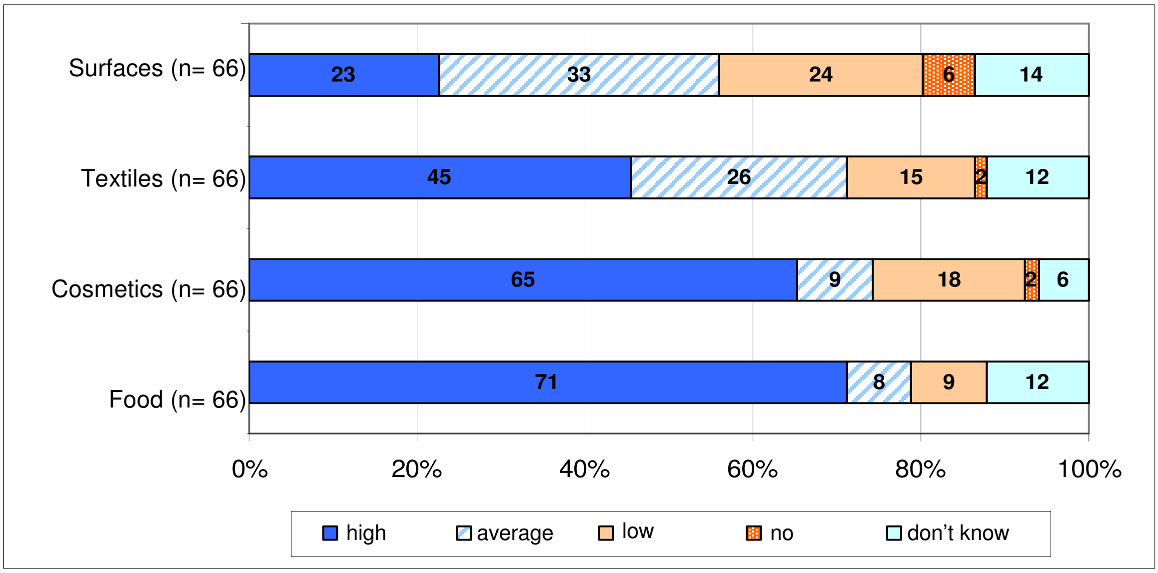
At the present time consumers cannot tell whether products contain nanomaterials. There is no mandatory labelling for nanoproducts. Consumers can only recognise the use of nanomaterials when manufacturers push their products by referring to the use of nanotechnology. Based on the advertising for a product alone, however, no statements can be made as yet about whether it actually contains nanoparticles or other nanomaterials. Hence various non-governmental organisations (e.g. BUND 2008) and consumers are calling for the introduction of mandatory labelling for nanoproducts. The participants in the BfR Consumer Conference on Nanotechnology called for the declaration of products so that consumers can decide for themselves whether they wish to purchase products manufactured using nanotechnology or not (Zimmer *et al*. 2007).

In the Delphi survey the experts were, therefore, asked about the importance they attributed to consumer freedom of choice and the labelling of nanoproducts. The category ratings available to them were “high”, “average”, “low” and “no” as well as the category “don’t know.

6.3.1 Consumer freedom of choice

The importance of the criterion “consumer freedom of choice” varied relatively markedly between the product groups (Fig. 55). In the case of nanotechnology applications in the area of surface coatings, only 23% of experts were of the opinion that this criterion is of major importance. However, the closer the nanoproducts can come to the human body, the greater the importance attributed to this criterion by the experts. Already in the case of textiles 45% of experts attributed high importance to consumer freedom of choice. In the case of nanocosmetics this figure is already 65% and when it comes to the use of nanomaterials in food 71% of the experts say that major importance should be attributed to consumer freedom of choice.

Fig. 55: Importance of consumer freedom of choice in conjunction with nanotechnology applications in various product areas (number of responses in brackets)

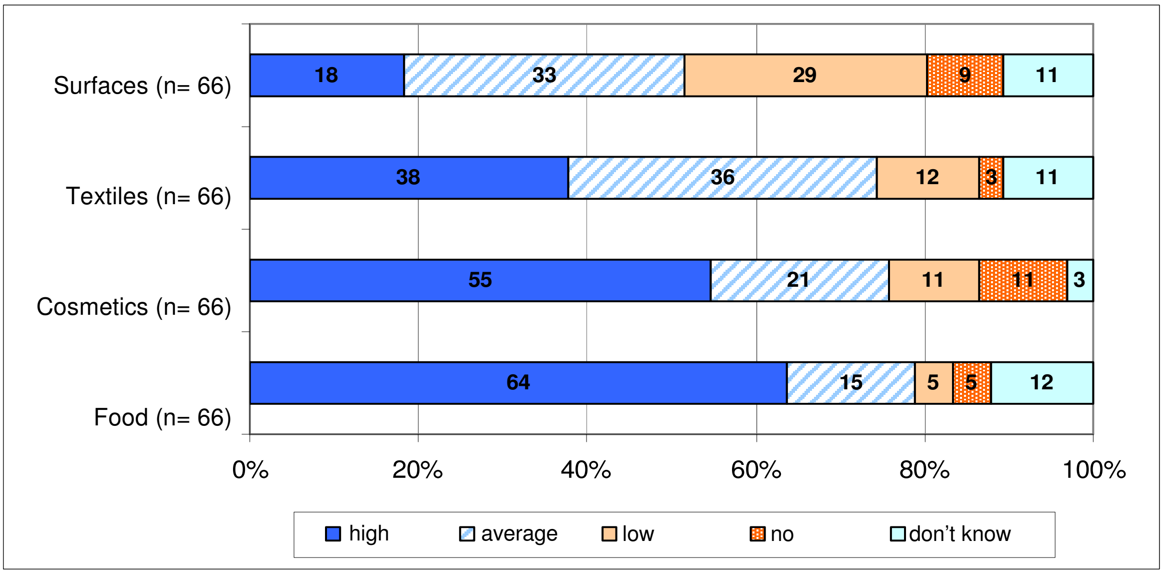


Explanation: percentages rounded up

6.3.2 Labelling of nanoproducts

One way of supporting consumer freedom of choice is to label nanoproducts. The importance attributed to the labelling of nanoproducts varies between the different applications (Fig. 56). For the application surface coatings only 18% of experts attribute major importance to the labelling of nanoproducts. Already 38% of experts believe that the labelling of nanoproducts in the area of textiles is very important and in the areas cosmetics and food the labelling of nanoproducts is deemed to be of major importance by well over half of the experts (55% and 64%).

Fig. 56: Importance of the labelling of nanoproducts from various product areas (number of responses in brackets)



Explanation: percentages rounded up

The question of the labelling of nanoproducts was discussed in depth at the expert workshop. In the opinion of industry representatives the importance of the labelling of nanoproducts may differ considerably depending on the sector. In the cosmetics industry, for instance, ingredients like titanium dioxide or zinc oxide are already labelled today – without any details of size. Information on nanoscale is available on the homepage but not on the packaging. The term labelling was understood in this corporate group rather as a “warning” and was largely rejected. The majority of industry representatives were critical of labelling and gave the following reasons for this:

- At the present time no standardised methods are available to measure performance criteria (Lotus effect, self-cleaning surfaces). Preliminary work on standardisation within DIN/ISO is already being undertaken but will still continue for several years.
- Labelling was dependent on an international standardised definition about what had to be labelled and which properties define a material as a nanomaterial.
- The option of introducing self-defined labelling would in the opinion of industry lead to more confusion than clarity as the quality criteria were not standardised.

For the representatives of the environmental organisations and consumer protection, the following points were raised about the term labelling:

- The labelling of nanoproducts leads to greater transparency, acceptance by consumers and confidence in the manufacturers.
- The labelling of nanoproducts should not take on the character of a warning but simply facilitate consumer’s freedom of choice. The basis for freedom of choice is informed choice and the possibility for consumers to easily access information in the public domain.

The scientific representatives touched in particular on the following points in conjunction with the labelling of nanoproducts:

- The exchange of information on materials used in industry had to improve and the joint discussion of research questions encouraged. To this end, information on mechanisms of action could be provided on downstream websites.
- The sharing of knowledge should not be a “one-way communication street”. Improved coordination and cooperation between industry and the research programmes of the senior federal authorities is desirable (UBA, BAuA, BfR).

The public authorities focus on the following points in the labelling discussion:

- Information should be provided about which products currently contain nanomaterials. In this context information was also required on ingredients and particle sizes.
- On the basis of this data, classification is deemed to be useful based on the German Hazardous Substances Ordinance in “irritating”, “toxic” and “environmentally hazardous”.

In the discussions the insurers advocated the labelling of nanoproducts from the angle of traceability and the causal attribution of possible damage. The detailed listing of nanomaterials was important in conjunction with product recalls as well in order to be able to exchange data on comparable products in cases of damage and undertake safety assessments.

6.4 Conclusions

Nano-specific regulations

- Overall most of the experts interviewed in this Delphi procedure advocate the moderate adaptation of regulations. A completely new, nano-specific regulation is, however, rejected by the majority of these experts.
- Voluntary undertakings are deemed to be useful by the vast majority of the experts interviewed here. The workplace assessment and safety assessment of end products are deemed to be the most important elements in these undertakings.
- More detailed information on the elaboration of safety data sheets and a guide on the consistent implementation of the provisions were recommended for the use of nanomaterials, too.

Action strategies for risk avoidance and risk minimisation

- Action strategies like the systematic recording of biological effects, assessment of nanoproducts along their entire life cycle and systematic research into interaction with natural and artificial substances were deemed to be useful or very useful by the experts.
- Networking activities and various forms of dialogue were also deemed to be useful instruments in order to work together on avoiding or minimising potential risks.
- The experts called for more expert dialogues and citizen dialogues – depending on the goals – for the purposes of the joint generation of knowledge between the experts in all stakeholder groups and between experts and citizens.

Product labelling and freedom of choice

- The closer nanoproducts come in terms of their envisaged use to the human body (surface coatings, textiles, cosmetics, food), the greater the importance of consumer freedom of choice in the opinion of the experts.
- Consumer freedom of choice can best be achieved according to the majority of the experts interviewed here via the labelling of nanoproducts.

7 Summary

In 2006 the Federal Institute for Risk Assessment (BfR) conducted a Delphi study on the risks of nanotechnology in the areas of food, cosmetics and consumer products. Parts of the study were undertaken in cooperation with the Centre for Interdisciplinary Risk Research and Sustainable Technology Development (ZIRN) of Stuttgart University.

A total of 100 experts were asked to identify and assess the potential risks of nanotechnology applications in the areas food, cosmetics, surface coatings and textiles. One-third of the participants came from industry (basic substance manufacturers, users from the food, cosmetics, textile and surface industry, associations), one-third from scientific institutions (basic and application-oriented research) and one-third from institutions which deal rather with the risks of nanotechnologies (public authorities, environmental organisations, consumer protection associations, trade unions, technology impact assessment institutions/networks, insurance companies).

In the study the experts forecast a moderate to major increase in the consumption of all nanomaterials used at the present time. Airborne nanomaterials were identified by the experts as the group with a particularly high hazard. Inhalational exposure to nanomaterials should be avoided. According to the majority of the experts, however, the risk potential of nanomaterials can only be identified and assessed in each individual case. To this end, nine general test criteria were elaborated for nanomaterials too, and nine additional nano-specific test criteria in the Delphi study.

The criteria build on the existing test criteria for chemicals and consciously encompass aggregates and agglomerates of nanomaterials or nanoscale systems. They apply to the entire life cycle of a product and provide information for workplace assessment. At the same time, they mean that companies will be assigned more responsibility and the public authorities can only assume their supervisory function in very close cooperation with the companies. Cooperation requires the trust of all social groups. Hence, the experts recommend the extension of cross-stakeholder dialogues for the generation of neutral knowledge about the properties of nanomaterials for the further development of measurement measures and for occupational health and safety.

The bioavailability of nanomaterials, their persistence and a generally inadequate knowledge base on these materials were identified as the important criteria for extended risk assessment. They should be taken into account in action strategies for risk avoidance and risk communication like, for instance, the systematic recording of biological effects, the life cycle analysis of nanoscale products and systematic research into interaction with natural and artificial substances.

Experts see the largest growth potential for nanoproducts in the area of surface coatings. They predicted moderate growth for nanoproducts in the areas of textiles and cosmetics. No major market development was expected for nanoproducts in the food sector. Experts do not, however, expect to see any new risks for consumers arising from the greater market availability of nanoproducts. 22 out of 30 nanoproducts covered in the survey are safe in the opinion of experts. Minor harmful effects were expected for 7 products. Only in the case of fullerenes in cosmetics were greater harmful effects on human health expected. Not one single nanoproduct was placed in the category “major harmful effects”. With the exception of the food sector the experts interviewed here assumed that nanoproducts will be accepted by consumers. However, it should be borne in mind that consumer freedom of choice should be guaranteed. This could require the labelling of nanoproducts particularly in the area of food. Another decisive factor was a timely dialogue with citizens in order to deal with critical questions early on and to facilitate informed assessment of the opportunities and risks of nanotechnology applications.

Overall the majority of experts interviewed in this Delphi method were against a separate "nanoregulation" but were in favour of the moderate adaptation of existing provisions. Voluntary undertakings by industry met with high approval ratings. Nano-specific workplace assessments and the safety assessment of end products should be part of voluntary undertakings in the opinion of the experts interviewed.

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9 Annex

9.1 Questionnaire Survey Round 1

Risiken erkennen – Gesundheit schützen

Universität Stuttgart

Delphi survey on nanotechnologies in the areas food, cosmetics and consumer products

After completing the questionnaire, please save the file with your entries. Thank you.

Form of address:	Organisation:
Title:	Street:
First name:	Postal code and place:
Name:	Tel.:
Function:	Email:

1 Economic importance of nanotechnologies

1.1 Total sales revenues with nanoproducts

At the present time total annual sales revenues of approximately US$ 52 billion are generated with nanoproducts around the world. According to a study by Lux Research the market for all products to do with nanotechnologies will grow annually by 70% and total sales revenues would already amount to around US$ 1,400 billion by 2012. Do you think that the growth forecast of 70% is accurate?

	too low	accurate	too high	don't know
... for nanoproducts over all	☐	☐	☐	☐
... for food based on nanotechnologies	☐	☐	☐	☐
... for cosmetics based on nanotechnologies	☐	☐	☐	☐
... for textiles based on nanotechnologies	☐	☐	☐	☐
... for surface coatings based on nanotechnologies	☐	☐	☐	☐

Remarks?

1.2 Consumption of nanomaterials

The global consumption of nanomaterials in 2001 and 2006 is indicated in the table below [according to Haas, K.-H. 2003][3]. How do you estimate the future development in the product categories listed up to 2015? Please assess the development for 2015 in the drop down list. Please activate the various response options with a mouse click and select one.

Products/materials	**2001 in mass (1000 t)**	**2001 in value (millions $)**	**2006 in value (millions $)**	**development up to 2015**
Metals	1-2	35-70	approx. 200	
Aluminium nanocoatings	1,7	193	252	
SiO_2 (pure nanostructures)	370	1200	1600	
Metal oxides (Al, Zr, Zn, Ti, Fe) Pyrolytic Wet-chemical	 4.5 190	 100 1300	 >200 1850	
Effect pigments	15	400	500	
Nanotones/layered silicates Polymer nanocomposites	0.2 4	1.5 15	25 300	
Carbon: fullerenes, nanotubes, nanofibres	< 0,1	approx. 5	25 - 70	
Organic materials: dendrimers, highly branched polymers, POSS*	<<	< 1	5-15	

* **POSS** = **P**olyhedral **O**ligomeric **S**il **S**esquioxane

Remarks?

[3] Haas, K.-H.; Hutter, F.; Warnke, P.: Wengel, J.: Produktion von und mit Nanopartikeln – Untersuchung des Forschungs- und Handlungsbedarfes für die industrielle Produktion. Supported by BMBF Support reference: 02PH 2107, project promoter PTF. Würzburg July 2003.

2 Toxicity

In the following section on the toxicity of nanomaterials we ask for your assessment:

2.1 In your opinion do these nanomaterials have toxic potential in the following aggregate states?
2.2 What can toxicity be attributed to?
2.3 Can you describe the mechanism of action?

	2.1 Aggregate states						**2.2 Cause for toxicity**				**2.3 Mechanism of action**
	as volatile particles	in an aerosol	naturally aggregated	coated	in a liquid medium/in a solvent	embedded in a matrix	solubility	size (details in the range, e.g. < 70 nm)	shape	surface and reactivity	Can you describe the mechanism of action? (e.g. genotoxicity, oxidative stress…)
Silicon dioxide	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Titanium dioxide	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Zinc oxide	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Chromium(III)-oxide	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Nickel oxide	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Aluminium oxide	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Iron oxide	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Silicates	☐	☐	☐	☐	☐	☐	☐		☐	☐	

	2.1 Aggregate states						2.2 Cause for toxicity				2.3 Mechanism of action
	as volatile particles	in an aerosol	naturally aggregated	coated	in a liquid medium/in a solvent	embedded in a matrix	solubility	size (details in the range, e.g. < 70 nm)	shape	Surface and reactivity	Can you describe the mechanism of action? (e.g. genotoxicity, oxidative stress …)
Inorganic dye pigments	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Organic dye pigments	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Carbon nanotubes	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Fullerenes	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Polymers	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Nanocomposites	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Silver	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Vitamins	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Degradable materials: lipid compounds, biopolymers	☐	☐	☐	☐	☐	☐	☐		☐	☐	
Nanotones/layered silicates	☐	☐	☐	☐	☐	☐	☐		☐	☐	

Remarks?

3 Exposure

3.1 Exposure pathway

What importance do the various exposure pathways have for negative health effects? Please assess the importance of the following materials concerning exposure pathways in the drop down list with “no importance”, “minor importance”, “average importance”, “major importance” or “don’t know”.

	Oral	Dermal	Inhalational
Silicon dioxide			
Titanium dioxide			
Zinc dioxide			
Chromium(III)-oxide			
Nickel oxide			
Aluminium oxide			
Iron oxide			
Silicates			
Inorganic dye pigments			
Organic dye pigments			
Carbon nanotubes			
Fullerenes			
Polymers			
Nanocomposites			
Silver			
Vitamins			
Degradable materials (lipid compounds, bio-polymers?)			
Nanotones/layered silicates			

Remarks?

3.2 Consumer exposure to nanomaterials

In your opinion are consumers exposed to nanomaterials *from abrasion* in conjunction with textiles of surface coatings? If so, what effects do you expect? Can you attribute specific effects to specific materials?
Yes ☐ No ☐ Don't know ☐
Effects (where appropriate attribute to materials):

Do you expect consumer exposure through the use of nanomaterials *in aerosols?* If so, what effects do you expect? Can you attribute specific effects to specific materials?
Yes ☐ No ☐ Don't know ☐
Effects (where appropriate attribute to materials):

Do you expect consumer exposure to nanomaterials *in food and food supplements?* If so, what effects do you expect? Can you attribute specific effects to specific materials?
Yes ☐ No ☐ Don't know ☐
Effects (where appropriate attribute to materials):

Do expect consumer exposure to nanomaterials in *cosmetics and pharmaceutical products?* If so, what effects do you expect? Can you attribute specific effects to specific materials?
Yes ☐ No ☐ Don't know ☐
Effects (where appropriate attribute to materials):

Remarks?

3.3 Dermal, inhalational and oral exposure pathways

Do you agree with the following theories?

3.3.1 Dermal exposure pathway

1. "The skin is largely impermeable to nanoparticles if it can assume its protective function and is not impaired or exposed to mechanical strain."

   Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

   Comments:

2. "In the case of skin injuries, strong mechanical strain and very small nanoparticles (< 5 – 10 nm) the protective function is probably impaired."

   Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

   Comments:

3. "Dermal strain results amongst other things from manual activities with dust- shaped or suspended particles. If the nanoparticles are embedded in a solid matrix, the skin burden is low."

   Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

   Comments:

4. "Liposomes cannot pass the intact horny layer nor can they improve the intake of active ingredients."

   Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

   Comments:

5. "No genotoxic or photo-genotoxic risks for man are to be expected from the normal use of nanoscale TiO_2 particles."

   Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

   Comments:

6. "Nanoscale TiO_2 protects the skin from the genotoxic and carcinogenic effects of UV light."

   Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

   Comments:

7. "Nanoparticles can penetrate the skin and cause systemic exposure of the organism."

   Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

   Comments:

Remarks?

3.3.2 Inhalational exposure pathway

1. “The use of particles in a non-dust form or in a liquid suspension (solid in liquid), which is not sprayed and the embedding of particles in a solid matrix (solid in solid) can markedly reduce inhalational exposure.”

Yes ☐ No ☐ Don’t know ☐ It depends, …. (please comment))

Comments:

2. “Following inhalational intake nanoparticles have a carcinogenic effect.”

Yes ☐ No ☐ Don’t know ☐ It depends, …. (please comment)

Comments:

3. “ As nanoparticles are more toxic than microparticles, inhalation leads to new toxicities.”

Yes ☐ No ☐ Don’t know ☐ It depends, …. (please comment)

Comments:

4. “Inhaled nanoparticles are systemically ingested and influence the cardiovascular system and the brain.”

Yes ☐ No ☐ Don’t know ☐ It depends, …. (please comment)

Comments:

5. “In areas of nanotechnology where nanotubes are used, there may be health consequences similar to those for asbestos fibres as the nanotubes may possibly behave in a similar way to larger respirable fibres.”

Yes ☐ No ☐ Don’t know ☐ It depends, …. (please comment)

Comments:

Remarks?

3.3.3 Oral inhalational pathway

1. "The oral intake of nanoparticles leads to systemic exposure of the organism."

Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

Comments:

2. "Metallic nanoparticles are not ingested by the body via the gastro-intestinal tract."

Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

Comments:

3. "Nanoparticles need specific receptors in order to be ingested at all."

Yes ☐ No ☐ Don't know ☐ It depends, …. (please comment)

Comments:

Remarks?

4 Consumer-relevant applications

4.1 Nanotechnology and food

Application	Toxicity/negative health effects of the end products	Consumer acceptance	Positive health effects	Implementation period	Comments
Application L 1: Vitamins or amino acids are encapsulated in nanocontainers (e.g. liposomes). These **capsules**, measuring between 10 and 100 nm in size, are more soluble, more mobile and more robust than conventional food additives in microdroplet form.					
Application L 2: Membranes from (multiple-walled) **carbon nanotubes** are used to separate biomolecules with functional value (e.g. proteins, peptides, vitamins and minerals). They can be used to fortify food or to produce dietetic additives or medicines.					
Application L 3: Colloidal salicylic acid or **silicon dioxide** is used as a **trickling agent** or carrier material because of its high absorption capacity to prevent the baking together of sodium chloride crystals and food.					
Applications L 4: There are plans to coat chocolate bars with a **titanium dioxide** layer that is only a few nanometres thick and is neutral in taste in order to ensure that they **still look attractive** even if they have been lying around for some time.					
Applications L 5: Highly disperse salicylic acid is said to be used in ketchup as an efficient **thickening agent**. The nanoparticles have a diameter of 5 to 30 nm. The ketchup which is viscous when at rest is to be rendered runny by shaking.					
Applications L 6: Nanotechnology **anti-oxidant** systems are to help food stay fresh longer. Nanoscale **micelles** are to be used as the carriers for anti-oxidants.					
Applications L 7: Silver particles dissolved in pure water (diameter 0.8 nm, concentration 10ppm) are available as food supplements. The charge of silver and its nanoscale formulation are said to increase a feeling of wellbeing and boost the **immune system**.					

4.2 Nanotechnology and its cosmetics

Applications	Toxicity/negative health effects of the end products	Consumer acceptance	Positive health effects	Implementation period	Comments
Application K 1: With the help of **hydroxylapatite** nanoparticles the weakened dental enamel can be restored whilst brushing teeth. The chemical structure of the material is identical to that of the dental enamel. After application the particles form a thin film which covers the gaps.					
Application K 2: Nanoparticles (**zinc oxide** und **titanium dioxide**) are used to produce the latest generation of contact lenses. The lenses are not completely coloured but have an interrupted pattern with various pigments. In this way nanoparticles are to create a natural-looking **eye colour**.					
Application K 3: Sun creams contain materials made from **titanium dioxide** particles with a diameter of 15 to 20 nm as **UV filters**. The smaller the particles are, the more closely they are aligned on the skin and the better they are said to protect the skin from UV light.					
Application K 4: Hydrophilic or hydrophobic dispersions made of **ZnO** (particle size 100nm) are said to ensure transparent cosmetic **UV protection**.					
Application K 5: Nanoemulsion with avocado oil or jojoba oil is used in **hair masques**. The drops in this emulsion are 100 times finer than in a normal emulsion and are said to make the hair combable, shiny and silky in just a few seconds.					
Application K 6: Silver nanoparticles (diameter approx. 7nm) can be used in soaps for to **clean and disinfect the skin.** This is said to prevent the onset of acne and activates skin cells.					
Application K 7: C60 fullerenes are used as **anti-oxidants** in creams. Fullerenes are said to neutralise free radicals and, in this way, to prevent premature aging of the skin.					

4.3 Nanotechnology and textiles

Application	Toxicity/negative health effects of the end products	Consumer acceptance	Positive health effects	Implementation period	Comments
Applications T 1: Titanium dioxide is used as an UV-absorbing nanolayer in textiles. The small size of the pigment particles of around 20nm ensures a high absorption potential combined with low level of light scattering. This means that the particle layer is transparent and the sun protection invisible.					
Applications T 2: A new anti-**odour** technology embeds **silver** nanoparticles (diameter 15nm) in the fibres of socks, shoes and cloths. The silver particles kill odour-forming bacteria or inhibit their growth.					
Applications T 3: Nanocontainers with fragrances and active ingredients are integrated into textiles (clothing as well as carpets and settees). The capsules form when fragrance isocyanine oil droplets (from 100nm in size) are incorporated into an aqueous polyamide solution and the **isocyanine** molecules react on the surface of the oil droplets with the surrounding **polyamines** in water. In this way they encapsulate the fragrance. Capsules with a porous shell continue to release even amounts of the substance over a period of months.					
A**pplications T 4: Halamides** (polymer molecules) are used to coat textiles. Materials are formed which trap and kill viruses and bacteria. **The antimicrobial** materials are used to protect medical personnel and farmers who work with pesticides.					
Applications T 5: Single-walled and double-walled **carbon nanotubes** are used to improve the electrical and thermal **conductivity** of fibres.					
Applications T 6: Fibres acquire **antistatic** properties by coating them with **Ag, Al or Ti nanoparticles**.					
Applications T 7: The integration of **layered silicates** (e.g. Montmorilonit) and **nanotones** into bicomponent fibres improves temperature stability and the **flame-retardant** properties of textiles.					
Applications T 8: Nanoparticles made of **SiO_2** are used to form nanostructures surfaces on fibres. This gives the textiles dirt-repellent properties.					

4.4 Nanotechnology and surface coatings

Applications	Toxicity/negative health effects of the end products	Consumer acceptance	Positive health effects	Implementation period	Comments
Applications O 1: The use of nanostructured materials (nanocomposites made from modified **aluminium layered silicates** and **polymers**) in food packaging can considerably extend the shelf life of processed food by means of improved **barriers** to oxygen, carbon dioxide and humidity.					
Applications O 2: Plastic films into which particles of **titanium dioxide** (diameter 10- 20nm) have been incorporated, block **UV** rays and, in this way, prevent chemical processes in food. The packaged product still looks appetising several days later.					
Applications O 3: Silicon nanoparticles, which contain fluorescent dye molecules and antibodies help to **detect bacteria**. When the antibodies dock onto the antigens of a bacterium, this can be indicated by the fluorescent illumination of the nanoparticles.					
Applications O 4: Antimony zinc oxide (Sb:Sn ration = 1:9 purity 99.5+% particle size 30nm) is admixed to coatings in order to improve the **antistatic** properties of surfaces.					
Applications O 5: Ink jet paper and films which are coated with amorphous nanoparticles made of **salicylic acid** or mixed oxides (e.g. **silicon dioxide** and **aluminium oxide**) **adhere well and rapidly absorb** the ink droplets.					
Applications O 6: A 30% dispersion of aluminium (**Al_2O_3**) nanoparticles (particle size 45 nm) in hexane diocrylate (HDDA) is used to improve the **scratch resistance** of parquet and furniture varnishes.					
Applications O 7: Nanoscale **$CaCO_3$** (particle size approximately 50nm) is used as a functional filler for paper and coatings in order to improve **rigidity and stability**.					
Applications O 8: A wall paint, in which nanometre size **silver particles** are evenly distributed, **prevents mould formation** in indoor areas and algae growth on façades. The particles release silver ions that block nutrient-transporting enzymes, destroy important proteins, dock onto hereditary material and intervene in cell wall synthesis.					

5 Further aspects of risk assessment, communication, management and the dialogue with stakeholders

In the case of new technologies further aspects are to be included aside from toxicity and exposure in risk characterisation. Please indicate the **importance of the following topics** for the areas food, cosmetics, textiles and surfaces:

	Foods	Cosmetics	Textiles	Surfaces
Bioavailability/degradability in nature				
Persistence				
Reversibility				
Inadequate knowledge				
Uncontrollability				
Mobilisation potential of the public at large				
Consumer freedom of choice				
Labelling of products				

Remarks?

6 Identification of open research and regulatory questions/monitoring

Please answer the following questions in a detailed manner:

Do the existing statutory provisions (REACH) suffice? Please state your reasons.
Answer:

Is there a need to adapt existing statutory provisions for nanomaterials? If so which ones?
Answer:

Do new nanoprovisions have to be elaborated? Please state your reasons.
Answer:

On the basis of what information can regulatory recommendations be developed (e.g. classifications, limit values, recommendations)?
Answer:

Do you think that the voluntary undertaking of companies (best practice guidelines) are helpful? Please state your reasons.
Answer:

What should voluntary undertakings contain?

	Yes	No	Don't know
Template for detailed nanosafety data sheets	☐	☐	☐
Instructions for workplace assessment	☐	☐	☐
Safety assessments for all individual links in the production chain	☐	☐	☐
Safety assessment of the end product	☐	☐	☐
Use of the precautionary principle down to adjustment of the provisions	☐	☐	☐

Remarks?

7 Development of action strategies for risk avoidance/risk minimisation

How useful do you think the following proposals are:

	Not useful at all	Not very useful	Useful	Very useful	Don't know
Systematic recording of biological effects	☐	☐	☐	☐	☐
Live cycle analysis of nanoproducts	☐	☐	☐	☐	☐
Systematic research on interaction of natural and artificial substances	☐	☐	☐	☐	☐
Improved networking/cooperation between the information providers (industry, research, public authorities)	☐	☐	☐	☐	☐
Open result-oriented dialogue between the stakeholders on joint risk assessment	☐	☐	☐	☐	☐
Stakeholder dialogues on the joint development of voluntary undertakings of industry	☐	☐	☐	☐	☐
Citizen dialogues/consumer conferences on selected topics of nanotechnology	☐	☐	☐	☐	☐

Remarks and further action strategies:

On behalf of the Federal Institute for Risk Assessment and Stuttgart University we thank you for taking the time to complete this questionnaire.

Please ensure that you have saved all your entries before you send the questionnaire back to us.

If you wish to give us any other feedback or make any general remarks please do so here:

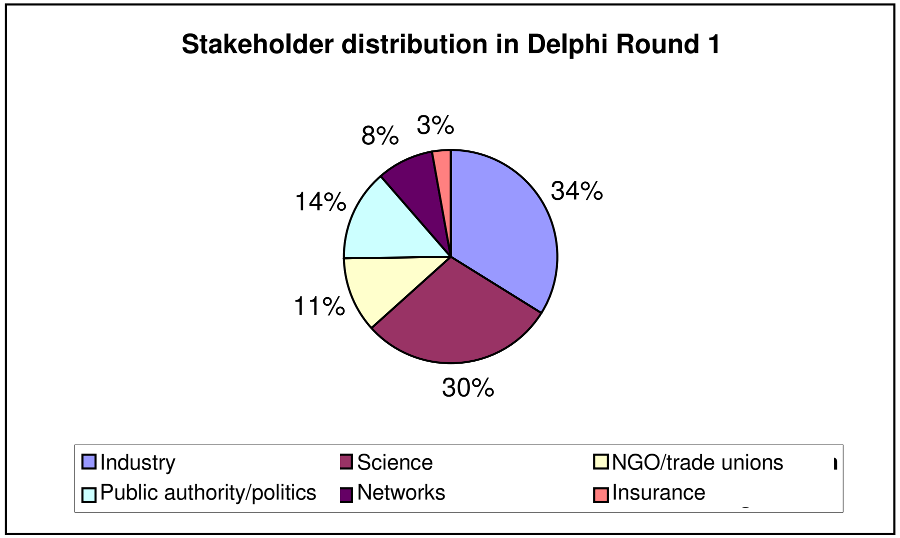
9.2 Questionnaire Survey Round 2

Round 2 of the Delphi survey on nanotechnology in the areas food, cosmetics and consumer products:

Only the questions marked in red are to be answered! Please save the file with your entries after completing the questionnaire. Thank you!

Form of address:	Organisation:
Title:	Street:
First name:	Postal code and place:
Name:	Tel.:
Function:	Email:

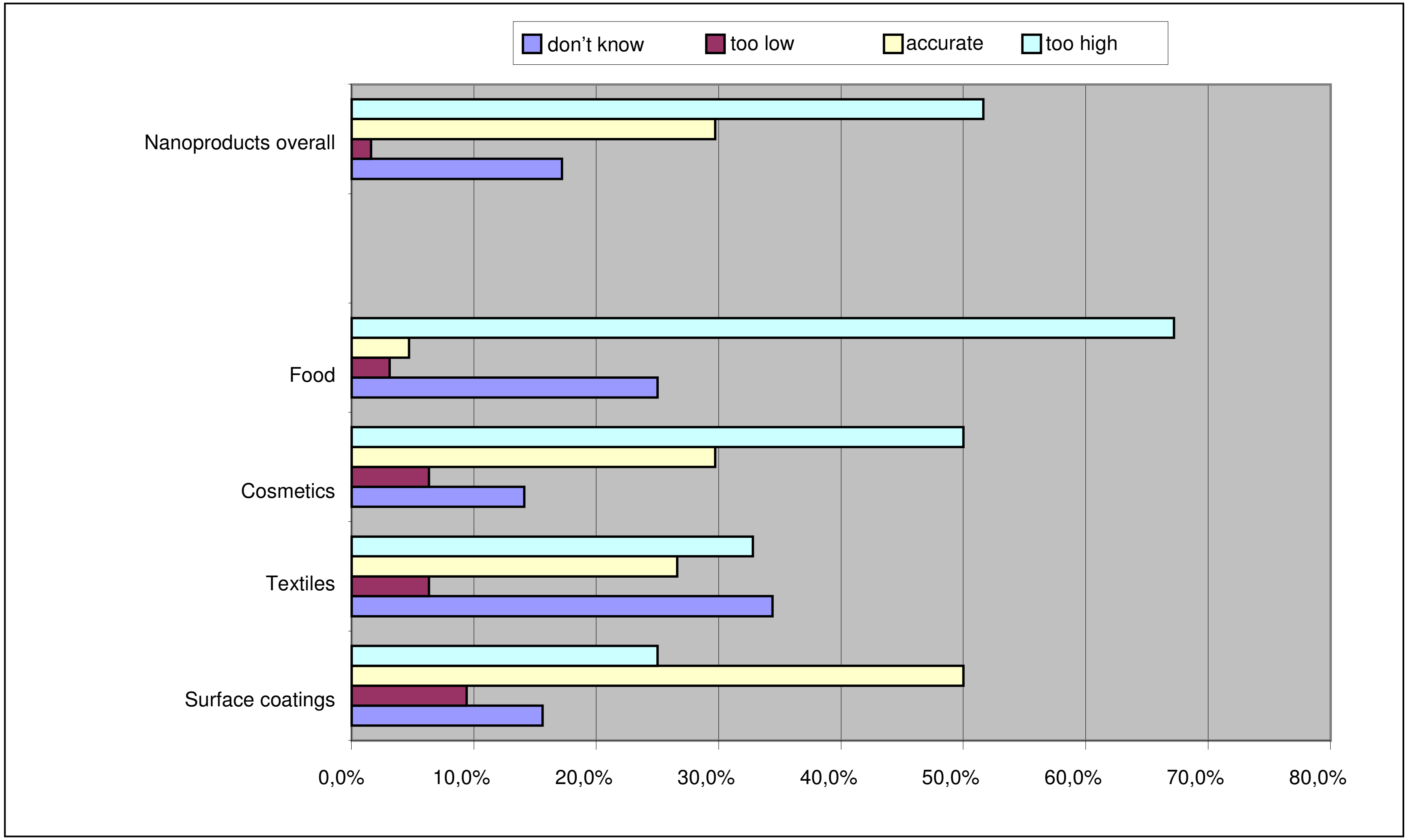
Sociodemographic data: Results Round 1



71 of the 100 questionnaires sent out in the first round of the expert Delphi were completed and returned by the stipulated date. There were 54 male and 7 female participants. The first group are experts from research and application-based industry (23 individuals). The second group encompasses scientists (21 participants). A third, highly heterogeneous group with 27 participants consists of experts who primarily work in institutions on the risk assessment of nanotechnologies (public authorities = 10, NGOs = 8, environmental organisations, consumer protection groups and trade unions, network institutions = 7, insurance companies = 2).

1 Economic importance of nanotechnologies

Total sales revenues with nanoproducts: assessment of the growth potential of 70%: Results of Round 1



Detailed questions 1.1:

From the comments from all stakeholder groups it became clear that the estimation of the amounts and growth potentials mainly depend on whether materials are classified as “new” nanomaterials or have already been produced for many years and are described as “old”.

1.1.1 Which criteria for classification as “new” and “old” nanomaterials do you think are appropriate?

Criteria to describe a nanomaterial as “new”?

Criteria to describe a nanomaterial as “old”?

2 Toxicity results from Round 1

The following substances were deemed to have toxic potential by participants in Round 1: orange indicates substances with more than 21 mentions, yellow substances with between 11 and 20 mentions.

Substance	as volatile particles	in an aerosol	naturally aggregated	coated	in a liquid medium	in a matrix
Silicon dioxide	26	28	4	9	8	1
Titanium dioxide	32	29	5	10	12	2
Zinc oxide	32	28	8	8	14	3
Chromium(III)-oxide	22	29	11	12	15	4
Nickel oxide	24	30	14	13	17	7
Aluminium oxide	21	25	4	7	9	3
Iron oxide	21	26	4	7	10	3
Silicates	17	23	8	6	6	2
Inorganic dye pigments	19	28	7	5	11	3
Organic dye pigments	17	25	6	5	11	3
Carbon nanotubes	25	31	13	7	15	4
Fullerenes	25	26	7	8	18	2
Polymer	15	18	4	4	8	3
Nanocomposites	13	17	3	4	5	1
Silver	17	21	10	7	11	4
Vitamins	6	8	4	3	6	1
Degradable materials: Lipid compounds, biopoly-mers	7	9	4	6	2	5
Nanotones/layered silicates	10	16	5	4	6	3

Across all substance aggregate state combinations, aerosols are deemed to have toxic potential the most frequently (417 positive mentions) followed by the category “as volatile particles” (349 positive mentions). The categories “in a liquid medium (184), “coated” (125), “naturally aggregated” (121) and “in a matrix” (54) follow much further behind. In the category with the highest number of mentions (orange) there are only mentions of the aggregate states “as volatile particles” and “in an aerosol”. This highly uniform top group is followed by a group with an average number of mentions (yellow) in which various aggregate states are given.
We kindly ask you to again evaluate toxicity in the second, yellow group.

In depth question: Which mechanisms of action do you attribute to the substances or do you see other ones?

Substance	Aggregate state	Mentions Round 1	Toxicity	Mechanisms of action	Other/Comments
Inorganic dye pigments	as volatile particles	19			
Fullerenes	in a liquid medium	18			
Polymers	in an aerosol	18			
Nickel oxide	in a liquid medium	17			
Nanocomposites	in an aerosol	17			
Silicates	as volatile particles	17			
Organic dye pigment	as volatile particles	17			
Silver	as volatile particles	17			
Nanotones/layered silicates	in an aerosol	16			
Chromium(III)-oxide	in a liquid medium	15			
Carbon nanotubes	in a liquid medium	15			
Polymers	as volatile particles	15			
Zinc oxide	in a liquid medium	14			
Nickel oxide	naturally aggregated	14			
Nickel oxide	coated	13			
Carbon nanotubes	naturally aggregated	13			
Nanocomposites	as volatile particles	13			
Titanium dioxide	in a liquid medium	12			
Chromium(III) oxide	coated	12			
Inorganic dye pigments	in liquid medium	11			
Organic dye pigments	in liquid medium	11			
Silver	in liquid medium	11			
Chromium(III) oxide	naturally aggregated	11			

2.2 Are the criteria used sufficient?

2.2.1 Aggregate states:

as volatile particles
in an aerosol
naturally aggregated
coated
in a liquid medium/in a solvent
embedded in a matrix

The list is sufficient Yes ☐ No ☐ Don't know ☐

Comments or more precise details:

2.2.2 Causes of toxicity

Solubility
Size (given in the range e.g. < 70 nm
Shape
Surface and reactivity

The list is sufficient Yes ☐ No ☐ Don't know ☐

Comments or more precise details:

3 Exposure: results from Round 1

The following table contains a **selection** of substances marked in red which were attributed high or average importance of the exposure pathway for negative health effects by more than 50% of the experts. The substances in yellow are the ones to which more than 33% of experts attributed high or average importance. Substances were selected for which not only the inhalational pathway was mentioned primarily but which were attributed high or average importance for negative effects for other exposure pathways, too.

Exposure pathway of the substances (listed by number of mentions)	**Number of mentions**	**Oral [in %]**	**Dermal [in %]**	**Inhalational [in %]**
Carbon nanotubes	**135**	33.3	22.2	**88.9**
Fullerenes	**123**	36.6	43.9	**78.0**
Silver	**108**	36.1	27.8	**63.9**
Vitamins	**108**	47.2	16.7	30.6
Nickel oxide	**105**	**60.0**	48.6	**65.7**
Degradable materials (lipid compounds, biopolymers?)	**102**	35.3	20.6	26.5
Chromium(III)-oxide	**99**	**51.5**	39.4	**84.8**
Organic dye pigments	**93**	32.3	41.9	**77.4**

3.1 Please evaluate this selection again:

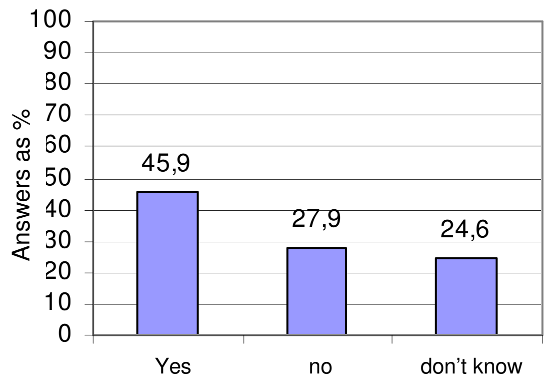
What importance do the various exposure pathways have for negative health effects? Please assess the importance of the exposure pathways of the following materials in the drop down list.

Substance	**Oral**	**Dermal**	**Inhalational**	**Reasons**
Carbon nanotubes				
Fullerenes				
Silver				
Vitamins				
Nickel oxide				
Degradable materials (lipid compounds, biopolymers)				
Chromium(III)-oxide				
Organic dye pigments				

Comments?

3.2 Consumer exposure to nanomaterials

The figure opposite contains the results from Round 1 for the question: “In your opinion are consumers exposed to nanomaterials from the abrasion of textiles or surface coatings?” “



3.2.1 Do you agree with the following statements?

3.2.1.1 Surface coatings (e.g. varnishes, easy-to-clean coatings)

There may be abrasion of nanomaterials	Yes ☐	No ☐	It depends ☐	Don’t know ☐
Abrasion may be nanoscale	Yes ☐	No ☐	It depends ☐	Don’t know ☐
Abrasion is in the micrometer range and does not show any nanospecific effect	Yes ☐	No ☐	It depends ☐	Don’t know ☐

Please state reasons:

3.2.1.2 Textiles

There may be abrasion of nanomaterials	Yes ☐	No ☐	It depends ☐	Don’t know ☐
Abrasion may be nanoscale	Yes ☐	No ☐	It depends ☐	Don’t know ☐
Abrasion is in the micrometer range and does not show any nanospecific effects	Yes ☐	No ☐	It depends ☐	Don’t know ☐

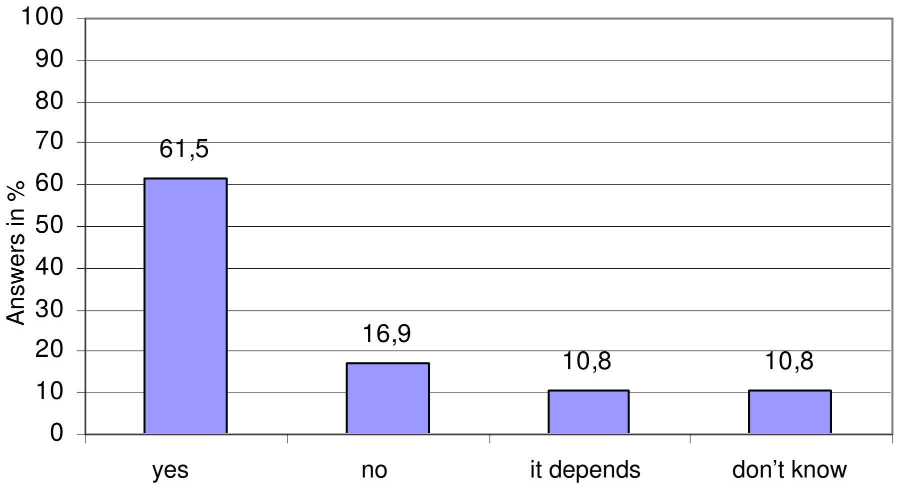
Please state reasons:

3.3 Dermal, inhalational and oral exposure pathways

In the following section general theories were examined in order to identify a basic trend in the assessments. Some new questions arose from the remarks, which are given below the result graphs.

3.3.1 Dermal exposure pathway

Results for theory 1: "The skin is largely impermeable to nanoparticles when it can assume its protective function and is not free from damage or mechanical strain"



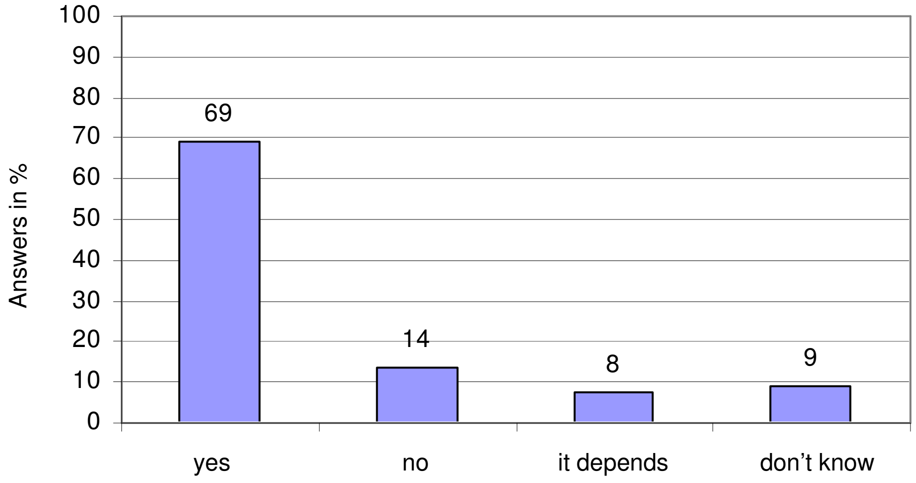
3.3.1.1 New question triggered by the remarks:

In your opinion is there an elevated risk of allergies when nanomaterials come into contact with the skin?

Yes ☐ No ☐ It depends ☐ Don't know ☐

Please state reasons:

Results for theory 2: “In the case of skin injuries, strong mechanical strain and very small nanoparticles (< 5 – 10 nm) this protective function is probably impaired.”



3.3.1.2 New question triggered by the remarks:

Do you expect a negative health effect when nanomaterials come into contact with stressed skin which can be attributed to the nano-scale of the substances?

Yes ☐ No ☐ It depends ☐ Don’t know ☐

Please state reasons:

Do you expect contact with very small nanoparticles (<5-10 nm) to have negative health effects on healthy skin?

Yes ☐ No ☐ It depends ☐ Don’t know ☐

Please state reasons:

Results for theory 4: “Liposomes can neither pass through the intact horny layer nor can they improve the intake of active ingredients.”

3.3.1.3 Additional questions triggered by the remarks:

3.3.1.3.1 Can liposomes pass through the intact horny layer?

Yes ☐ No ☐ It depends ☐ Don’t know ☐

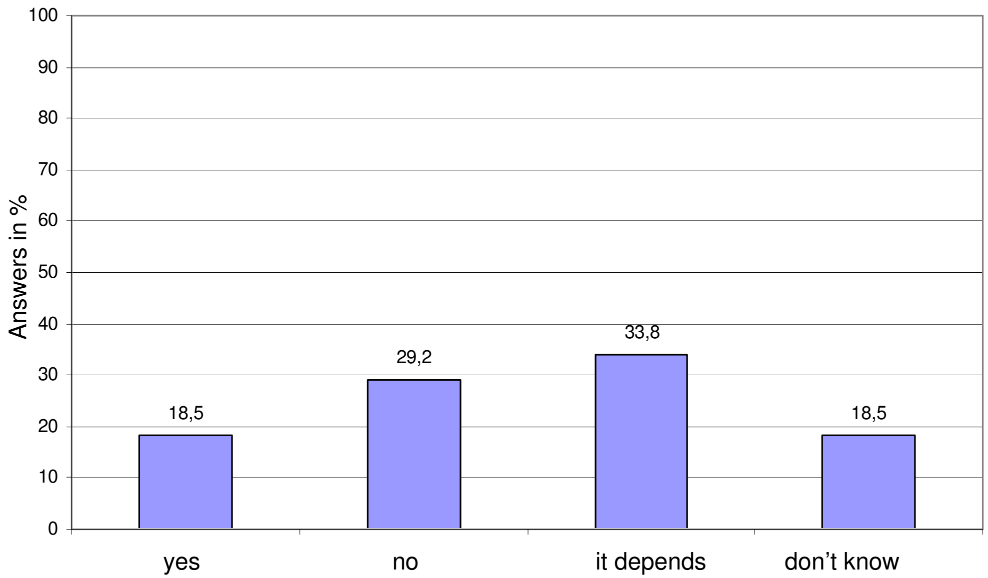
Please state reasons:

3.3.1.3.2 Do they improve the intake of active ingredients?

Yes ☐ No ☐ It depends ☐ Don’t know ☐

Please state reasons:

Results for theory 7: “Nanoparticles penetrate the skin and cause systemic exposure of the organism.”



The remarks of numerous participants differ when it comes to the question of systemic exposure by substances. Fullerenes are mentioned particularly frequently as a negative example.

3.3.1.4 Additional questions triggered by remarks on fullerenes:

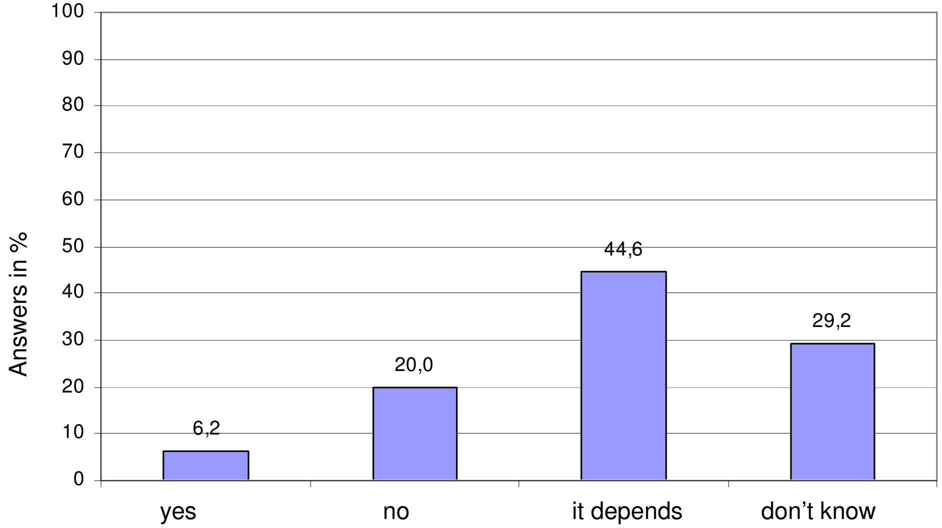
Do you expect dermal contact with **fullerenes** to lead to systemic exposure?

Yes ☐ No ☐ It depends ☐ Don't know ☐

I do not expect any negative health effects ☐

I expect one negative health effect and that is:

3.3.2 Results for theory 2: Inhalational exposure pathway. "Following inhalational intake nanoparticles have a carcinogenic effect."



3.3.2.1 Additional questions about the dependency factors

In the remarks various dependency factors were identified which could trigger carcinogenicity.

Please assess these factors:

The carcinogenicity of nanomaterials depends on...

Dependency factor	**Assessment**	**Remark/reasons**
Persistence of the particles		
Surface reactivity		
Potential to produce free radicals		
Dose		
Type of substance		
Coating		
Form		
Distribution in tissue		
Charge distribution between the molecules		
Degree of agglomeration		
Oxidative mechanisms		
Size		

Remarks?

4 Consumer-relevant applications: results

The frequencies of the selected mention are given. The option “don’t know” is not contained in this overview. The highest value is indicated.

Please assess a few selected applications again.

4.1 Nanotechnology and food

Application	Toxicity/negative health effects of the end products	Consumer acceptance	Positive health effects	Implementation period	Remarks
Application L 3: Colloidal salicylic acid or **silicon dioxide** is used as a **trickling agent** or carrier material because of its high absorption capacity in order to prevent the baking together of sodium chloride crystals and food.	none 45.7 % few 10.9 % average 6.5 % high 6.5 %	none **4.3 %** few **15.2 %** average **39.1 %** high **28.3 %**	none **47.8 %** few **21.7 %** average **15.2 %** high **8.7 %**	On the market **47.8 %** 1-2 y. **8.7 %** 2-5 y. **8.7 %** 5-10 y. **0.0 %**	
Applications L 4: There are plans to coat chocolate bars with a **titanium dioxide** layer that is only a few nanometres thick and is neutral in taste in order to ensure that they still **look attractive** even if they have been lying around for some time.	none **27.1 %** few **14.6 %** average **10.4 %** high **4.2 %**	none **16.7 %** few **33.3 %** average **29.2 %** high **6.3 %**	none **56.3 %** few **22.9 %** average **8.3 %** high **0.0 %**	On the market **8.3 %** 1-2 y. **29.2 %** 2-5 y. **10.4 %** 5-10 y. **0.0 %**	
Applications L 6: Nanotechnology **anti-oxidant** systems are said to help food stay fresh longer. Nanoscale **micelles** are to be used as the carriers for anti-oxidants.	none **27.9 %** few **14.0 %** average **7.0 %** high **2.3 %**	none **7.0 %** few **25.6 %** average **48.8 %** high **7.0 %**	none **16,3 %** few **32.6 %** average **37.2 %** high **7.0 %**	On the market **7.0 %** 1-2 y. **14.0 %** 2-5 y. **25.6 %** 5-10 y. **0.0 %**	
Applications L 7: Silver particles dissolved in pure water (diameter 0.8 nm, concentration 10ppm) are available as food supplements. The charge of silver and its nanoscale formulation are said to increase a feeling of wellbeing and boost the **immune system**.	none **11.9 %** few **26.2 %** average **23.8 %** high **7.1 %**	none **16.7 %** few **38.1 %** average **26.2 %** high **4.8 %**	None **59.5 %** few **21.4 %** average **14.3 %** high **0.0 %**	On the market **28.6 %** 1-2 y. **19.0 %** 2-5 y. **7.1 %** 5-10 y. **0.0 %**	

4.2 Nanotechnology and cosmetics

Application	Toxicity/negative health effects of the end products	Consumer acceptance	Positive health effects	Implementation period	Comments
Application K 6: Silver nanoparticles (diameter approx. 7nm) are used in soaps to **clean** and **disinfect the skin.** This is said to prevent the onset of acne and activate skin cells.	none **22.4 %** few **22.4 %** average **12.2 %** high **6.1 %**	none **4.1 %** few **10.2 %** average **57.1 %** high **22.4 %**	none **4.1 %** few **28.6 %** average **32.7 %** high **10.2 %**	on the market **16.3 %** 1-2 y. **18.4 %** 2-5 y. **4.1 %** 5-10 y. **0.0 %**	
Application K 7: C60 fullerenes are used as **antioxidants** in creams. Fullerenes are said to be able to neutralise dangerous free radicals and in this way prevent premature aging of the skin.	none **10.9 %** few **15.2 %** average **19.6 %** high **8.7 %**	none **6.5 %** few **23.9 %** average **34.8 %** high **15.2 %**	**none** **23.9 %** few 41.3 % average 13.0 % high 2.2 %	on the market **21.7 %** 1-2 y. **10.9 %** 2-5 y. **4.3 %** 5-10 y. **2.2 %**	

4.3 Nanotechnology and textiles

Applications T 2: A new anti-**odour** technology embeds **silver** nanoparticles (diameter 15nm) in the fibres of socks, shoes and cloths. The silver particles kill odour-forming bacteria or inhibit their growth.	none **26.9 %** few **23.1 %** average **11.5 %** high **3.8 %**	none **1.9 %** few **9.6 %** average **34.6 %** high **42.3 %**	none **26.9 %** few **28.8 %** average **26.9 %** high **9.6 %**	on the market **53.8 %** 1-2 y. **13.5 %** 2-5 y. **0.0 %** 5-10 y. **0.0 %**	
Applications T 3: Nanocontainers with fragrances and active ingredients are integrated into textiles (clothing as well as carpets and settees). The capsules form when fragrance isocyanine oil droplets (from 100nm in size) are incorporated into an aqueous polyamide solution and the **isocyanine** molecules react on the surface of the oil droplets with the surrounding **polyamines** in water. In this way they encapsulate the fragrance. Capsules with a porous shell continue to release even amounts of the substance over a period of months.	none **20.5 %** few **15.9 %** average **11.4 %** high **9.1 %**	none **4.5 %** few **25.0 %** average **43.2 %** high **15.9 %**	none **56.8 %** few **31.8 %** average **6.8 %** high **4.5 %**	on the market **15.9 %** 1-2 y. **22.7 %** 2-5 y. **9.1 %** 5-10 y. **0.0 %**	
Applications T 4: Halamides (polymer molecules) are used to coat textiles. Materials are formed that trap and kill viruses and bacteria. **The antimicrobial** materials are used to protect medical personnel and farmers who work with pesticides.	none **5.3 %** few **31.6 %** average **7.9 %** high **10.5 %**	none **0.0 %** few **15.8 %** average **34.2 %** high **39.5 %**	none **2.6 %** few **15.8 %** average **34.2 %** high **31.6 %**	on the market **10.5 %** 1-2 y. **18.4 %** 2-5 y. **10.5 %** 5-10 y. **0.0 %**	
Applications T 8: Nanoparticles made of **SiO_2** are used to form nanostructured surfaces on fibres. This gives the textiles dirt-repellent properties.	none **46.2 %** few **0.0 %** average **23.1 %** high **1.9 %**	none **1.9 %** few **1,9 %** average **19.2 %** high **67.3 %**	none **32.7 %** few **15.4 %** average **30.8 %** high **13.5 %**	on the market **32.7 %** 1-2 y. **17.3 %** 2-5 y. **3.8 %** 5-10 y. **0,0 %**	

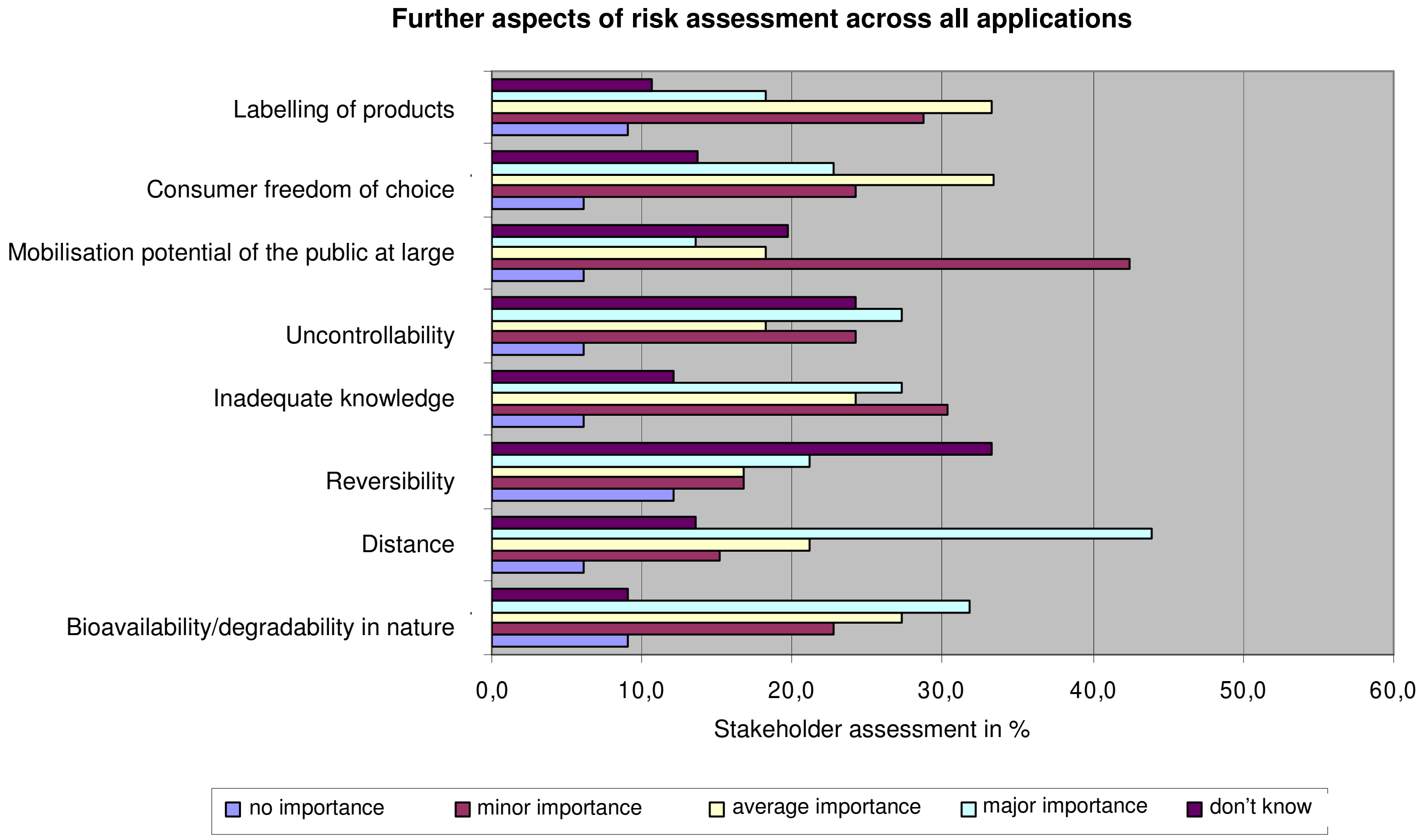
4.4 Nanotechnology and surface coatings

Applications O 3: Silicon nanoparticles, which contain fluorescent dye molecules and antibodies, help to **detect bacteria**. When the antibodies dock onto the antigens of a bacterium, this can be indicated by the fluorescent illumination of the nanoparticles.	none **26.2 %** few **23.8 %** average **7.1 %** high **4.8 %**	none **4.8 %** few **14.3 %** average **45.2 %** high **23.8 %**	none **14.3 %** few **4.8 %** average **47.6 %** high **23.8 %**	on the market **4.8 %** 1-2 y. **9.5 %** 2-5 y. **21.4 %** 5-10 y. **00 %**	
Applications O 4: Antimony zinc oxide (Sb:Sn ratio = 1:9 purity 99.5+% particle size 30nm) is admixed to coatings in order to improve the **antistatic** properties of surfaces.	none **23.9 %** few **17.4 %** average **8.7 %** high **13.0 %**	none **2.2 %** few **19.6 %** average **45.7 %** high **8.7 %**	none **37.0 %** few **26.1 %** average **13.0 %** high **2.2 %**	on the market **15.2 %** 1-2 y. **19.6 %** 2-5 y. **10.9 %** 5-10 y. **0.0 %**	
Applications O 6: A 30% dispersion of aluminium (**Al_2O_3**) nanoparticles (particle size 45 nm) in hexane diocrylate (HDDA) is used to improve the **scratch resistance** of parquet and furniture varnishes.	none **29.4 %** few **23.5 %** average **7.8 %** high **2.0 %**	none **0.0 %** few **3.9 %** average **39.2 %** high **45.1 %**	none **51.0 %** few **5.9 %** average **21.6 %** high **7.8 %**	on the market **29.4 %** 1-2 y. **15.7 %** 2-5 y. **5.9 %** 5-10 y. **2.0 %**	
Applications O 8: A wall paint, in which nanometre size **silver particles** are evenly distributed, **prevents mould formation** in indoor areas and algae growth on façades. The particles release silver ions that block nutrient-transporting enzymes, destroy important proteins, dock onto hereditary material and intervene in cell wall synthesis.	none **23.1 %** few **30.8 %** average **5.8 %** high **9.6 %**	none **1.9 %** few **7.7 %** average **46.2 %** high **32.7 %**	none **17.3 %** few **19.2 %** average **34.6 %** high **19.2 %**	on the market **36.5 %** 1-2 y. **19.2 %** 2-5 y. **3.8 %** 5-10 y. **0.0 %**	

Remarks?

5 Further aspects of risk assessment, communication, management and dialogue with stakeholders

5.1 Results from Round 1:



5.1.1 In the areas food and cosmetics we ask for renewed assessment and the statement of the reasons for your point of view

	Food	Reasons	Cosmetics	Reasons
Bioavailability/degradability in nature				
Persistence				
Reversibility				
Insufficient knowledge				
Uncontrollability				
Mobilisation potential of the public at large				
Consumer freedom of choice				
Labelling of products				

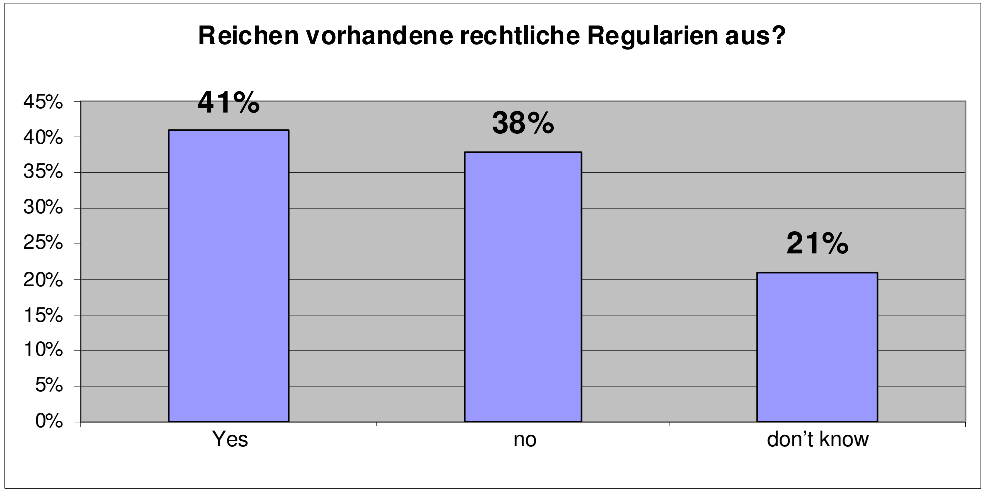
Remarks?

6 Regulatory questions

6.1 Results from Round 1: Are the existing statutory provisions (REACH) sufficient?

6.1.1 Please assess again: Are the existing statutory provisions (REACH) sufficient?

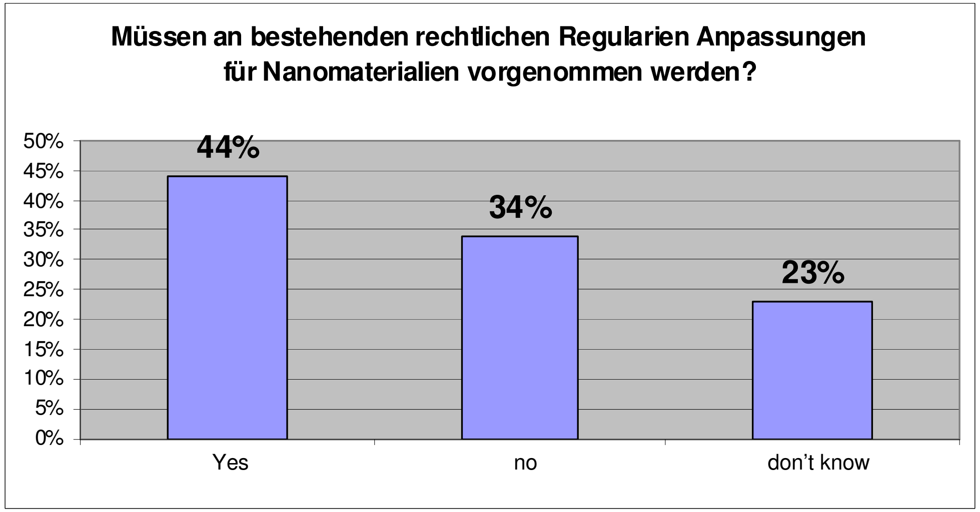
Yes ☐ No ☐ Don't know ☐



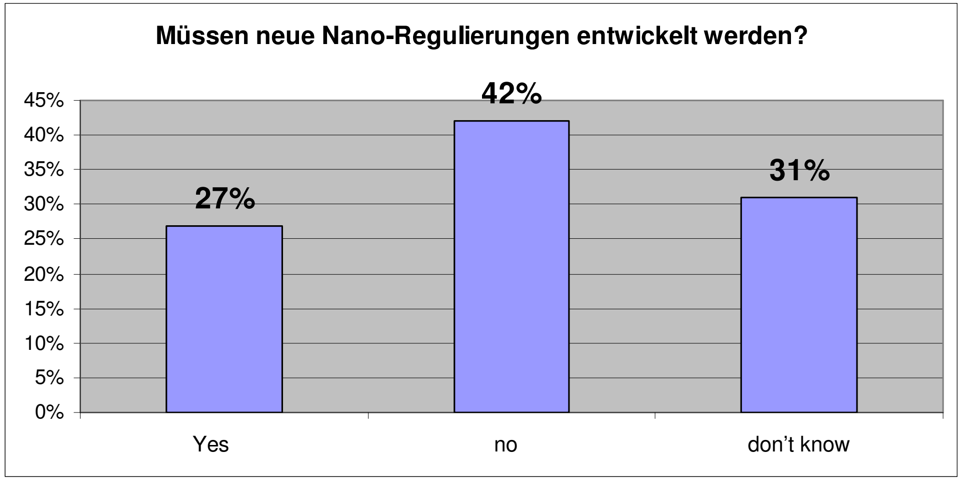
6.2 Results from Round 1: Is there a need to adapt the existing statutory provisions for nanomaterials?

6.2.1 Please answer the question again: Is there a need to adapt the existing statutory provisions for nanomaterials?

Yes ☐ No ☐ Don't know ☐



6.3 Results from Round 1: Must new nanoprovisions be developed



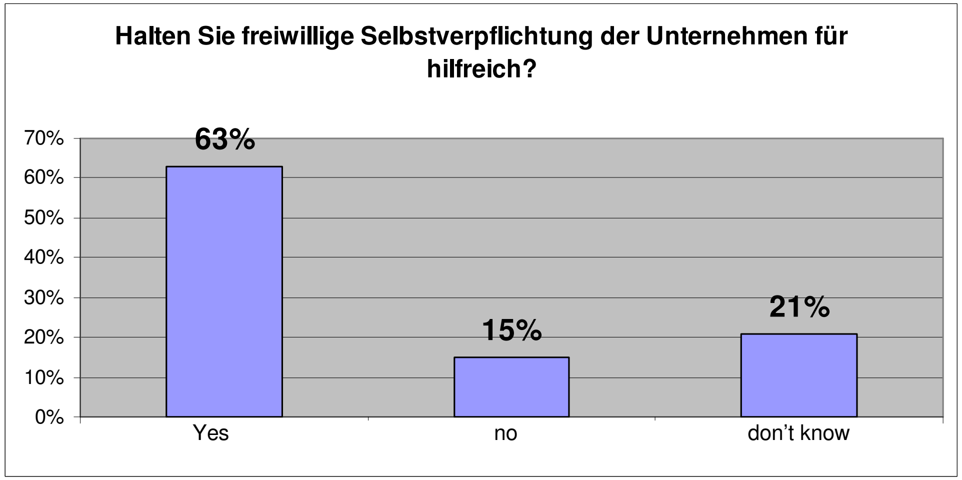
6.3.1 Please assess this again: Must new nanoprovisions be developed?

Yes ☐ No ☐ Don't know ☐

6.4 Results from Round 1: Do you believe that voluntary undertakings of companies (best practice guidelines) are helpful?

6.4.1 Please assess this again: Do you believe that voluntary undertakings of companies (best practice guidelines) are helpful?

Yes ☐ No ☐ Don't know ☐



6.5 Results from Round 1: What should voluntary undertakings contain? All values higher than 50% are indicated

What should voluntary undertakings contain?	**Yes**	**No**	Don't know
Instructions for workplace assessment	**87.3 %**	4.2 %	8.5 %
Safety assessment of the end product	**85.9 %**	7.0 %	7.0 %
Safety assessment for all links in the production chain	**67.6 %**	16.9 %	15.5 %
Use of the precautionary principle down to adaptation of provisions	**62.0 %**	18.3 %	19.7 %
Template for detailed nano safety datasheets	**59.2 %**	28.2 %	12.7 %

We ask for renewed assessment:

6.5.1 What should voluntary undertakings contain?

	Yes	**No**	**Don't know**
Template for detailed nano safety datasheets	☐	☐	☐
Instructions for workplace assessment	☐	☐	☐
Safety assessment for all links in the production chain	☐	☐	☐
Safety assessment of the end product	☐	☐	☐
Use of the precautionary principle down to adaptation of provisions	☐	☐	☐

Remarks?

7 Development of action strategies for risk avoidance/risk minimisation

Results from Round 1: How useful are the following proposals?

The values in orange are the ones with the highest approval. The values in yellow have the second highest approval rate.

	Not useful at all	Not very useful	Useful	Very useful	Don't know
Systematic recording of biological effects	2.8 %	2.8%	35.2%	**57.7%**	1.4%
Life cycle assessment of nanoproducts	4.2%	4.2%	38.0%	**47.9%**	5.6%
Systematic examination of interaction with natural and artificial substances	12.7%	8.5%	29.6%	**45.1%**	4.2%
Improved networking/cooperation with information providers (industry, research, public authorities)	0%	1.4%	38.0%	**57.7%**	2.8%
Open, result-oriented dialogues between the stakeholders on joint risk assessment	0%	5.6%	**50.7%**	39.4%	4.2%
Stakeholder dialogue on the joint development of voluntary undertakings by industry	2.8%	12.7%	**64.8%**	15.5%	4.2%
Citizen dialogues/consumer conferences on selected nanotechnology topics	8.5%	23.9%	**46.5%**	15.5%	5.6%

7.1 Please assess again:

How useful do you think the following proposals are:

	Not useful at all	Not very useful	Useful	Very useful	Don't know
Systematic recording of biological effects	☐	☐	☐	☐	☐
Life cycle assessment of nanoproducts	☐	☐	☐	☐	☐
Systematic examination of interaction with natural and artificial substances	☐	☐	☐	☐	☐
Improved networking/cooperation with information providers (industry, research, public authorities)	☐	☐	☐	☐	☐
Open, result-oriented dialogues between the stakeholders on joint risk assessment	☐	☐	☐	☐	☐
Stakeholder dialogue on the joint development of voluntary undertakings by industry	☐	☐	☐	☐	☐
Citizen dialogues/consumer conferences on selected nanotechnology topics	☐	☐	☐	☐	☐

Remarks and other management strategies:

On behalf of the Federal Institute for Risk Assessment and Stuttgart University we thank you once again for your support and the time you spent on the second Delphi round.

The final report with all the results will be handed over to our client in December and will be made available as soon as possible to all participants.

Kind regards,
Dr. Antje Grobe, ZIRN, Stuttgart University and Dr. René Zimmer, Federal Institute for Risk Assessment, Berlin

Here you have an opportunity to give us further feedback or make general remarks:

10 List of Figures

11 List of Tables

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