Report 2019:1

SweNanoSafe

Swedish National Platform for Nanosafety

National Workshop on Nanosafety Research & Education

13 June 2018, Stockholm, Sweden

Nanosafety Research & Education

A report from the National Workshop, 13 June 2018, Stockholm, Sweden

Preface

On 13th June 2018, SweNanoSafe, the Swedish National Platform for Nanosafety, gathered around fifty participants at Karolinska Institutet for a workshop on research and education within the area of nanosafety. The discussions focused on research needs and implementation of research results for regulation, development and safe use of nanomaterials.

The event brought together participants from different stakeholder groups, mainly from academia but also from research institutes, public health-care, authorities and industry, thereby providing opportunities for networking and further cooperation among stakeholders. Researchers from nine Swedish universities participated in the workshop.

On behalf of SweNanoSafe, we express our gratitude to all participants for their valuable contribution to the discussions and results of the workshop. We also thank Ami Palmin and Jonas Förare for contributing to the practical arrangements and communication of the workshop.

Bengt Fadeel, Chair SweNanoSafe Expert Panel, and the SweNanoSafe Project Team

SweNanoSafe

Swedish National Platform for Nanosafety

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Jonas Förare

The report can be downloaded at
www.swenanosafe.se

Stockholm, June 2019

Contents

Abbreviations

AOP	Adverse outcome pathway
CLP	Classification, Labelling and Packaging
DNEL	Derived No Effect Level
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EHS	Environment, Health and Safety
EU	European Union
EUON	The European Union Observatory for Nanomaterials
GU	Gothenburg University
H2020	Horizon 2020
ICT	Information and Communication Technology
ISO	International Organization for Standardization
KEMI	Swedish Chemicals Agency
LCA	Life Cycle Assessment
OECD	Organisation for Economic Co-operation and Development
MISTRA	Swedish Foundation for Strategic Environmental Research
NGO	Non-Governmental Organisation
NP	Nanoparticle
NM	Nanomaterial
OEL	Occupational Exposure Limit
PI	Principal investigator
QSAR	Quantitative structure–activity relationship
REACH	Registration, Evaluation, Authorisation and restriction of Chemicals
RIVM	National Institute for Public Health and the Environment (The Netherlands)
SbD	Safe-by-Design
SDS	Safety Data Sheet
SME	Small and medium-sized enterprise
SOP	Standard Operating Procedure
SU	Stockholm University
UU	Uppsala University
WHO	World Health Organization

About the Organisers

The workshop was organised by the SweNanoSafe Expert Panel and Project Team. The work was led by Ulrika Carlander (SweNanoSafe Project Manager) in collaboration with Bengt Fadeel (Karolinska Institutet, Chair SweNanoSafe Expert Panel) and Gregory Moore (Swedish Chemicals Agency and SweNanoSafe Expert Panel) with the support of members of the SweNanoSafe Project Team: Rune Karlsson, Marie Beckman, and Elina Drakvik, as well as Heike Hellmold, Ami Palmin and Jonas Förare at Swetox.

Ulrika Carlander, Karolinska Institutet, and Project Manager of SweNanoSafe, Swetox Södertälje

About the Report

The report is aimed at stakeholders in the field of nanosafety such as academia, regulatory authorities, industry, and NGO's and interested members of the public. It provides a condensed summary of the discussions and suggestions for future actions (see Summary of Group Discussions). The report was prepared by Rune Karlsson, reviewed and revised by predominantly Heike Hellmold, Bengt Fadeel, Gregory Moore and Marie Beckman. Layout and final editing: Marie Beckman. Guidance for the group discussions is included in Annex

II. As a background, the notes from the discussions, taken by Jonas Förare, Elina Drakvik, Heike Hellmold, Rune Karlsson and Ulrika Carlander, have been adapted by Rune Karlsson and included in Annex III.

About SweNanoSafe

SweNanoSafe, the Swedish National Platform for Nanosafety, is an assignment from the Swedish Government. The platform was originally established in 2016 at Swetox, an academic research center. Since January 1, 2019, the platform is hosted by the Institute of Environmental Medicine, Karolinska Institutet.

In order to promote safe use and handling of manufactured nanomaterials, the platform aims to strengthen the communication and cooperation between different stakeholders to ensure knowledge exchange in the field of nanosafety. One important objective for the platform is to increase the knowledge on hindrances to the safe use and handling of nanomaterials and how these hindrances can be addressed.

The platform consists of a Steering Committee, a Project Team, a Cooperation Council, an Expert Panel. In addition, the platform has developed a web-based forum for information and knowledge exchange (www.swenanosafe.se) and further information on the organisation and the various activities can be found there.

In brief, stakeholders are represented in the Cooperation Council that consists of members from authorities, industry, NGO's and academia. Currently, the council has approximately thirty members. Through the council, the needs of information and knowledge about nanosafety among those who work within the field can be highlighted. Therefore, the council plays a key role in the platform ensuring that the benefit of the platform is maximised for the actors involved.

The Expert Panel of SweNanoSafe consists of members with expertise from different disciplines within the field of nanosafety ranging from toxicology to risk assessment. An important task of the panel is to ensure the quality and actuality of the knowledge generated and communicated via the platform.

Overview of the Workshop

Åke Bergman, Head of Swetox, introduced the workshop by welcoming everyone and presenting SweNanoSafe's activities.

The main aim of the workshop was to provide an opportunity to discuss strengths, needs and priorities of Swedish nanosafety research and how research and results can be made useful for societal and regulatory needs (see the agenda, Annex I). The goal was to develop proposals for measures based on identified needs. The focus of the discussions was on manufactured nanomaterials and identification of proposals that may be realized nationally in the short-term (1-5 years) or medium-term (5-10 years). The workshop also aimed to increase collaboration and knowledge transfer between different actors in the field of nanosafety.

Professor Åke Bergman, Chair SweNanoSafe Steering Committee and Head of Swetox, opened the workshop by welcoming everyone and presenting the background, aims and activities of SweNanoSafe. Subsequently, Professor Bengt Fadeel, Karolinska Institutet, presented the work of the Expert Panel (chaired by him) and the Swedish network of experts, which was inaugurated at the workshop. The network has been created on the initiative of SweNanoSafe to support interdisciplinary collaboration, to highlight and to increase the visibility of nanosafety research in Sweden, and to identify research needs and

priorities for future research. Heike Hellmold, Chair SweNanoSafe Cooperation Council, concluded the introduction by speaking about the platform's work to identify existing hindrances and possible measures for the safe management of nanomaterials.

Following these introductory remarks, the workshop participants were divided into several smaller groups, and discussions took place in the morning as well as in the afternoon, using a predefined set of questions. Bengt Fadeel and Gregory Moore introduced and chaired the morning and afternoon sessions, respectively. The smaller break-out groups were chaired by Bengt Fadeel, Gregory Moore, Alexander Lyubartsev (Stockholm University and SweNanoSafe Expert Panel), Joachim Sturve (Gothenburg University and SweNanoSafe Expert Panel) and Åke Bergman. Notes from the discussions in these respective groups, were taken by Jonas Förare, Elina Drakvik, Heike Hellmold, Rune Karlsson and Ulrika Carlander. In the afternoon, each group reported their findings. Finally, Ulrika Carlander discussed the topic of education, and Bengt Fadeel concluded with reflections on the discussions and the way forward, including future activities of the national research network.

Introduction to Group Discussions: Nanosafety Research & Innovation

Bengt Fadeel, Karolinska Institutet, Chair SweNanoSafe Expert Panel, inaugurated the national network of nanosafety experts initiated by SweNanoSafe.

Bengt Fadeel introduced the topic and gave examples of Swedish and international research projects and research collaborations such as the Swedish Mistra Environmental Nanosafety Programme and the European Union (EU) NanoSafety Cluster. He also highlighted ongoing research and current issues on nano-specific effects, classification and grouping of nanomaterials, advanced in vitro methods and systems biology concepts. The aim of the group discussions was to identify 1) strengths and trends and 2) needs and priorities in nanosafety research, as well as proposals for actions that could strengthen future Swedish nanosafety research.

Introduction to Group Discussions: Nanosafety Research – Making it Useful

Gregory Moore began by demonstrating the importance of nanosafety research for Swedish and global goals for sustainable development and a non-toxic environment. He provided examples of actors and research funding bodies in the field, such as the EU, the Organisation for Economic Cooperation and Development (OECD), the World Health Organization (WHO), Vinnova, Mistra and Formas. He expressed the need for a link between nanosafety research and regulatory activities, highlighting the ProSafe White Paper (ref 4), where 14 recommendations were presented to promote this goal.

Gregory Moore, Swedish Chemicals Agency, Member of SweNanoSafe Expert Panel

Education and Training

Ulrika Carlander presented the work that has been performed to understand needs in education and training in nanosafety. In the survey conducted by the platform, only a few courses in nanosafety have been found. This can be explained to some extent by the fact that nanosafety is included as a part-time subject in other courses. The platform will appreciatively showcase courses, programs and other educational activities on SweNanoSafe's web portal. Participants were therefore encouraged to send information about courses and other educational events to the platform and to further consider activities needed to strengthen education and training in nanosafety.

National Network of Researchers

The network has been created to support national cooperation in the field of nanosafety research. The network currently includes approximately 75 participants from 13 Swedish universities and research institutes, and its members span across different disciplines from material production and characterization to toxicology, risk assessment and life cycle analysis. The present workshop represents the official kick-off of the network.

Towards the end of the day, Bengt Fadeel discussed what the next steps for the research network and of SweNanoSafe should be. One suggestion was to follow up on research in industry with a workshop for academics and industry researchers, possibly with a focus on Safe-by-Design (SbD). Another proposal was to make visible relevant research information and research networks to facilitate research collaboration.

If you would like to join the network, please visit the page Research Network on the SweNanoSafe web portal or contact Rune Karlsson (rune.karlsson@swenanosafe.se).

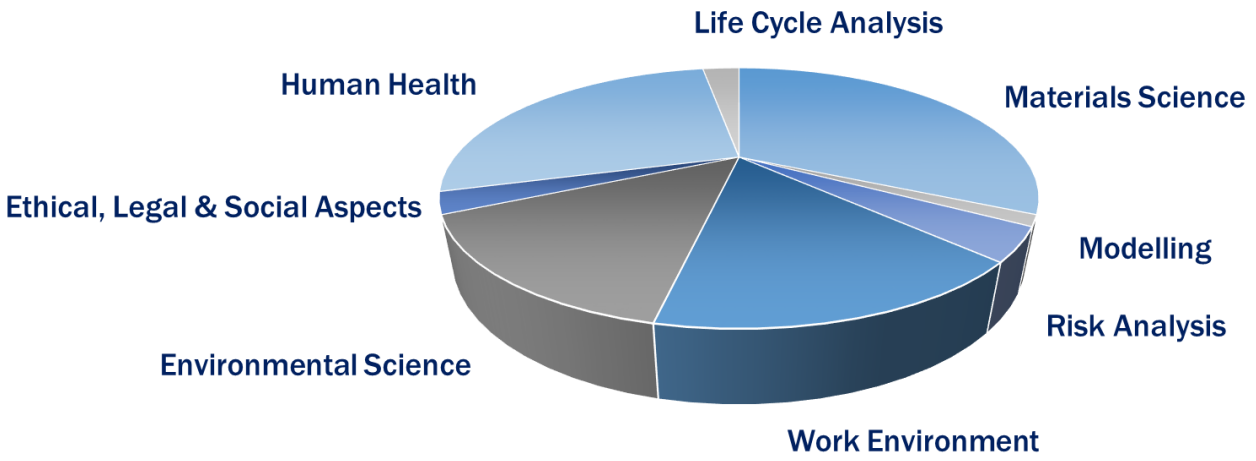

Illustration of research disciplines that are currently represented within the network.

Summary of Group Discussions

In particular, the following main areas were discussed in parallel groups with secretaries taking notes that were further processed and summarised by the project group. The discussions resulted in suggestions for future needs in research and continued activities of the research network (see also the Annex which documents in detail the various group discussions). The suggestions from the individual participants are categorised and summarised in ten different areas, see below:

Data

Recent activities have been focused on gathering and consolidating data and building databases, thereby supporting modelling efforts. Because there is a mismatch between required and available data, one focus is on generating the data needed for modelling and regulatory purposes. Data driven approaches, such as Quantitative Structure–Activity Relationship (QSAR), is based on rigorous methodologies leading to regulatory relevant

data (4). A need to build large databases was similarly identified, for example to enable QSAR-modelling. The quality and accessibility of data continues to be important issues. For example, it was suggested to retrieve all data that industry has produced and make it available to researchers and regulators. The quality of input data should be controlled to guarantee the usability and reliability of databases. All data should have open access. One way to support this, would be for funding agencies to already at the application stage require formatted "open-data" results.

To harmonise, better utilise and ensure quality data, the meeting suggested to use Big Data techniques (statistics, machine learning, data mining etc.), defined nanosafety terms (ontologies) (cf. 7), rigorous and systematic data management (standardised data collection, curation, analysis, storage). Meticulous data management should also be financially supported by funding agencies. It was recommended that data storage should be centralised at the EU-level (the EU Observatory for Nanomaterials, EUON), but also to some degree at national levels.

Terms with similar meaning like "zero-effect", "no-effect" and "negative effect" – data are used by different stake holders. It was suggested to elaborate on the meaning of, and suggest a definition for these terms with involvement of both researchers and regulators (cf. 7).

Methods and test systems

As characterisation is coupled with safety aspects, proper and good-quality information should be included in safety data sheets (SDSs), for example data of appropriate quality obtained from industry.

The quality of information about nanomaterials in the SDSs that industry provides may be low because proper characterisation has not been done. It was suggested that lack of quality of the SDSs is more of an enforcement issue/responsibility issue rather than a research question (there are already appropriate characterisation methods in place and so no need to develop new ones).

In addition, current Standard Operation Procedures (SOPs) should be collected and made available. Existing SOPs needs to be adapted to new nanomaterials with novel properties (for example regarding coating and surface functionalisation). More research may be required to improve the scientific basis of the EU nanomaterial definition. Furthermore, the definition should be open for modification if scientifically justified.

Interdisciplinary cooperation is important for developing methods and test systems. A major challenge lies in knowing which methods should be used, validated and

standardised. The meeting requested guidelines on what parameters to assess, as well as guidance documents for testing. Characterisation methods need to be adapted to biological media, and standardised methods for testing in biological systems are required. QSAR models should be developed further.

Adverse outcome pathways (AOPs), a method for structured representation of biological events leading to adverse effects, can be used toward application of in silico and in vitro data as a complement to basic testing.

More standard materials should be made commercially available for validation and calibration. In addition, it was suggested to develop a validated high through-put screening method and a testing matrix of parameters as a start for risk assessment. Generally agreed criteria/decision-tree is needed to demonstrate application of grouping and read-across concepts, that is predicting properties of a nanomaterial based on information from similar nanomaterials.

Developing a method to measure actual exposure in air was considered to be high priority, which means to accurately measure very low real-time nanoparticles concentration. There is also a need to increase knowledge about occupational exposure and health effects through human biomonitoring and epidemiology. In addition, new methods should be developed to handle waste and waste streams, to be selected and used based on the form, composition and quantity of the waste materials.

Exposure

Even though there are regulations for the work environment, very little knowledge exists about real-life occupational exposures. Safety awareness training was considered important for avoiding potential exposure in the working environment. It was suggested to translate the precautionary approaches into guidelines and basic requirements for protection, combined with labelling with a risk symbol for nanomaterials. The information requirements of SDSs need to be enforced according to laws since quality is an issue. Further knowledge on occupational exposure, predicting exposure scenarios, and setting of Occupational Exposure Limits (OELs) is required.

Specifically address potential high-risk manufacturing exposure scenarios, for example by enforcing regulation protecting workers or to only use known safe nanomaterials in fabrication processes. One could build on the asbestos tradition regarding measurements, risk assessment etc. and adapt to fibres that physically resembles asbestos such as certain carbon nanotubes.

For exposure scenarios in general (occupational, consumers, environment), knowledge of realistic exposures combined with toxicological data of new materials is required.

Life cycle analysis and fate

There are still many gaps in knowledge with regard to environmental fate, for example on where nanomaterials end up in the environment and which effects they may have. It was noted that more data is required for material flows and life cycle analysis (LCA). Additional data should be collected for environmental fate analysis, for example by measuring concentrations of nanomaterials in the environment and further information on the fate and behaviour such as trophic transfer (the extent to which nanoparticles can be reintroduced to the ecosystem via various food chains) and assessing biodegradation in soil and water.

Environmental fate modelling and exposure scenarios needs to be further developed. It was also suggested to investigate and perhaps regulate who can be considered responsible for safe handling of nanomaterials throughout the life cycle (for example manufacturers, users, re-users and/or waste handlers).

Calls and funding

It is desirable to enable coordination at the national level in order to increase the application- and success rates for national nanosafety research. Sweden should be more active in attracting EU-funding and also aim at EU-project coordination. National activities should be coordinated with international ones, especially with EU and OECD efforts in mind. Funding agencies should make targeted nanosafety calls. There are also requests for more minor interdisciplinary research calls in specific areas as well as more multidisciplinary calls with several principal investigators (PIs) with involvement of industry and authorities.

Education, training, communication

Education was considered essential at all levels, professional, university and applied research. Industry needs more knowledge, both by way of education and regulation. Education on REACH and nanomaterials should be emphasized. Competence in the field should be maintained through basic education and by recruiting younger researchers. It is important with good popular scientific information, for example communicated through workshops for the general public. Communication areas include: possible risks (for researches, workers, consumers), new research relevant to regulation and SweNanoSafe Research Network's views.

Regulation, test guidelines

In order to get regulatory approval sooner for new approaches, methods and concepts (testing, grouping, modelling etc.), it was suggested to initiate a forum for regulators and researchers to start discussion and the continue dialogue on this issue. There needs to be resources and funding for validation phases. Swedish scientists (for example at KEMI) should get involved in the evaluation of REACH, such as in case studies on REACH appendices, maybe funded by Sweden. Also, Swedish involvement in the evaluation of cosmetic and food packaging regulation etc. should be encouraged as well. It was suggested to adjust the tonnage limit in REACH and also to apply registration of articles with nanomaterials. There need to be arenas for regulators to collaborate with researchers. A specific suggestion was for researchers to develop a compendium on specific Environment, Health and Safety (EHS)-data that regulators could use.

For example, OECD's Testing Programme of Manufactured Nanomaterials is long-term work and research at universities is often shorter (projects, employment, etc.). Therefore, standardisation institutes/research institutes were considered better suited for such testing. Funding opportunities for researchers' contributions to work in the OECD, ISO, etc. were requested. Contributions to the organisations from national regulators and scientists, should be coordinated.

Safe innovation

At some applied research institutes, safety is designed-in from the very beginning of the innovation process. A suggestion was to further adapt the SbD-concept, that is to make it understandable and practical to the nanotechnology sector by collaboration between the academy, industry and regulators (cf. 5). Also, determine a definition of SbD, preferable with support and active involvement of Swedish funding agencies. Gather and disseminate information regarding calls on safe innovation/SbD for funding at the EU level. Apply risk-benefit analysis to SbD (for example, would it be justified to use a hazardous nanomaterial if you have a ground breaking application?) and use smarter tools for safe development of nanomaterials. Advanced knowledge on safety aspects, safety culture and sustainable innovations, could be used as business advantages for promoting Swedish industry in comparison to other countries.

The following specific needs in Swedish nanosafety research were identified:

- Explore and understand national scientific/applied research needs and answering to these needs by applying for funding concerning smaller Swedish research projects.

- Measurements of real exposure as a basis for more relevant and reliable risk assessments.
- Depending on products being developed, both basic and/or applied research may be needed.
- *In silico* evaluations are critical to target development towards relevant research.
- A better understanding of mechanistic action of NMs is required to predict possible toxic effects.

Suggestions on what SweNanoSafe could do:

- Arrange workshops: 1/Follow-up workshop, for example on the SbD concept, for the nanosafety research network (invite both industry and research funders) 2/ Characterisation workshop for industry researchers.
- Be responsible for national nanosafety data management, including list of contact persons.
- Initiate activity with members from the research network aimed at attracting more EU funding to Sweden,
- Coordinate the Swedish participation in, and coordination of, EU projects
- Develop a short educational PowerPoint on OECD activities and publish on the portal
- Develop an action plan and nanosafety research strategy for Sweden

Conclusions

At the end of the workshop, Bengt Fadeel concluded that Sweden has played a leading role in nanosafety research with excellent research in several areas, for instance in work environment, exposure measurements, bioavailability, material science, inhalation science, nano(eco)toxicology, advanced *in vitro* methods, systems biology & bioinformatics, and safety culture. The researchers also highlighted that existing and future data need to be harmonised and exploited better, for example for modelling and regulatory purposes. In some areas such as exposure scenarios and waste management, participants proposed that research should be strengthened. In these areas, Sweden should also have good opportunities to lead the required research forward. Several experts stated that research on underlying factors is required, for example on the parameters that are critical in the calculation models and on the mechanisms that control nanomaterial toxicity. The characteristics and behaviours of nanomaterials differ not only between different nanomaterials and their surface modifications, but also on the surrounding environmental media that may cause transformations, altering their behaviours (fate, transport, and toxicity). SbD was a recurring concept that several participants considered to have a

potential, but it needs to be further defined, made concrete and made practically applicable. Finally, the participants discussed potential future activities of the research network and topics for future workshops. Several participants expressed their interest in a workshop to engage with industry, for example on the theme of “Safe by design”. In terms of future challenges, questions were raised on how to maintain relevant competences in Sweden and attract new researchers into the field.

Comments from the participants after the workshop included appreciation of the "getting-to-know-people"-aspect with researchers from very different backgrounds working on nanosafety. The event was seen as a good opportunity to build networks as foundation for upcoming collaboration projects. The group discussions about research gaps and what is needed, were seen as very useful. Other appreciated topics included working with the OECD and the relationship of academic researchers to industry.

Sammanfattning (Abstract in Swedish)

Den 13 juni 2018 samlade SweNanoSafe cirka femtio deltagare på Karolinska Institutet för en workshop om forskning och utbildning inom nanosäkerhetsområdet. Dagen var också kick-off för ett nationellt forskarnätverk inom området. Diskussionerna under workshopen inriktades på forskningsbehov för att svara mot krav som finns vad avser reglering, utveckling och säker användning av nanomaterial. Workshopen förde samman olika aktörer, främst från akademin men även från forskningsinstitut, näringsliv och myndigheter, vilket gav utmärkta möjligheter till nätverkande mellan olika aktörer.

På workshopen konstaterades att Sverige spelar en viktig roll inom nanosäkerhetsområdet med världsledande forskning på flera områden, till exempel inom arbetsmiljö, säkerhetskultur, exponeringsmätningar, biotillgänglighet, materialvetenskap, inhalationsvetenskap, nano(ekotoxikologi) inklusive avancerade in vitro-metoder, systembiologi och bioinformatik. Under dagens gruppdiskussioner framkom att befintliga och framtida data måste harmoniseras och utnyttjas bättre, till exempel som underlag för modellering och riskbedömning. På vissa områden såsom exponering och avfallshantering, ansåg deltagarna att forskningen behöver stärkas. Inom just dessa områden bör Sverige också ha goda möjligheter att ha en ledande roll, till exempel genom att koordinera EU-projekt men också naturligtvis på nationell nivå. Flera experter menade att ytterligare forskning om underliggande faktorer fordras, till exempel för att fastställa kritiska parametrar i beräkningsmodeller och klargöra mekanismer som styr nanomaterialens toxicitet. Materialens egenskaper och beteenden skiljer sig åt, inte bara mellan olika nanomaterial och olika ytbehandlingar, utan också i förhållande till materialets omgivning det vill säga den biologiska miljön i eller utanför kroppen. "Säker design" (eng. Safe-by Design, SbD) var också ett återkommande begrepp som flera deltagare ansåg ha potential, men det behöver definieras ytterligare, konkretiseras och göras praktiskt tillämpbart. Vidare diskuterade deltagarna eventuella framtida aktiviteter i forskarnätverket och forskningsområden för framtida workshops. Flera deltagare uttryckte sitt intresse för att närmare följa upp forskningen inom industrin med en workshop för forskare inom akademi och industri, eventuellt kring begreppet SbD. Framtida utmaningar inklusive vilken roll SweNanoSafe har att spela som ett forum för svensk nanosäkerhetsforskning togs också upp.

Mer information på svenska om workshopen finns på följande länk: Nytt svenskt forskarnätverk inom nanosäkerhet invigt på SweNanoSafes workshop. Information om forskarnätverket hittar du här: SweNanoSafe / Vad vi gör / Forskarnätverk / Research Network.

References

1. Swedish Action Plan for the Use and Management of Nanomaterials, SOU 2013:70, 2013
2. Nanosafety in Europe 2015-2025, FIOH, 2013
3. Nanotechnology Research Directions for Societal Needs in 2020, WTEC, 2010
4. ProSafe White Paper – Towards a more effective and efficient governance and regulation of nanomaterials, ProSafe Project Office, 2017
5. NanoReg2 safe by design concept
6. Teunenbroek TV, Baker J, Dijkzeul, A, Towards a more effective and efficient governance and regulation of nanomaterials. Particle and Fibre Toxicology (2017) 14:54.
7. JRC Technical Reports: NANoREG harmonised terminology for environmental health and safety assessment of nanomaterials. Edited by Stefania Gottardo Authors Stefania Gottardo Laia Quiros Pesudo Sara Totaro Juan Riego Sintes Hugues Crutzen, 2016.

Annex I. Agenda

SweNanoSafe National Workshop on Nanosafety Research & Education

TIME: 10 - 16, 13th of June 2018

VENUE: INGHESALEN, WIDERSTRÖMSKA HUSET

TOMTEBODAVÄGEN 18, KAROLINSKA INSTITUTET, SOLNA

09.30	**REGISTRATION & COFFEE**
10.00	**Opening -** Åke Bergman • Short about SweNanoSafe
10.05	**Introduction** • The expert panel and the research network – Bengt Fadeel • Safe handling of nanomaterials – Heike Hellmold
10.30	**Group discussions: Nanosafety research & innovation** Bengt Fadeel • *Tour de Table* • *Research needs and funding priorities* • *Nanosafety – opportunity or threat?*
12.00	**Report from group discussions**
12.30	**LUNCH**
13.30	**Group discussions: Nanosafety research – making it useful** Gregory Moore • *Safe-by-design* • *From research to regulation*
14.30	**REFRESHMENT BREAK**
15.00	**Report from group discussions**
15.30	**Nanosafety education – Ulrika Carlander**
15.50	**Closing remarks – Bengt Fadeel**
16.00	**Close of the workshop**

Annex II. Guidance for group discussions

This chapter provides information and instructions for the group discussions at the workshop.

Group discussion – practical issues

There will be two sessions of discussions, one in the morning on "Nanosafety research & Innovation" and one in the afternoon on "Nanosafety research and making it useful".

During the discussion please motivate the needs (why, who) and concretize the proposals (how, who and when).

Background information is provided for each session with the aim to highlight relevant topics. Specific questions have been prepared for each session to help stimulate and focus the discussions, see below.

At the end of each session, discussions will be summarised and the most important conclusions will be presented in plenum. A group secretary will take notes.

Participants will be divided into the groups in advance and grouping will be sent out before the workshop.

Group discussion (1) on nanosafety research & innovation

Topics: Research needs & funding priorities; Nanosafety: opportunity or threat

Background

Nanomaterials and nanomaterial-enabled products have a huge economic potential with applications in many different sectors from energy to ICT (Information and Communication Technology) to medicine to environmental remediation to various consumer products. However, safe and sustainable development of the nanotechnologies demands that these new and emerging materials are tested with respect to potential effects on human health and the environment. A key challenge is to assess whether existing test methods for assessment of traditional chemicals are also applicable for engineered nanomaterials and how they need to be adapted. More information is needed on the actual exposure in occupational or other settings and attention should be put on safety assessment of nanomaterials from a life cycle perspective.

Considerable efforts have been made, not least in the FP7 and, more recently, in H2020 Framework Programme of the European Commission. Around 5 years ago, the EU Nanosafety Cluster published a strategic research agenda in which several cross-cutting issues were identified as being important in order to promote the growth of the nanotechnology industry including, e.g. standardization and development of the regulatory framework, and development of infrastructures for research, education and innovation, along with international collaboration. The report also provided a roadmap for 2015-2025 centred on the four main areas: materials, hazard, exposure, and risk.

An important focus in recent years has been on the development of a predictive nanotoxicological paradigm based on a detailed mechanistic understanding of nanomaterials and material features

that account for their health and environmental effects. This could aid in the grouping or categorization of nanomaterials and the development of adverse outcomes pathways with which to support decision making in risk assessment. However, at the same time, it is equally important to promote fundamental research to further our understanding of the biological interactions of nanomaterial.

Questions

1. Which are the current topics and trends in nanosafety research in Sweden, at the EU-level and beyond?
2. What are the research needs and priorities in Sweden and why, both short-term and medium-term?
3. Opportunity or threat? Discuss nano(eco)toxicology (nanosafety) activities in the context of innovation and suggest ways forward.
4. How can nanosafety research in Sweden benefit from collaboration?
5. What additional questions should be addressed at this workshop – please bring them with you?

During the discussion please motivate the needs (why, who) and concretize the proposals (how, who and when).

Group discussion (2) on nanosafety research and making it useful

Topics for discussion: the safe-by-design concept; From research to regulation

Background

Regulation of chemical substances is considered essential to ensure the safety of human health and protect the environment. Regulation in itself must be able to clearly define what is to be regulated, how it will be detected, identified, characterised and assessed, and how all this based on set criteria will be translated into regulatory decisions, which in turn can be enforced. Clear and understandable regulations supported by relevant guidance documents are essential to assure legal clarity and avoid ambiguity for regulators and stakeholders. High quality, robust and relevant information in the form of analytical, physical, chemical and human (toxicological) and environmental (ecotoxicological) effect information are essential for the adequate function of regulations for chemical substances. The contribution of so-called academic and applied science is thus linked to regulation and the quality and direct applicability of science/research is essential to assure better and more effective regulation. Much information required for assessment is based on OECD standardized Test Guidelines grounded on Good Laboratory Practice (GLP) to ensure Mutual Acceptance of Data (MAD) and additional Guidance (on GLP).

Currently there exists at least nine pieces of EU regulations dealing with nanomaterials (NM). There also exist several definitions of nanomaterials. More recently, an update of REACH to include registration /assessment/enforcement of physical-chemical properties, human health and

environmental data including a definition for NM was agreed and is expected to be fully applied by 1 January 2020. Soon it is also expected that a revised harmonised definition for NM will be available to ensure consistent application across various pieces of legislations.

Recently, the coupling between research and regulatory needs for nanomaterials has been analysed in several EU funded projects, notably: NANoREG and ProSafe. A main goal has been to translate findings to recommendations aimed at more efficient and effective governance of nanomaterials and thus increase nanosafety. The ProSafe project aimed to link scientists, regulators and policy makers in order to support evidence-based policy for the governance of manufactured nanomaterials and nano-enabled products at the EU level. A disappointing conclusion was that purely science-oriented research often results in experimental data that cannot be used in a regulatory context where data have to be well defined, standardized, reliable, reproducible and exchangeable. An inspiring development was the introduction of a concept/approach termed SbD). The SbD approach looks at ways to identify, and thus avoid, possible adverse effects of nanomaterials from the earliest stages of the design/innovation process onwards based on chemical and other properties – this is now further explored in NanoReg2. Application of SbD principles is considered crucial for a cost-effective risk management of Manufactured NMs. Safe by Design is one of 14 main recommendations identified in the ProSafe White Paper with the subtitle "towards a more effective and efficient governance and regulation of nanomaterials".

Currently, several other recommendations in the White Paper are already being worked on e.g. work on OECD test guidelines, a follow up Conference held on 17-18 April 2018 in Holland "Future-proof nanomaterials", and consequently the recommendation to explore future-proof approaches.

Questions

1. There is much Environmental Health Safety data, but how do we assure the quality and usefulness of the data in terms of reproducibility, comparability and relevance? How do we make zero effect data and all data available? How do we ensure/enforce access to all relevant data on NM?
2. How can we contribute to grouping of NM, assessing low tonnage volumes, new methods and approaches for NM testing (Mode of Action, Adverse Outcome Pathways, *in silico* and *in vitro* High Throughput Screening), materials characterisation, modelling? What is ongoing? What needs more focus? Are all applicable to regulation?
3. How can we assure that reliable test guidelines for NM are available/developed? What works well? What could be improved?
4. How can science aid/contribute to the upcoming changes in REACH annexes? More physical chemical data will be required, inhalation toxicology is empathised, toxicokinetics is required, dissolution rate with solubility and/or biodegradation testing is required, and more extensive ecotoxicology is recommended.
5. How can the SbD approach be applied? How do we couple this approach to the Discovery/Invention/Development stages in the product development chain? Who is responsible?

6. How do we deal/prepare for the assessment of a wider family of advanced materials which exploit nanoscale properties, such as advanced ceramics?
7. What additional questions should be addressed at this workshop – please bring them with you?

Annex III. Documentation of group discussions

NOTE: As a background to this report, the following notes from the group discussions are provided in an adapted but less edited form.

1. Nanosafety Research & Innovation

Bengt Fadeel introduced the first part of the workshop and this was followed by discussions in five smaller break-out groups. These groups were chaired by Bengt Fadeel, Gregory Moore, Alexander Lyubartsev, Joachim Sturve and Åke Bergman. Notes were taken by Jonas Förare, Elina Drakvik, Heike Hellmold, Rune Karlsson and Ulrika Carlander, respectively.

1.1 Swedish nanosafety research

It was discussed that current trends and topics in nanosafety research include for instance characterisation in biological systems, nano(eco)toxicology, proteomics, modelling, measure actual exposure, LCA perspective, validation of in vitro methods for high through-put screening. It was noted that there has been much focus on read-across and grouping, databases, and activities that are relevant for regulation.

It was highlighted that Sweden is at the forefront of many fields within nanoscience: research on biocoronas, materials science, work environment (which was strong even before nano-issues were relevant), inhalation science, bioinformatics and transcriptomics. Furthermore, there is drive towards connecting exposure measurements with lung dosimetry so that we understand actual exposure levels, (for example as already performed at Precise Inhale, Novum).

On the other hand, it was noted that the starting point for research often is material development and not nanosafety.

There are national research initiatives towards innovation, proof of concept, on applications such as research on combustion as requested by road authorities and police. Also initiatives towards making use of existing data and its utilization in applications and at businesses exist. Interdisciplinary collaboration and work is obvious today and virtually a requirement to get funding.

The EU's latest roadmap emphasizes the newer concept of "nanoinformatics", which, like other research, has to be part of the main areas of nanosafety and toxicology: material, exposure, hazard and risk. It was brought up that EU-funded nanosafety research seems to be more integrated than our Swedish research. Funding for pure nanosafety research projects has been decreasing, and the EU trend is towards integration of safety aspects into the innovation process and the whole value chain from design and production to end-of-life. Frequently the EU projects are very large and interdisciplinary. This can lead to extensive administration and several smaller part-projects.

Many of the workshop participants stated that there is need for smaller Swedish projects aimed at exploring and understanding specific scientific/applied research questions. Data on new NMs was requested and should be relevant from exposure perspective when required for risk assessment.

Characterize the material in different life cycle steps, and link to exposure as a part of life cycle assessment (LCA). It was concluded that in-silico evaluations are important to target the development towards relevant research. Both basic and applied research were considered important, depending on products being developed.

We need to know how to handle NPs, screen out the high risk ones (validation of in vitro methods for high through-put screening), accepted by both academia and industry. Nanomedicine was considered as a special area which nanosafety has potential much to learn from and build on.

Prioritise research tools for implementing predictive models, disseminating knowledge about models, data curation and disseminating knowledge outside the research area (authorities, companies etc.).

The results obtained by researchers are subject to certain conditions. If these are generalized and applied in other areas, the researchers usually say it does not go because it has not been tried. A dilemma for researchers is that generalizations can easily be truths that do not reflect reality.

Researchers are good at developing methods but when these are developed, funding for validation is lacking.

More knowledge on secondary effects of production is needed, where nanosubstances arise after processing of materials, such as after grinding and abrasion. Further, knowledge that leads to mechanistic predictions; development of predictive analyses. Currently there is little knowledge on the distribution of nanomaterials in the environment. And some research misses to clearly identify that "nano" (i.e. in the nano size range) is part of some ongoing research areas, such as with diesel particles, and micro- and nanoplastics.

The following needs were identified:

- Enforce open data (funders should require sharing of data)
- Smaller Swedish projects aimed at specific research questions so to explore and understand national scientific/applied research needs
- Measurements of real exposure as basis for more relevant and reliable risk assessments
- Depending on products being develop, both basic and/or applied research may be needed
- *In silico* evaluations critical so to target development towards relevant research
- A better understanding of mechanistic action of NMs is required to predict possible toxic effects

1.1.1 DATA AND DATABASES

Strengths and trends

Much of the current activities are focused on consolidating and gathering data, building databases and thus also promoting the modelling efforts. Much data have been and are generated, including safety data. However, the accessibility and quality of data has been and continues to be an important issue.

It was emphasised that knowledge is required for using processed data and that this may be difficult for example, for statisticians to use. For example, data from toxicity tests often require

further analysis and processing of data. From the eNanoMapper-project, there was experience that data formats can pose a problem. Standardization efforts for the data formats are therefore needed. Today, industry has a much data that researchers are not able to access. Hence, there is a need for more openly accessible data that could be used also by researchers and regulators.

Needs and priorities

It was noted that a lack of coordination and possibility where to find data is a basic problem. There is much data that is not utilized for various reasons; however, not all of this data is of adequate quality for use. It was emphasized that it is important to control the quality of input data to ensure the usability and reliability of databases. It was also pointed out that the rigorous and systematic data management is not financially supported by funding agencies making it more difficult to ensure the reliability and relevance of information.

There is a need for relevant information in large databases. Addition of new data and possible modifications of structure are long term needs and require collaboration with EU member states and internationally. Data handling should be steered from the EU. Open access data should be implemented, with the same principles as for open access publication. Correct data in proper and standardized formats are essential. This should include also the harmonisation of ontologies.

The current libraries of available nanoparticles are too small (some tens of particles/substances) to provide meaningful results when they are fed into QSAR models: Databases built on maybe thousands of NMs would be required.

Funding agencies should require formatted "open-data", but it is important to raise the status of data management and not just data production, as data curation requires both funding and time.

Future priorities should see further development and utilization of a big data methods (machine learning) and data ontologies (defined nanosafety terms) to harmonize and better exploit data. Data collection into data repositories should be carried out according to a standardized system. It is important to define which metadata are important to enable relevant studies.

It was recommended that the data should be centralized, not only at an EU-level (The European Union Observatory for Nanomaterials, EUON), but that some degree of coordination at a national level might be needed. It was suggested that perhaps SweNanoSafe could be responsible at a national level for data coordination. It was also discussed that by having access to data does not necessarily provide the entire solution, as we should also have access to meta-data and lists of contact persons to facilitate further enquiries.

Proposals (short-term)

- Enforce open data (funders should require sharing of data)
- Address todays mismatch between required and available data
- Coordination, consolidation (curation), standardisation of data collection and data bases
- Retrieve data on what is produced industrially
- Use big data methods (machine learning) and data ontologies (e g terms linked to functionalization) to harmonize and better utilize data (requires standardization of

protocols)

Proposals (medium-term)

- Expand relevant information in databases to enable meaningful results for QSAR – modelling

Proposals (actions by SweNanoSafe)

- Responsible for data coordination in Sweden, including list of contact persons

1.1.2 MATERIAL CHARACTERISATION & SAFETY DATA SHEETS

Strengths and trends

The experiences discussed showed that at least at some applied research institutes, safety is designed-in from the very beginning. However, the laboratory-scale and industry-scale represent two very different situations. There is a large mismatch between small- and large-scale technology and environment in terms of knowledge, needs and requirements. It was also emphasized that the quality of the material information and safety data sheets (SDS) that the industry provides is often low, and there is no proper characterization of nanomaterials. It was discussed that this is actually more of an enforcement issue/responsibility rather than a research question nowadays. If you look at older toxicology journals, you can see that material characterization was not as extensive as expected today, indicating that the quality of research is improving. However, as this area is also coupled with safety aspects, it was therefore considered that proper and good-quality SDS information should be urgently addressed.

Needs and priorities

It was concluded that much of the knowledge is already available in terms of methods for material characterization. However, there should be a significant combined effort invested to collect the available SOPs, make them accessible and raise awareness (among industry and research groups). Focus in this area should be on standardization and spreading the knowledge, in addition to proper enforcement to obtain data of appropriate quality from industry and material producers.

Many standards (SOPs) are still missing, for example there are no standardized approaches for how to characterize coating and surface functionalization. Test protocols (SOPs) need to be adapted for different types of nanomaterials which is a challenge. Physicochemical characterization of the pure nanomaterial can be done on a routine basis, but there is still need for characterization in biological media (for addressing nano-bio compatibility). Furthermore, it was suggested to introduce a labelling symbol for NMs to make nano-content more visible and transparent.

Proposal (short-term)

- Enforce information requirements of SDSs (quality of data is an issue)
- Collect current SOPs and make them available
- New characterisation methods in biological media
- Adaption of SOPs to different nanomaterials
- Labelling and risk symbols for NMs

1.1.3 METHODS AND MODELS

Strength and trends

The existence and development of many different methods were discussed. A major challenge lies in knowing which methods should be used, validated and standardized. To make methods useable, there is a risk that they are simplified too much and no longer reflect real life. Another challenge is to gain acceptance for new methods by regulators.

There must be tests for controlling nanomaterial risks in the work environment, but complex testing systems such as for exposure measurements may not be used here. Complex systems probably fit better in an early stage of development. When knowledge is built up, it can then be used to develop simpler systems adapted for regulatory purposes. One challenge is to get acceptance for new methods.

It is difficult to standardize a method to study the corona in the environment since there are so many different compartments, particular rivers, lakes, sediments, etc. We need to understand aging of the corona; fresh exposure is usually more dangerous than old. Particular issues with analysis of NPs in biological media, buffer problems and so on. It has to do with study of the corona and its formation. Modified buffers needed without proteins that can lead to agglomeration.

It is difficult to measure the correct parameters in cell systems and to develop good in vitro methods needed to screen nanomaterials and nanoforms. There is a need for these as alternatives to in-vivo test methods for REACH registration. However, cell systems can be complex like ALI (Air Liquid Interface) and Organ-On-The Chip, difficult to scale up and so far difficult to use for screening. These methods are also in their own fields of research. The idea of some projects is to develop methods that contract laboratories can execute.

Grouping and read-across are considered complex. Tools have been developed to enable grouping, but generally agreed criteria/decision-tree is needed to facilitate the understanding and application of these approaches. From an occupational health perspective, you have to be careful with grouping since you don't see the details of individual NPs, workers handling specific NPs may be suffering in the end.

Needs and priorities

There is a need for predictive models, such as QSAR and grouping tools, which incorporates mechanistic information. Data from toxicity test often requires further analysis and processing, which may be challenging for statisticians to use. Proper material characterization and good quality data is a pre-requisite for modelling.

A specifically expressed need was discussed to measure very low airborne NP concentrations in the working environment continuously at a reasonable cost. The nanoparticles cannot today be traced by standard measuring equipment.

Also, methods to measure NPs in waste streams correctly, from research labs, industrial processes etc., was requested.

It is almost impossible to test all variants of nanomaterials, as there are so many forms and

environments and the resources are limited. To address this, groupings have been suggested. Today's state of knowledge is not yet enough to make groupings and classifications. They considered that ongoing research on underlying factors, such as the parameters in the calculation models that are critical and which mechanisms control nanomaterial toxicity (toxicity), is required. The characteristics and behaviours of nanomaterials differ not only between different nanomaterials but also depend on the surrounding environment. There needs to be e.g. a similarity assessment and a quantitative assessment, and the surface chemistry and other physical-chemical properties need to be taken into account. The conclusion from GUIDEnano was that quite much further work is required before we fully understand how to apply these approaches. The problem is that there is no standardized approach e.g. how to characterize the coating and surface functionalization.

Proposals (short-term)

- Develop QSAR modelling
- Method to measure very low airborne NP concentrations
- Approaches for grouping and read-across

1.1.4 DEFINITION OF NANOMATERIAL/NANOFORM

Strengths and trends

It was suggested it may be a problem that the proposed EU definition does not link to actual risks. Sizes from 1 to 100 nm and at least 50% of the number size distribution, may not be the most optimal definition. Update of the REACH annexes will clarify the registration requirements for nanoforms of substances, and the new requirements are expected to be fully applicable by 1 January 2020.

Needs and priorities

More detailed research is needed (e.g. material characterization research) to improve the scientific evidence base of the EU definition. The definition should be a living definition, open for modification when more scientific knowledge become available. Currently, it is easy to "play around" with the material and change a parameter in the structure (referred to as a "shadowing" technique, also "masking") so that it is no longer considered as nano according to the EU definition.

Some participants wondered if particles not engineered for particular uses, such as diesel particles in the air and plastic particles in water/sediments should be included in the definition since some of these obviously are in the nano-range.

Proposals (short-term)

- Research to improve the scientific basis of the nanomaterial definition (EU)
- If scientifically justified, the EU-definition should be open for modification

1.1.5 OCCUPATIONAL EXPOSURE

Strengths and trends

There is still very little knowledge about the real-life occupational exposures even though there are

regulations for the work environment. This means there is a poor foundation for exposure assessments. For that we need good models and good characterization. Different nanoforms from the same nanomaterial may be formed depending on surface area, functional groups on the surface etc.

Although the regulation is in place, it seems that it is not followed. Workers and companies should be made more aware of the legislation. Experiences has shown that many small companies believe that safety measures are not that crucial. It was suggested that one reason that measures are not followed, is that there are too few Occupational Hygienists.

It was considered important to measure/estimate true exposure levels, for example in the research area for lung dosimetry to understand actual exposure levels

Participants expressed concerns with specific airborne NPs, such as nanowires in research laboratories, secondary nanoforms formed by industrial scale printing of 3D objects and grinding processes.

Workers could be exposed to mixtures of NPs and other materials. One trend is therefore to use particles collected from real world exposure in working environment. This can be difficult to collect a mixture of NPs, other compounds mixtures, on both the nano- and micro-scale. There may even be an interaction on the collecting grid/filter which misrepresents the "real world" exposure.

Because historically much work has been conducted in Sweden on asbestos, there is a tradition and knowledge base to measure and perform risk assessment for other fibre like particles.

Furthermore, it was advocated that international harmonization of OELs would be beneficial so that same level of protection would be achieved in Europe, US and internationally.

Needs and priorities

Occupational settings are highly relevant from a risk perspective (i.e. exposure situations). More information on the persistence of nanomaterials and also on the hazardous properties of the NM is important to know and should be collected.

It is necessary that workers know how to protect themselves and that new and more effective measures are developed. In some cases machines run all the time which may result in continuous exposure. It's essential that workers follow protocols, use PPE when relevant but can't wear "space suits" all the time. In summary, there is a need to promote safety culture and implement engineering controls, improve methods to measure, as well as decreasing the prices of measuring devices and instruments.

Exposure scenarios that mimic reality can be studied by following a process or product from start to finish. If nanoparticles are spread in one of the sub-steps, the next step should be to analyse what is happening and in what form the spread occurs. If a product contains e.g. metallic nanoparticles, spreading is probably not in the form of nanoparticles but as the release of metals that form colloids in nano sizes with potentially new properties. The question is whether there is a problem and how it can be addressed.

Accurate measurement of actual exposure is already performed such as by some companies.

However, better methods need to be developed for real-time measurements of, for example, very low particle concentrations.

In the future, REACH and its tools, e.g. exposure scenarios and safety data sheets, can be used to bridge the gaps (and also better coordinate OELs and DNELs). It was considered that more human biomonitoring and epidemiology linking work would be needed long-term to increase knowledge about occupational exposure and health effects.

More knowledge is needed about secondary effects of production where nanosubstances arise after processing of bulk materials such as grinding and using abrasives in grinding fluid. 3D printing is growing fast and expanding with more and more nanosized elements. Predictive analyses are required. Already traditional ink contains more and more components in the nanoform and deserves more research.

One example is a Swedish project on nanomaterial exposure associated with additive manufacturing (3D) where it really couldn't be proved that workers are exposed since nanoparticles couldn't be detected. This points to a need for better methods for real-time particle counting as well as chemical characterization since there is an uncertainty. Such a tool would be an instrument that can continuously measure very low airborne nanoparticle (preferable together with chemical characterisation).

It was also highlighted that there are available methods but they are too expensive for monitoring. It is possible to capture particles on grids, count and characterize them by EM, but this is very expensive on a routine basis, and the problem is that it can't be made continuously.

A collaboration between researcher, method developers, and instrument manufacturers was proposed, to develop an instrument to measure real-time nanoparticle number concentrations in air.

Attention to specific applications, such as NPs in food. Also to specific nanomaterials such as nanocellulose that has an asbestos-like shape but is soft, but for example, what happens if these fibres enter the human body?

Proposals (short-term)

- Methods for accurate measurements of actual exposure.
- Work towards predicting exposure scenarios, setting OELs
- Address potential high-risk manufacturing exposure scenarios
- Methods (instruments) to measure real-time nanoparticle number concentration in air
- Build on the "asbestos tradition" (measurements, risk assessment) for fibre NPs
- Use only well-characterised ("safe") NMs in manufacturing
- Safety awareness training: translate the precautionary approaches into guidelines and basic requirements for protection
- Knowledge on occupational exposure and setting the OELs

Proposal (medium-term)

- Increase knowledge about occupational exposure and health effects through human

biomonitoring and epidemiology

1.1.6 OTHER EXPOSURE SCENARIOUS

Strengths and trends

It was discussed that there is essentially a mismatch between the materials that are studied and the real-life exposures. There is also a tendency to mainly study the same materials (for example the OECD list), which means that there is much data on the same few nanomaterials but less or no data on others which could be important and relevant.

There are many studies on metal oxides in the environment. Another area is plastic particles, both micro and nano sized.

NPs in waste streams have been somewhat studied, one form is silver NPs in sewers ending up in the environment. Some participants had concerns about how to handle the waste correctly through the life cycle.

It was emphasized that some NP applications are seen as unnecessary, such as silver NPs for antibacterial effects in clothing. High levels of silver ions have been detected from sewer plants, and the usefulness of some NMs (e.g. nanosilver) should be questioned.

Needs and priorities

Few case studies are available/have been started to study what we are exposed to and to identify realistic (and prospective) exposure scenarios. Some further case studies would be needed as there is a need for better insight into what the organisms and cells are truly being exposed to.

General exposure is difficult to evaluate and applies to all chemicals. There is a need to develop exposure scenarios and link to risk assessment

Studies and data on new nanomaterials are needed, but they should be relevant from an exposure perspective when needed for risk assessment. The surface chemistry and functionalization etc. of NM complicate the picture as they can influence the toxicity.

It was discussed that there is essentially a mismatch between the materials that are studied and the real-life exposures. There is also a tendency to mainly study the same materials (e.g. OECDs list of eleven NM) which means that there is much data on the same few nanomaterials but less or no data on others (which could be important and relevant).

Proposal (short-term)

- Knowledge on realistic exposure scenarios and toxicological data of new materials

1.1.7 LIFE CYCLE ASSESSMENT, FATE ANALYSIS, RELEVANCE

Strengths and trends

There are still many gaps in knowledge with regard to the environmental fate, how nanomaterials end-up in the environment and which effects they will have. Models are being built to predict NM fate in the environment, for example in water and sediments. In addition, there is a large variability

in the identity, grade and even purity of nanomaterials that are produced which is a great challenge, also affecting attempts to develop reliable modelling tools.

Needs and priorities

It is important to study and characterize the material life cycle, and this again links to the exposure as a part of LCA. Few case studies are available/have been started to study what we are exposed to and to identify realistic (and prospective) exposure scenarios. Some further case studies would be needed as there is a need for better insight into what the organisms and cells are truly being exposed to. In order to understand what is happening in the environment and degree of exposure, one would need to collect the samples from real-life settings in the environment. It was concluded that more research is needed on survey and monitoring studies on environmental fate and there is a need to develop protocols and guidelines, especially for industry.

In order to understand what is happening in the environment and degree of exposure, one would need to collect the samples from real life settings in the environment. It was concluded that more research is needed on survey and monitoring studies on environmental fate and there is a need to develop protocols and guidelines especially for industry. One area to study is if NPs can be released from sediments through trophic transfer.

Proposals (short-term)

- More data for material flows and LCA
- Measure concentrations in the environment
- Fate analysis (e.g. transfer in the food chain, trophic transfer)
- Develop exposure scenarios and fate modelling
- Methods to handle waste/waste streams

1.1.8 RISK ASSESSMENT

Strengths and trends

The researchers background (chemist, physicist, and biologist) influence the risk assessment process of nanomaterials.

Needs and priorities

Communication between disciplines is desirable to understand other people's risk data. There is a lack of data on exposure scenarios and links are weak to risk assessment.

The precautionary principle should be translated into precautionary approaches, meaning concrete guidelines and basic requirements for protection when handling nanomaterials. This can be combined with a labelling of articles with nanomaterials, which would link to the precautionary principle.

Safety awareness training directed from senior management in the organization is crucial for safe work with nanomaterials and sustainable development. Perspectives on safety awareness among actors and between disciplines varies, often due to lack of knowledge.

It is important for start-up companies and SMEs to participate in safety awareness training, but they may lack resources to engage in research projects.

Proposal (short-term)

- Translate the precautionary principle into precautionary approaches (development of guidelines and basic requirements for protection combined with a labelling of articles)

1.1.9 REGULATION

Trends

In reality, legislation is based on the assumption that chemicals are not an environmental and health problem, but a product that may be sold freely on the market, imported and exported, i.e. free movement. Thus, from a legal perspective, companies are free to set chemicals on the market until the point where the authorities show that there are risks with the chemicals. REACH is created for companies to submit pre-information so that some data about the chemical is available. In reality, for most chemicals there are no restrictions.

Using research resources in regulatory contexts is something that some research groups are constantly working on. The difficulty is that test methods need to be simplified over and over again. Finally, the test method no longer reflects the complex reality of nanoparticle interactions that researchers want to transfer to the protocol. The researchers find it frustrating not to be able to include all known factors that affect the methods.

On a positive note, many EU-projects have contributed to building on similar measurements for various nanoparticles, with the purpose of generating data and developing standardized methods that can then be accepted for use in the regulatory process.

Needs and priorities

Researchers should be better aware of the regulatory aspects, and how that affects their field, as regulations and approval of nanomaterials drive innovations and development. Validation of systems is generally considered not to be research but is required for acceptance of the methods for regulatory purposes. There is a need for assigned resources for validation of methods. Furthermore, here were questions about articles with NPs and if these should be registered too? It was proposed that KEMI should look into this.

Proposals (short-term)

- Speed up the process for acceptance of novel models and concepts by regulators
- Resources and funding for validation phases

Proposal (medium-term)

- Registration of articles with NMs

1.1.10 CONSORTIA AND RESEARCH FUNDING

Strengths and trends

Funding for nanosafety research is limited compared to development of new nanomaterials and its applications. Researchers must promise great progress to get funding, but small steps and careful characterization are not rewarded, which makes it difficult to conduct systematic and careful research. It was suggested that there should be additional criteria for research and impact assessment, for example, to promote data collection and curation

Researchers are looking for funding, but there seems to be few calls that fit. Current topics seems diffuse, and major efforts have been made already. There are still opportunities to apply for nanoscience research funding, but in large constellations, and if you are not already included in these, it can be difficult to participate

Many projects are aimed at standardization, meaning many routine experiments. However, alternative projects are also needed. For doctoral students and post docs, it can be hard to be included in these projects as their task is "basic" and "excellence science". It is unclear whether doctoral students will undertake a project based on repeating the experiments many times, as that could be perceived as insufficiently developing and challenging for doctoral studies. Likewise, it may be hard to motivate doctoral students and post docs to do this type of projects, especially in small research groups where there are no side projects where several may contribute. It was noted that it is important for Sweden to work strategically and secure research funding both at the national and EU level. In the long-run, the national level funding and coordination of research activities would be reflected also in the better success rates at EU funding opportunities. Sweden participates in many EU projects, but they are not coordinated by the Swedish actors. It was highlighted that Sweden should become more courageous and strive to coordinate more EU projects in the future. The participants also called for a need to become more organized in Sweden to apply for EU level calls, inspired by UK's successful example in gaining EU funding. It was concluded that this is a very important aspect and perhaps something that the platform or another actor could take forward in Sweden.

It was noted at the workshop that nanosafety research by itself has decreased whereas the funding is directed more towards developing nano-specific applications and other innovations using nanotechnology. At the EU-level, nanosafety research is often part of major multidisciplinary research projects that include several steps in the life cycle of nanomaterials. These major projects were considered important but some researchers have experienced these as being administrative and economically challenging. Therefore, additional research funding was requested for smaller but targeted and better coordinated projects.

Needs and priorities

Participants hoped that there would be more opportunities for targeted and smaller projects. On the other hand, it was argued that most research groups deliver what is promised, but often it becomes the cost of something else. Thus, there is also a need for a larger research groups, staff and equipment, so that it is possible to have "side projects" that are not included in the main project.

More minor interdisciplinary research announcements focusing on national priorities as well as for supporting/contributing to the international developments and efforts.

Proposals (short-term)

- Enabling environment to promote the coordination at the national level and to increase the application and success rates for Swedish nanosafety research
- More minor interdisciplinary research grant opportunities
- Multidisciplinary calls with involvement of industry and authorities
- Sweden should be more active in attracting EU-funding (meaning financial support for EU proposal preparations) and also aim at coordination

Proposal (medium-term)

- Involve funding agencies for targeted calls

Proposals (actions by SweNanoSafe)

- Create a joint national forum for facilitating discussions to attract more EU funding to Sweden
- Coordinate the Swedish participation and coordination of EU projects, i.e. initiatives and links to EU/international research and regulatory work

1.1.11 COLLABORATION

The nanosafety field is so multidisciplinary and complicated that there is a need to collaborate on national, European and international levels.

Many ecotoxicology groups have reduced funding and are becoming smaller; therefore, there is an acute need to collaborate to maintain competence, and in the near future attract new people to the field. The same is true in the human toxicology field, many people are leaving the field without renewal or increase in personal.

Collaborations to strengthen research and higher education through basic education. Ensure that this policy is supported by industry since there is a missing link from basic research to industrial applications. Update regulation reflecting state of current knowledge.

Focus on the benefits of geographic proximity. This includes collaboration around generation of expensive, comparable data, such as sharing of equipment and facilities (instruments, clean rooms, super-computers etc.).

Collaboration around education and training is desirable at all levels: professional, university level and applied research. Ensure to maintain competence through basic education and recruiting younger researchers into the field. This policy should be supported by industry, thereby addressing the missing link between basic research and industrial applications.

It was highlighted that Sweden should combine its efforts to coordinate common activities, especially concerning EU and OECD collaboration. Many current topics and challenges require EU and/or global level efforts. We should become more active in attracting the EU funding to Sweden

and coordinating the Swedish participation and coordination in EU projects. However, this requires that the national funding base is sufficient, strategic and promotes such an enabling environment. Important to get suggestions that can be implemented in Sweden from EU and other projects.

There is a clear need for creating a joint forum for facilitating such discussions, initiatives and links to EU/international & regulatory work. Possible role/co-role for SweNanoSafe to coordinate/facilitate this? Research collaboration can facilitate access to expensive analysis and equipment needed for interdisciplinary projects, such as clean rooms and TEM (transmission electron microscope). Collaborations in Sweden can benefit from geographical vicinity.

Proposals (short-term)

Workshops

- Follow-up workshop for the nanosafety research network, invite both industry and financiers.
- Characterization workshop for industry to educate and train experts
- Workshop on the safe-by-design concept

Calls

- Promote multidisciplinary calls with several principal investigators (PIs)

International

- Combine national activities, especially with EU and OECD efforts in mind

Proposal (action by SweNanoSafe)

- Arrange follow-up workshops

1.2 Education, training, awareness raising, consumers and citizen science

Education and training are needed at all levels; professional, university level and applied research. It was suggested that a characterization workshop for industry should be organised to educate and train industry experts. Also, the general public and consumers should be added to platform's target group, and public awareness should be increased with awareness raising and other activities. Citizen science was also lifted as that is included in the next Framework Programme, Horizon Europe and funding discussions. Sweden could promote these aspects more visibly to become a forerunner in safe and sustainable innovations while guaranteeing societal dialogue and trust. In France, the involvement of general public is strong in many chemical safety questions as the citizen involvement is rooted in their constitution.

Communicating the network's views is extremely important. Partly through personal meetings in lectures for students, associations, etc. But also in media/trade media such as larger newspapers, online publications, the medical newspaper, etc.

Proposals (short-term)

- Desirable at all levels; professional, university level and applied research

- Maintaining competence through basic education and recruiting younger researchers into the field
- Workshops for general public
- Communication around possible risks (industry, consumers, …)
- Communicate the research network's views

1.3 Nanosafety as an opportunity or threat to innovation

The question was asked how can safety aspects be transformed into an opportunity for research. Promoting sustainable innovations leading to competitive advantages of Swedish industries in the long-run maybe an argument for the need of research to focus on safety aspects. In many cases, industry is requesting regulations, which indicates that something that can be perceived as a threat/need also constitutes an opportunity for future research efforts and development of new products.

There is a need to address the gap between research and applications and information from researchers to SMEs needs to be formatted and adjusted. Many larger companies are also in an urgent need of information. Especially important for small businesses that are dependent on one or a few products.

Companies seek support from researchers, but researchers also seek help from companies and it is not always these actors know each other. Consequently, there is a need for two-way communication, matchmaking and a discussion forum.

It was argued that some companies no longer want to be associated with nanomaterials, previously seen as a market advantage but not now anymore. Many companies still have too little knowledge, for example, don't even use control measures for regular chemicals. Specific information needed for handling, storage, and destruction.

There is already a lot of data, but it seems that it is not available where it is needed and in the right format. For example, businesses would like help from researchers to identify which materials should be avoided to ensure that the materials used will be well received and that no unpredictable risks will arise in the future.

It was noted that the EU nanosafety research is more integrated than our national one. In Sweden, the funding is more scattered, small and diffuse. In other words, it has not been a priority area, a vision and strategy for Swedish nanosafety research has been lacking.

Companies that wants to take the lead should be encouraged. We should" invest" in companies that want to develop and implement new workplace safety measures linked to innovation. Vinnova provides funding for several innovation projects. There should be a possibility to promote projects wanting to couple safety aspects with business needs. This could be possibly linked to SDSs (safety data sheets) and CLP (regulation on Classification, Labelling and Packaging). To pursue the safety process throughout the production chain), industry needs more knowledge about scientific and regulatory matters: education was considered to be a key factor to achieve this aim. It was concluded that we need a national action plan on nanosafety research for Sweden. That would

promote sustainable innovations and competitiveness of Swedish industries in the long-run. It was noted that other countries e.g. Germany has had an ongoing and updated national action plan for over ten years.

Proposals (short-term)

- Industry need more knowledge, both education and regulation
- Smarter tools to choose nanomaterials in development
- Turning safety aspects into opportunities by promoting safety culture and sustainable innovations
- Promote sustainable innovations as contributing to competitiveness of Swedish industries
- Action plan and nanosafety research strategy and vision for Sweden

2. Nanosafety Research – Making it Useful

Gregory Moore introduced the second part of the workshop and this was followed by discussions in four smaller break-out groups. These groups were chaired by Ernesto Alfaro-Moreno, Alexander Lyubartsev, Joachim Sturve and Åke Bergman, respectively. Notes were taken by Jonas Förare, Heike Hellmold, Rune Karlsson and Elina Drakvik/Ulrika Carlander, respectively.

2.1 Quality and usefulness of EHS data

It is important to first identify what parameters require assessing and not on the details how to assess them. Thereafter guidelines on how to carry out research, such as required minimum amount of data, should be developed. The guidelines should also include all relevant "settings" (filter sizes, etc.). Standardization is desirable and important. But the systems differ. In biological systems, very different outcomes may occur depending on, for example, cell type, or on low concentrations effects of substances. It is easier to characterize particles as they are. From a strictly scientific point of view we should ask critical questions such as, can we do the experiment? Do we need to do it?

Very often regulators are not good at explaining their needs from researchers. Development of a compendium was suggested as useful tool to explicitly detail and communicate the specific needs of regulators from researchers and thus avoid “finger pointing”. Such a compendium could be a short term goal, but implementation probably would take a longer time.

Proposal (short-term)

- Develop a compendium to explicitly detail and communicate the specific needs of regulators from researchers

2.1.1 ZERO EFFECT DATA

On the topic of zero effect data it was unanimously considered that it is important to both define the term and publish such data. At present the definition of zero effect data differs between stakeholders leading to misunderstanding. Indeed, many terms a currently used e.g. “negative effect” the same as “no effect”, “zero effect” and “not an effect” causing ambiguity. Also negative

effect is a common term in toxicological research. Therefore, a clear and commonly accepted definition is needed to ensure clarity and certainty for stakeholders. There are some journals aimed specifically at publishing negative results but these type of journals are not so popular to publish in. Such publications are important to enlarge knowledge on non-effects and the rigidity of the study. A firm understanding of the study design and hypothesis are important to understand the robustness and relevance of the results which may be further used to justify a finding or redesign a study.

Often there are not enough resources to carry out research studies in such a way that they are valid for risk assessment, also regarding zero effects. Many times it is difficult to conclude that the result is truly zero effect or show something else.

A published and EU-level agreed definition, and nomenclature, of zero-effects would be desirable to have. A dialogue with ECHA, EFSA, KEMI, authorities and researchers together should be initiated. (Short-term goal to start the dialogue, ending will be a long-term goal).

Proposal (short-term)

- A draft definition for zero-effect (no-effect, negative effect etc.), involve regulators KEMI, ECHA, EFSA etc., but also researchers

2.1.2 DATA MANAGEMENT

Good examples that could be implemented for EHS-data were mentioned. An example is Danish contract labs that have a rigorous system to quantify and assure quality of data as scoring systems, filters, and processes. In proteomics, the reporting of data is standardized from raw data to results. This is obligatory, or else the results cannot be published.

The exact format is difficult to standardize since data may be produced from different aspects. Requirements should include ontologies, format of SOPs etc. Journals should have minimum requirements for publication as in omics or a guidance document.

Characterisation of the crystal structure in another good example on how to report data and results, proposing standardized protocols for publication. Would be useful to have a similar system for reporting nanosafety results, even though it might be more difficult as toxicity is more complex than crystal structure.

A guidance document for EHS-data management should be published, the question is who will do it? A funder and contractor are needed. Funding may be available on the EU level.

When projects are still active, plans should be made for how to make data accessible after a project is concluded. Important to make negative data available, it can be done in other ways than publication, for example report format, but quality needs to be ensured (through a review process). (This is also important for postgraduate and postdoctoral students who have limited time). In many cases, more data is generated than really needed, researchers are used to measuring everything possible. Could be more critical in planning the projects and only measure relevant data.

Input of data for material flows and LCA is a shortage. It should be possible accessing additional data through collaboration with companies. Examples are concentrations and exposure levels affecting the transport of nanomaterials into the environment.

Proposal (short-term)

- Publish a guidance document for EHS-data management

2.1.3 REGULATORY REQUIREMENTS

Regulators need to develop more descriptive and collaborative communications including education with researchers. Often regulators are not good enough in explaining what they need from the researchers. Maybe a compendium would be useful on what a regulator needs to avoid finger pointing? Such a compendium could be a short term goal, but implementation probably takes longer time.

Proposals (short-term)

- Publish a compendium on what a regulator need
- Opportunities for regulators to develop communication skills and collaborate with researchers

2.2 Grouping of NMs, assessing low tonnage volumes, new methods and approaches

2.2.1 APPROACHES FOR NANOMATERIAL TESTING

It seems that regulators have a tendency to only slowly embrace new developments. For example, how can regulators accept new useful approach methods faster? Should regulators be involved already in the development stage? It is difficult to get acceptance for new approach methods in addition to standard OECD methods. Should there be a continuous dialogue between method developers and regulators? It was suggested that EU and OECD could provide forums and meeting places. Such forums should also include industry.

Proposal (short-term)

- Initiate forum for regulators and researchers to start discussion and dialogue to get regulatory" approval" sooner for new approach methods (testing, grouping, modelling)

2.2.2 GROUPING

Grouping of nanomaterials is a way forward to sort out the complexity and an opportunity as a basis for regulation. However, it is difficult to get relevant test systems in place that are precise and robust. Requires good characterisation and standardisation work for methods. Interdisciplinary cooperation is important for developing these test systems. Well-defined parameters, size, surface area, solubility, ion strength, solvent, pH etc., as basis for grouping is needed.

Proposals (short-term)

- Grouping/scoring, ranking and guidance needed (and guidance, e.g. GUIDEnano, GRACIOUS), UU+ RIVM and others
- Define prioritized parameters for grouping
- Interdisciplinary cooperation is important for developing test systems
- Develop a validated high through-put screening method and a testing matrix over parameters

2.2.3 STANDARDISATION

Standardisation is desirable and important. But the testing systems differ. In biological systems, you can get very different outcomes depending on, for example, cell types, or different concentrations of substances. Easier to physicochemical characterize particles in themselves then in biological systems.

Proposal (short-term)

- Standardize methods to test NMs in biological system

2.2.4 ADVERSE OUTCOME PATHWAY

Adverse outcome pathway (AOP) representation has been shown to be useful for initial indication for potential biological effects. It is faster in some cases, but does not provide a complete understanding, can be seen as a first indication. New methods are becoming more relevant as researchers are going away from linear approaches to build AOP networks and in the future these might become more quantitative.

The question was asked if AOPs could be used for safe-by-design approaches for nanomaterials. In drug development, for example, AOPs are used in high throughput screening.

Could be useful for some chemicals where we have knowledge about AOPs but for most chemicals there is not enough knowledge. AOP development takes time and there is a risk we delay necessary actions. In the meantime, we have to find alternative ways for regulators.

Regulation around AOPs is patched. Interesting development but more likely a 10-year project to implement. EU and OECD have an eye on AOPs, but has to be shown to be applicable. Industry has shown an interest for AOPs as well.

I was pointed out that regulators should not look at new methods as replacement, rather as complement. They should analyse and see if these provides more relevant and accurate data.

Proposal (short-term)

- AOPs to be further developed as first indicators (complement to basic testing and further examination of test result)

2.3 Availability and development of reliable test guidelines for NMs

Testing should preferably follow the same protocols as for regular chemicals but have to be adjusted for NPs. The meeting agreed that researchers should contribute to test guidelines, for OECD, standardisation bodies, at the EU-level. Researchers want to contribute to the development and testing of guidelines but they are limited by lack of compensation for costs and time perspectives (projects, employments etc.). The OECD mission seems to be working well.

Proposals (short-term)

- Testing should require a minimum of substances, as well as a minimum of methods. Guidelines on what parameters to assess are needed
- Testing should be applied to the complexity of NM, such as grouping and read-across approaches
- Development of e.g. OECD guidelines is long-term work and research at universities is often shorter (projects, employment, etc.). Therefore, standardisation institutes/research institutes are better suited for testing
- Need of funding for researchers' contributions to work in the OECD, ISO, etc.
- Coordinate contributions from regulators and scientists
- Develop more standard materials and make them commercially available (compare to NANoREG)

Proposal (action by SweNanoSafe)

- Develop a short educational PowerPoint on what OECD does and publish on SweNanoSafe´s web portal

2.4 Scientific contributions to the upcoming changes in REACH annexes

Annexes will be in place as of 1st of January 2020. When these are going to be applied, there will be a need for new information. There is an opportunity for scientists to get involved on for example how testing shall be carried out. After 2020 there will be a need for an evaluation, such as possible case studies on the REACH appendixes. Authorities in the Netherlands and Germany will be involved and partly finance the evaluation. It is ECHAs job and also KEMIs (Product registry) to decide scientific methods to generate data and scientific methods to check.

Some research labs produce very small amounts (piko-grams) but can still be potentially dangerous so maybe the tonnage limit of 1000 kg in REACH needs to be adjusted?

Communicate new research relevant to regulation. How science can contribute to REACH? Case studies funded by Member States? Medium-term goal to be involved in the review of how REACH is working for the nanomaterials (for example KEMI). In addition to scientific publications, it is important with good popular scientific information. Also, education on REACH and nanomaterials should be emphasized.

Proposals (short-term)

- Swedish scientists (e.g. KEMI) should get involved in the evaluation of REACH (flagship)
- Communicate new research relevant to regulation
- Important with good popular scientific information
- Emphasize education on REACH and nanomaterials
- Adjust the tonnage limit in REACH

Proposals (medium-term)

- Swedish scientists should get involved in the evaluation of cosmetic and food packaging regulation etc.
- Also get involved in case studies on REACH appendices, maybe funded by Sweden

2.5 Apply the Safe by Design approach

2.5.1 PRODUCT DEVELOPMENT AND SAFETY

When you develop a product it usually starts at the university on a research level. Next is the innovation step that involves applied researchers and industry. After that the product have to find a niche on the market. To get acceptance on the market, the product has to be considered safe. It is in this stage innovators start to look more into health and safety issues. One important aspect is the physico-chemical characterization as it defines the material properties. Material characterization is important to understand what you are working with. You select properties depending on intended use and evaluate them accordingly. In industry, the focus has been that the material performs, functions in the expected manner, not so much focus on safety testing. Bulk material properties are usually well known, but not nanomaterial properties, which may differ from bulk properties and behaviour. The properties, initially analysed at the research level, may change during the industry processing. Mode of action is not so well established for nanomaterials. Mechanistic understanding is required to predict possible toxic effects in the safe by design process.

We should characterize in several steps. What we develop, what we deliver to the market. Even if you initially analyse your material dry, the bulk and surface properties may differ. If that is required, the information has to be provided along the life cycle of the material. Methodology should be implemented in the early stage but requires integration.

There are so many types of NMs under development so classification/grouping is important also in the context of SbD, and more research is needed. Safe by Design is used in drug development. However, comparison of nanomaterials with drugs may not be relevant as drugs have a specific intended use and exposure, whereas nanomaterials may involve several steps and lead to uncontrolled exposure.

We have to be careful to use safe-by-design in a societal context. There is a risk if the concept is misused by politicians.

Financing of dissemination projects (knowledge transfer) and application of the concept of safe by design. Include the responsibility question in the project. Important to get business involved (interdisciplinary work). Scanning all the calls, at national and EU level, maybe a suitable Vinnova

announcement?

Proposal (short-term)

- Make the SbD concept more understandable and practical (involve industry and regulators)

Proposals (medium-term)

- Financing of dissemination projects (knowledge transfer) and application of SbD
- Scanning all the calls, at national (Vinnova) and EU level

2.5.2 DEFINITION

What is meant by "Safe by Design"? Safe by design is a promising but complex approach that provides information to help select better, safer materials to avoid risks (short-term goal to make SbD more understandable and practical). Applicability is challenging, needs to be further investigated and better defined. Probably most useful in the early phases of product development. Adapt the SbD-concept to nanotechnology and determine a definition (long-term). Sweden should take the lead, with support of funding agencies active involvement.

Proposal (medium-term)

- Adapt the SbD-concept to nanotechnology and determine a definition with support of Swedish funding agencies active involvement

2.5.3 RESPONSIBILITY

If you design a certain material with a certain function and sell it to another company, what will the next step be? Who is responsible for the safety evaluation? Safe by design may mean shared responsibility between producers, users, waste handlers over the life cycle. Many different scenarios could be expected. Depends on whether the manufacturer is considered responsible for use or not. And what role does the user and waste handlers have? Is communication from all sides necessary to ensure safe use?

Proposal (short-term)

- Investigate who can be considered responsible for safe handling of nanomaterials throughout the life cycle (manufacturers, users, re-users, waste handlers)

2.5.4 RISK-BENEFIT ANALYSIS

In the framework of SbD, risk-benefit analysis is an interesting concept that should be refined and applied to nanomaterials. In some cases, in may be justified to use hazardous NPs. For example, you have a ground breaking NP invention for solar panel applications but the NPs are toxic. Methods should be found to reduce exposure or mitigate toxicity, i.e. if we understand the biological mechanisms we can make better materials with less danger.

Proposals (short-term)

- Refine and apply risk-benefit analysis to safe-by-design of nanomaterials

Annex IV. List of participants (with GDPR approval)

Namn	Organisation
Anwar Ahniyaz	Research Institutes of Sweden, RISE
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Anna Furberg	Chalmers University of Technology
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