Report 2017:1 from SweNanoSafe,

The Swedish National Platform for Nanosafety

From Research to Regulation

A report from the Nanosafety Conference,

28 March 2017, Stockholm, Sweden

SWETOX

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Preface

In March 2017, the Swedish National Platform for Nanosafety, SweNanoSafe, arranged its first conference. The theme of the programme was "From Research to Regulation".

At the conference, an overview of the NANoREG project and its key outputs was provided by Tom van Teunenbroek and Hugues Crutzen. Roland Grafström presented the Swedish contributions to NANoREG together with an overview of NanoReg2 and CaLIBRAte. Current nanosafety research was presented by Bengt Fadeel and Joachim Sturve provided an overview of the Mistra Environmental Nanosafety Programme. In addition, Gregory Moore gave a regulatory update and David Azoulay provided a commentary from the NGO perspective. Short scientific talks were also given from Swedish participants of the NANoREG project and researchers in the Mistra Environmental Nanosafety Programme. The conference programme further included panel discussions between various stakeholders and reflections on the conference from a policy perspective by Eva Hellsten.

The event brought together more than eighty participants from different stakeholder groups – academy, authorities, industry and NGO´s – thereby providing valuable networking opportunities and setting the stage for further cooperation among stakeholders.

On behalf of SweNanoSafe, we express our gratitude to the experts who prepared and presented lectures at the conference and to the audience for taking part in the event. In addition, we are grateful to Eva Krutmeijer for moderating the conference, including preparing and facilitating the discussions between stakeholders. We also thank Ami Palmin, and Jonas Förare for

SweNanoSafe

The Swedish National Platform for Nanosafety at Swetox

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The report can be downloaded from www.swetox.se or www.swenanosafe.se (when operational)

Prepared and written by: Marie Beckman

Cover photo: Pixabay.com

Other photos by: Jonas Förare

Stockholm, May 2017

contributing to the practical arrangements and communication of the conference.

Regarding the organisation of the event, we are grateful for the collaboration with the Swedish partners of the EU-funded project NANoREG, the Swedish Mistra Environmental Nanosafety Programme and the Swedish Chemicals Agency. Furthermore, we thank Bengt Fadeel, chair of the SweNanoSafe Expert Panel and the members of the Expert Panel for playing a key role in the composition of the programme and at the conference.

Åke Bergman, Chair SweNanoSafe Steering Committee and Head of Swetox, and the SweNanoSafe Project Team

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Abbreviations

CASG nano – The European Commission Competent Authorities Sub-Group on Nanomaterials

CEFIC – European Chemical Industry Council

CEN – European Committee for Standardization

ChemSec – International Chemical Secretariat, an NGO

CIEL – Center for International Environmental Law

ECHA – European Chemicals Agency

EUON – European Observatory for Nanomaterials

FP7 – Seventh Framework Programme. The European Union's Research and Innovation funding programme for 2007-2013.

IPEN – International POPs Elimination Network

JRC – Joint Research Centre, the European Commission's science and knowledge service

NGO – Non-Governmental Organisation

NM – Nanomaterial

NIA – Nanotechnology Industries Association

OECD – Organisation for Economic Co-operation and Development

OECD's WPMN – OECD's Working Party on Manufactured Nanomaterials

QSAR – Quantitative structure-activity relationship

REACH – Registration, Evaluation, Authorisation and restriction of Chemicals, EU regulation on chemicals

RIVM – Dutch National Institute for Public Health and the Environment

SA – Safety Assessment

SOP – Standard Operating Procedure

Swetox – Swedish Toxicology Sciences Research Center. An academic research center for research and education within chemicals, health and environment.

About the Organisers

The conference was organised in collaboration with the Swedish partners of the EU-funded project NANoREG, the Swedish Mistra Environmental Nanosafety Programme and the Swedish Chemicals Agency.

The Organising Committee was led by Heike Hellmold (SweNanoSafe, Swetox) and included members of the SweNanoSafe Project Team at Swetox: Ekatherine Lagovardos, Elina Drakvik and Marie Beckman, together with Eva Krutmeijer (EKKO AB) and Ami Palmin (Swetox).

Åke Bergman (Swetox), Bengt Fadeel (Karolinska Institutet), chair of SweNanoSafe's Expert Panel, and the members of the Expert Panel, see the section "About SweNanoSafe", contributed to the composition and content of the programme together with Roland Grafström (Karolinska Institutet) and Eva Hellsten (Swetox). Jonas Förare (Swetox) contributed to communication of the conference.

About the Report

The report is aimed at stakeholders in the field of nanosafety such as academia, regulatory authorities, industry, retail and NGO's and interested members of the public.

In the first section entitled "About SweNanoSafe", an overview of the Swedish National Platform for Nanosafety at Swetox is presented. In the following sections, the presentations, panel discussions and interactive dialogues that were held at the conference are summarized.

The report is focused on giving an overview of the NANoREG project and its outcomes, an overview of the Mistra Environmental Nanosafety Programme and on highlighting individual voices from industry, retail, authority and NGO's.

More specifically, an account is given of the NANoREG project and its key outputs as presented by Tom van Teunenbroek and Hugues Crutzen. Similarly, accounts are provided of the Mistra Environmental Nanosafety Programme, as presented by Joachim Sturve, and of the NGO perspective from the Center for International Environmental Law given by David Azoulay.

For the content of the presentations of additional main speakers Roland Grafström, Bengt Fadeel and Gregory Moore, the reader is referred to the abstracts and/or slides from their presentations.

An account is also given of various perspectives from industry, retail and authority in the first panel discussion. The outcome of the second panel discussion, which included all stakeholder groups present at the conference, is summarized in bullet points. Finally, an account is given of Eva Hellsten's reflections from a policy perspective and of the closing of the conference by Åke Bergman. For the short scientific talks, abstracts and/or slides are provided.

The report is based on the speaker presentations and/or the abstracts submitted. Almost all abstracts and presentation slides have been made available for this report. The citations included are based on audio transcripts from the conference.

Presentation slides are available at the following link http://swetox.se/en/presentations-from-swenanosafes-first-annual-conference/

About SweNanoSafe

For the safe use and handling of nanomaterials, there is a need for more knowledge of their properties and their potential environmental and health risks. To promote knowledge in this area, Swetox was commissioned by the government to develop a national platform for nanosafety in cooperation with authorities, academia, industry and organisations dealing with environmental, health and safety issues of nanomaterials. Subsequently, the Swedish National Platform for Nanosafety, SweNanoSafe, was established in 2016 at Swetox, an academic research center for chemicals, health and environment. The platform was launched in May 2016 with a kick-off conference that gathered approximately a hundred participants.

Objectives

In order to promote the safe use and handling of manufactured nanomaterials, the platform aims to strengthen the cooperation between different stakeholders to ensure knowledge exchange in the field of nanosafety. In collaboration with various stakeholder groups, the platform aims to:

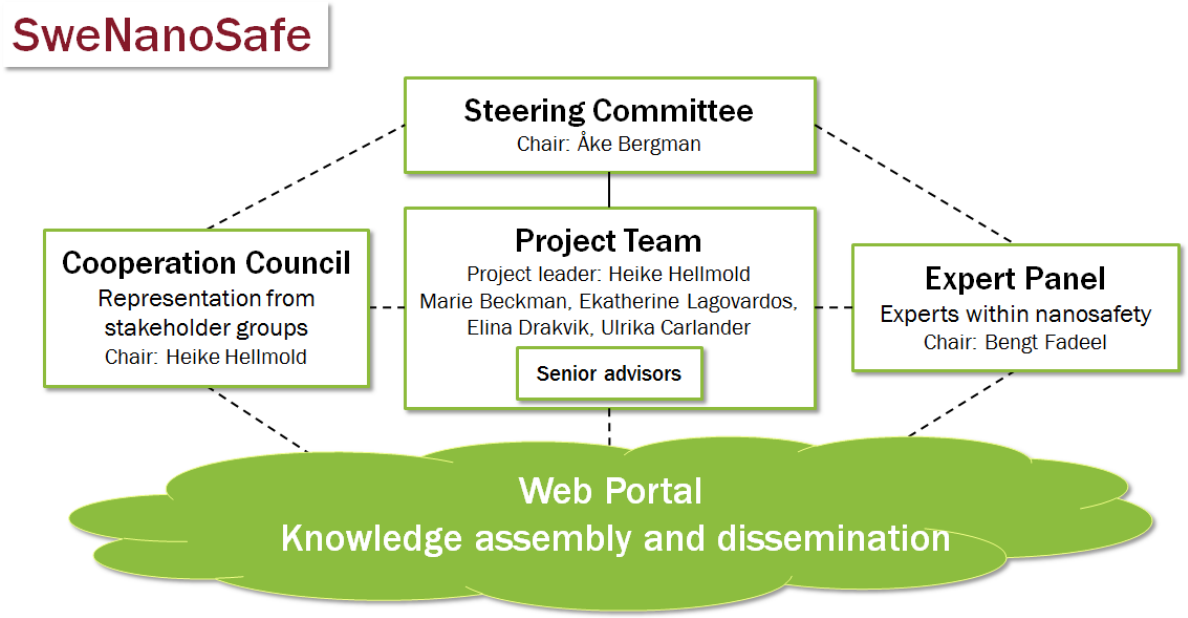
1. Ensure knowledge building; assemble and disseminate knowledge on environmental, health and safety issues of nanomaterials, including improving the knowledge base by making scientific expertise available.

2. Strengthen the education and training in nanosafety.
3. Increase the knowledge on hurdles to a safe use and handling of nanomaterials and how these hurdles can be addressed. An important aspect is the integration of nanosafety early in the innovation process.

The platform will not conduct research or perform safety assessments.

Organisation for Cooperation

The activities of the platform are organised by the **Project Team**, see organisational scheme below. Senior advisors within the field of nanosafety, including Eva Hellsten, and on communication contribute to the platform through a reference group. For efficient cooperation, an expert panel has been established and a cooperation council for stakeholder groups and a web portal are currently being set up.



The Cooperation Council will consist of representatives from authorities, industry, NGO's and academia. Currently, there is representation from the Swedish Chemicals Agency, the Swedish Environmental Protection Agency, the Swedish Work Environment Authority, the National Food Agency and the Medical Products Agency in Sweden. It is chaired by Heike Hellmold.

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 consists of members with expertise from different disciplines within the field of nanosafety and is chaired by Bengt Fadeel. For the members of the expert panel, see the table below. One task of the panel is to ensure the quality and actuality of the knowledge generated and communicated via the platform. Through its multidisciplinary composition, an illumination of nanosafety issues from different perspectives will be enabled. Furthermore, the panel will contribute to building a network of nanosafety researchers in Sweden to improve the knowledge base of the platform.

Area	Expert
Toxicology/Chair	Bengt Fadeel, Karolinska Institutet
Toxicology	Alexander Lyubartsev, Stockholm University
Ecotoxicology	Joachim Sturve, University of Gothenburg
Exposure	Maria Hedmer, Lund University
Materials Science	Kajsa Uvdal, Linköpings University Andrea Fornara, Research Institutes of Sweden
Risk Assessment	Gregory Moore, Swedish Chemicals Agency
Life Cycle Analysis	Rickard Arvidsson, Chalmers University of Technology

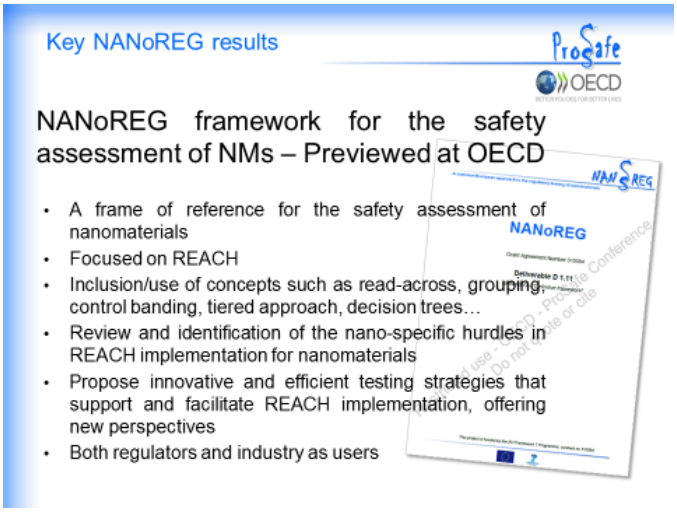
The platform is led by the **Steering Committee**, which is chaired by the head of Swetox, Åke Bergman. The Steering Committee consists of representatives from the Cooperation Council, the Expert Panel and the Project Team.

The Swedish Chemicals Agency contributes to the work of the platform through a constant dialogue and representation in the Steering Committee, the Cooperation Council and the Expert Panel.

The Web Portal (swenanosafe.se) is currently under development. The purpose of the portal is to serve as a source of knowledge in the field of nanosafety and to enable interaction between the different actors as a complement to the meetings, conferences and educational activities that the platform will organise.

Overview of the NANoREG Project and its Outcomes

Tom van Teunenbroek, Ministry of Infrastructure and the Environment, the Netherlands and Coordinator of NANoREG



Background, aims and basic conditions

Tom van Teunenbroek, coordinator of NANoREG, began by presenting the background and aims of the project. In NANoREG, 87 institutional partners – from EU member states (15), associated member states (2), the Republic of Korea and Brazil – have collaborated in developing reliable, reproducible and relevant methods for testing and assessing the effects of nanomaterials on human health and environment. "This amazing project, which is born out of frustration", as Tom van Teunenbroek described it, started in March 2013 and ended in February 2017. The industry has been involved, via individual companies, CEFIC (European Chemical Industry Council) and NIA (Nanotechnology Industries Association). Because the project concerns REACH, methodologies and applicability of methods, and standardization issues there have been official links to ECHA, OECD, ISO and CEN. There have also been links to former and ongoing EU FP7 projects. Roughly 2 500 people have been working in the project and the total budget was 50 million euro of which 10 million euro was provided by the EU (FP7) and 40 million euro by member states, regions, partners or other parties. Currently, reporting is still ongoing and the final progress report is expected in May 2017.

Tom van Teunenbroek further highlighted that NANoREG has been a "demand driven" project with a strong focus on both regulatory and scientific needs regarding methods and data that can be used in a regulatory context.

> "The demand side of the project was done with sixteen regulatory questions."

These questions were formulated by, among others, regulators and industry to ensure the generation of reliable and comparable data that could be of regulatory use. To fulfil the demands, the project partners had to comply with a so-called Guidance Document and agreements on test design, data management, etc.

A suite of well characterized nanomaterials and additional alternative materials were also selected for mandatory use. The approximately ninety different materials (metallurgic, fibre materials etc.) were deposited and subsampled at JRC (Joint Research Centre of the EU Commission). The materials are still in the depository at JRC and available for ordering via a web-based tool.

In addition, the same dispersion technique for the materials had to be used according to set standard operating procedures (SOPs).

> "Everybody had to characterize the material the moment it arrived in the laboratory. The moment they made a dispersion they had to characterize it again and the moment they did the an experiment on cells they had to characterize the solution again, so that we really would know whether the particle was transforming during the experiment and what the cells really were exposed to."

Sometimes this required collaboration with physicists and Tom van Teunenbroek emphasized that the only way out in solving many of the questions concerning novel materials i.e., nanomaterials, nano-enabled biomolecules and other materials, is interdisciplinary collaboration:

> "If we don´t have an interdisciplinary approach, we will get nowhere".

Regarding the *in vitro*-tests, they were performed with agreed cell lines and test media. Cell line stability was also checked by DNA-testing.

> "You think you can compare your results from the beginning to the end [of the experiment] but in reality you [may] have created a different cell line. // This is why a regulatory approach is so costly."

Results – a brief overview

Tom van Teunenbroek stated that the project has resulted in more than sixty scientific deliverables that will become publicly available at the end of the project, not just to the scientific community. Numerous SOPs, in stages from "proof of concept" to "validated", were also developed. Currently, all documentation is transferred to a website hosted by RIVM (Dutch National Institute for Public Health and the Environment) and will stay there for the next five years. To facilitate the dissemination of the results to different stakeholders, and because some deliverables may be over two hundred pages long, short fact sheets have been made for each deliverable. These fact sheets indicate the content of the deliverable and whether it could be of further interest. Everything is hyperlinked with links to the original documentation.

> "We have it all arranged so that everyone who wants to use it can use it in a user friendly way."

After the final meeting with the EU Commission in May, the final progress report of NANoREG will be published. It will contain an overview of the results, including hyperlinks to all the fact sheets, which in turn contain links to the original deliverables. The data has been standardized and opened up via FP7 **eNanoMapper** database. The original data set is also publicly available for use in for example QSAR studies.

> "The nice thing is that everybody used the same materials, everybody used the same SOPs and everybody used the same way of reporting it, making it, I think, one of the largest data sets around now on nano. It can be utilized to help us find the mode of action by computational type of approaches."

The results further include information on exposure and effectiveness of personal protective equipment.

> "I think this is a breakthrough type of documentation because it wasn't only shown but validated with measurements about the effectiveness of all sorts of protective equipment."

As an integrating output, the NANoREG Framework for the safety assessment of nanomaterials proposes forward-looking strategies for safety assessment under REACH. It will be released by JRC at the end of the project, for more details see presentation by Hugues Crutzen below. The forward-looking strategies include the nanospecific

prioritisation and risk assessment, the safe-by-design approach and life cycle assessment of nanomaterials.

A review of about forty key nanomaterial safety assessment terms has also been made by JRC to harmonise the terminology. It is downloadable from the EU Bookshop at the following link: http://doi.org/10.2788/71213

Finally, a toolbox from NANoREG and other initiatives at national and European level will be published soon, for more details see presentation by Hugues Crutzen below. Tom van Teunenbroek ended his presentation by stating that:

> "It is my clear intention that the outcome of the NANoREG project together with the tools, the datasets, the interlinkage of the datasets with eNanoMapper as well as the proposed Framework eventually is going to become a web-based tool."

However, NANoREG has ended and to provide this, more funding is needed.

To build on the results achieved, concerted action to expand the knowledge is needed.

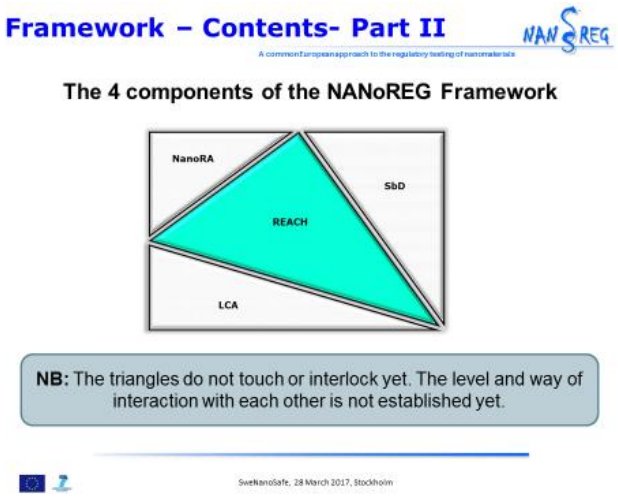
> "The biggest thing we have to learn from this is that the mindset has to be aimed at collaborating and data sharing."

All of NANoREGs deliverables, roughly 6 500 pages according to Tom van Teunenbroek, are available on the website hosted by RIVM at the following link: http://rivm.nl/en/About_RIVM/International/International_Projects/Completed/NANoREG/NANoREG_Results_Repository_sub_page_Publications

For additional information, see the slides from the presentation at the following link http://swetox.se/en/presentations-from-swenanosafes-first-annual-conference/

NANoREG Key Outputs: the Framework and the Toolbox

Hugues Crutzen, European Commission – Joint Research Centre



Hugues Crutzen, on behalf of the JRC, headed the NANoREG Work Package 1. In this work package, data, information and tools addressing environmental, health and safety aspects of nanomaterials, which were generated and/or evaluated during the project, were gathered. The knowledge was further framed into two outputs.

> "One is a framework, a kind of ideas document, perspective document, forward-looking document and the other one is a more technical collection of so-called tools".

The NANoREG Framework

Part I of the Framework document shows how REACH applies to nanomaterials, highlights the nanospecific considerations and points to the hurdles in nanomaterial safety assessment in REACH. Regarding the hurdles, Hugues Crutzen stated that some are already being addressed, some are not.

> "The advantage of the NANoREG framework is that we bring key information into one place. If you go through that document, you will find references and hyperlinks, for instance to ECHA guidance and other documents. Hopefully everything is there. If you go through it you get a complete picture and you know where to fish later on for more detailed information."

Part II of the Framework document is proposing forward-looking strategies. These are called 1) Nanospecific prioritisation and risk assessment, 2) Safe-by-design, and 3) Life cycle assessment.

The document is concluded with take-home messages that, together with the executive summary, can help to quickly identify remaining hurdles and suggestions for future work.

The forward-looking strategies propose three things:

1) Nanospecific prioritisation and risk assessment – ways to prioritise the risk assessment of nanomaterials, including the concept of grouping and read-across.

   > "This is done in the form of going through a decision tree, trying to make informed choices, to simplify the assessment so that you can push aside problems, or solve them, and try to come to a conclusion rather quickly and rather efficiently."

2) Safe-by-design – ways to bring safety concerns with nanomaterials up front at early stages of design and to consider these at each of the stages defined by the logic of an innovation model.

   > "At key moments when you have decision making [within an innovation model], go or no-go's, for those informed decisions you need to also consider the safety aspects. The safe-by-design logic proposes a logic to include these considerations at each step."

3) Life cycle assessment is based on ISO recommendations and EU directives.

   > "It is a holistic approach to the impact of chemicals on the environment and the society, but those who have written the [Life cycle assessment] chapter [of the Framework document] have suggested ways of linking it with the risk assessment of nanomaterials."

Hugues Crutzen pointed out that the possible use of the strategies within the REACH implementation process is currently debated in the scientific arena.

> "A lot of work still needs to be done to make sure these approaches work."

> "The Framework of NANoREG is done from the scientists' point of view. We are trying to help industry and regulators // it is not something that is being proposed as a piece of legislation or a regulatory document."

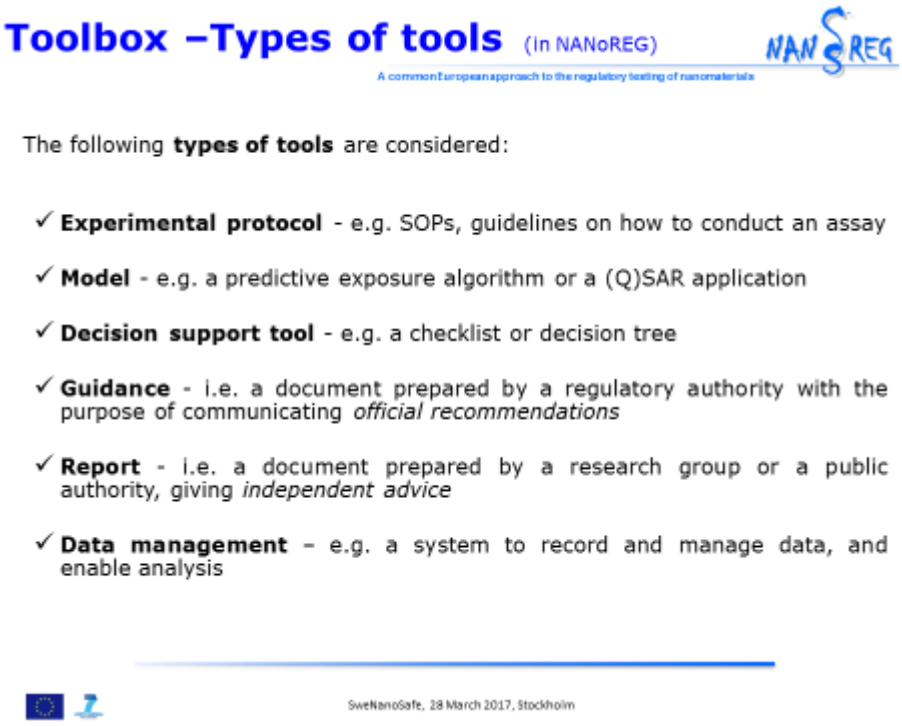
The JRC report on the NANoREG Framework has been published, doi: 10.2760/245972.

It is also available at the NANoREG results repository hosted by RIVM as deliverable D1.11.

The NANoREG Toolbox

The toolbox is a collection of tools for the safety assessment of nanomaterials. It is focused on working tools that are ready to use and accessible. For types of tools, see figure below. The tools are linked to the issues that are identified in the Framework:

> "You should be able to go to the toolbox, click on a tab which is reporting the same name and number as the paragraph in the Framework and find relevant tools to address that problem".



There are also tags to describe the regulatory status of a tool, i.e. from research product to regulatory document. This assessment was done to the best of JRC's ability. Currently, there may be unintentional errors or incomplete verifications present in the Toolbox.

Presently (March 2017), there are in total 207 unique tools in the Toolbox. Out of these, 175 are available and 32 are prospective tools. The most common type of tool is experimental protocol and the most common regulatory status is research product, followed by regulatory document. The possible future evolution of the Excel®-based toolbox is towards

a more user-friendly system. Until then, Hugues Crutzen proposed downloading the tables and transforming them into a preferred format.

> "It is open stuff, all there and available for everyone."
>
> "This Toolbox should be a living document. Anyone can build on it, complete it, if the ideas and criteria are followed, it can really grow and become a very interesting system."

The Toolbox has been released as deliverable D1.12. A JRC report on the toolbox development is expected in June 2017.

For additional information, see the slides from the presentation at the following link
http://swetox.se/en/presentations-from-swenanosafes-first-annual-conference/

NANoREG, NanoReg2 and CaLIBRAte

Roland Grafström, Institute of Environmental Medicine, Karolinska Institutet

Roland Grafström, the national coordinator of the Swedish partners in NANoREG, presented an overview of the Swedish contributions to the NANoREG project. In addition, he gave an overview of the two EU funded projects NanoReg2 and CaLIBRAte that are currently ongoing. These projects are focused on the development and implementation of grouping and safe-by-design approaches within regulatory frameworks and the next generation tools for risk governance of nanomaterials.

For additional information, see the slides from the presentation at the following link
http://swetox.se/en/presentations-from-swenanosafes-first-annual-conference/

Current Nanosafety Research: Lessons Learned

Bengt Fadeel, Nanosafety & Nanomedicine Laboratory, Division of Molecular Toxicology, Institute of Environmental Medicine, Karolinska Institutet and Chair SweNanoSafe Expert Panel

Abstract

We have witnessed an exponential growth in the number of publications on nanotoxicology in the last decade and it is important to take stock of where we are. Here, I provide a glimpse of recent achievements in nanotoxicological research and highlight some remaining challenges. The ability to manipulate matter at the nano-scale enables many new properties that are both desirable and exploitable, but the same properties could also give rise to unexpected (if not entirely novel) toxicities that may adversely affect human health. Understanding the physicochemical properties driving the toxicity of nanomaterials remains a challenge. However, if one could link material properties to toxicological outcomes this would enable the prediction of nanomaterial hazards and facilitate the design of nanomaterials that retain their useful properties, but display reduced toxicity (so-called safe-by-design). The view is emerging that interactions of nanomaterials with cells and tissues is determined by the combination of intrinsic, physicochemical properties of the materials (the 'synthetic identity') and the context-dependent properties arising from the so-called corona of adsorbed biomolecules on the surface of the materials in a biological system (the 'biological identity'). The bio-corona may be of particular importance for

nanomaterial interactions with the immune system, our main defence against foreign intrusion [Farrera & Fadeel. 2015]. It is challenging to achieve a comprehensive understanding of the mechanisms underlying the toxicity of new and emerging nanomaterials using conventional toxicological assays. Therefore, systems biology approaches based on global "omics" technologies coupled with computational methods to elucidate perturbations of genes or pathways are being progressively applied in nano(eco)toxicological research in order to develop predictive models of nanomaterial behaviour or toxicity in a biological system [Fadeel. 2015].

Fadeel B. Systems biology in nanosafety research. Nanomedicine (Lond). 2015;10(7):1039-41.

Farrera C, Fadeel B. It takes two to tango: Understanding the interactions between engineered nanomaterials and the immune system. Eur J Pharm Biopharm. 2015;95(Pt A):3-12.

Mistra Environmental Nanosafety Programme

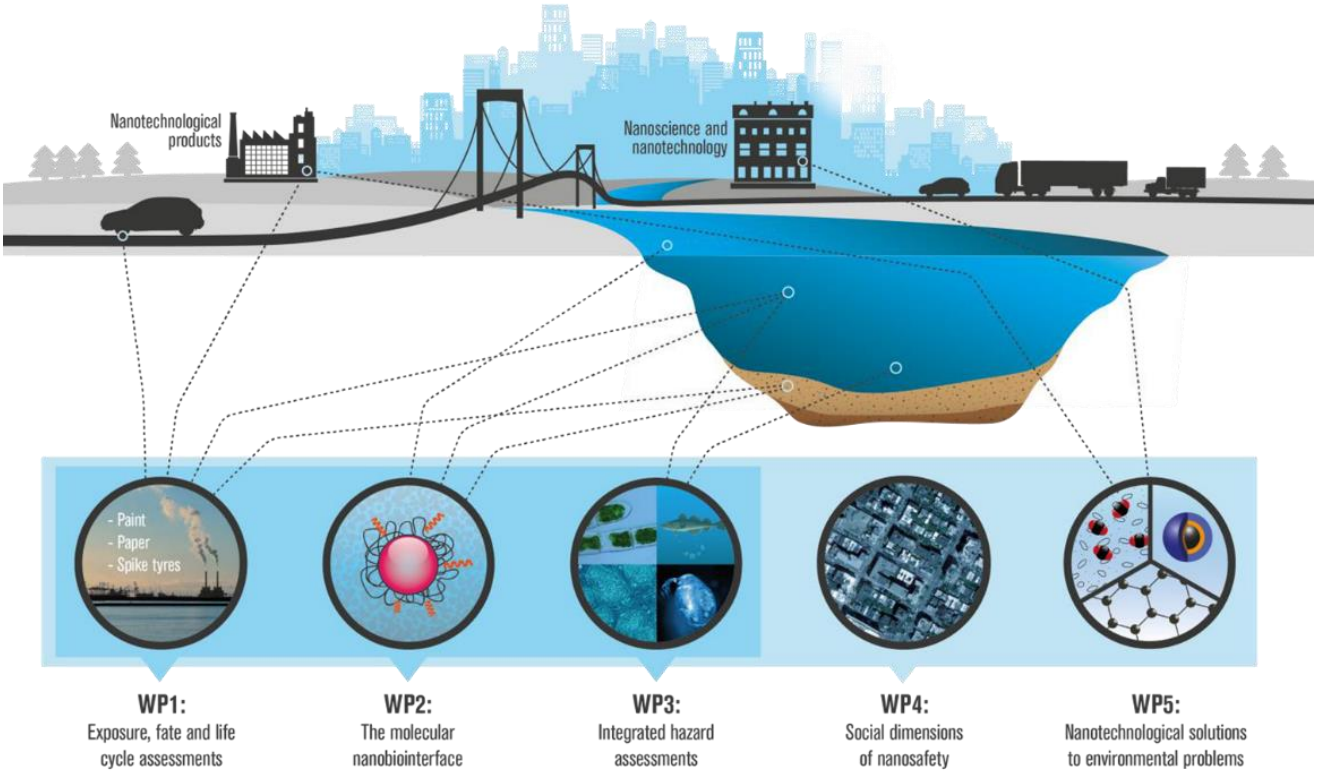
Joachim Sturve, Department of Biological and Environmental Sciences, University of Gothenburg

From Susan Woskie, Univ of Mass Lowell, 2014

The Mistra Environmental Nanosafety programme director is Julie Gold from Chalmers University of Technology and Joachim Sturve is co-coordinating the programme. The aim of the programme is to build knowledge to promote responsible use of nanotechnology in a sustainable society. Joachim Sturve stated that:

> "The research focus is environmental risks of nanomaterials, to look at properties of nanomaterials that should be avoided and how we can protect the environment from unacceptable emissions."

Joachim Sturve continued to describe the programme in more detail. It is divided into five work packages, see figure from the presentation below. The three following short scientific talks from researchers in the Mistra programme also reflect these work packages. The programme is further based on three main case studies. The first one is on commercial nanoparticles (silica nanoparticles, SiO_2, in paint and paper) and is performed in collaboration with AkzoNobel that provides the study with nanoparticles that exhibit different properties. The second case study is built on nanomaterials in road runoff (nanoparticles from studded snow tires) and the last one is focussed on future nanomaterials (graphene and other 2D materials).



Briefly, the particles bio-corona and the fate of the particles when they are released into the environment is under investigation. The nanoparticles are treated in different ways and the effects studied with a battery of biological monitoring tools. Currently, four model systems are used: the bacteria Pseudomonas, the algae Chlamydomonas, cell lines (for lung and gill) and zebra embryo toxicity test according to the OECD test guideline.

> "Zebra fish larvae locomotion and behaviour is [also studied] as a promising tool for screening on a sub-lethal level."

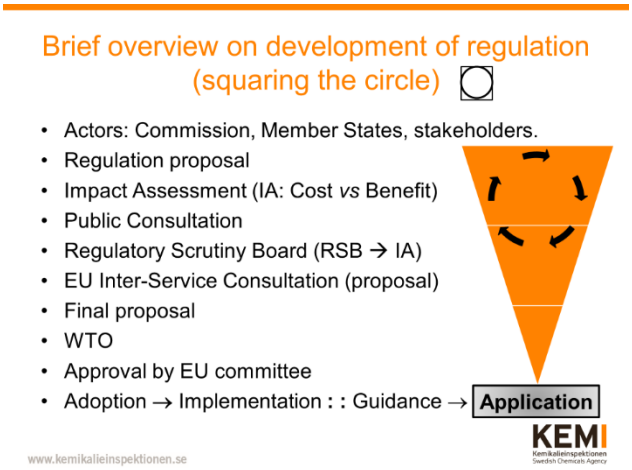
Partners in the programme consortium are Chalmers University of Technology, Gothenburg University, KTH Royal Institute of Technology, Lund University, Karolinska Institutet and AkzoNobel.

For additional information, see the slides from the presentation at
http://swetox.se/en/presentations-from-swenanosafes-first-annual-conference/

and visit the web page of Mistra Environmental Nanosafety Programme at
http://www.mistraenvironmentalnanosafety.org/

Regulatory Update

Gregory Moore, Swedish Chemicals Agency (KemI)



Abstract

The Second EU Regulatory Review on Nanomaterial (NM) in late 2012 in principle marked a milestone for activities to improve EU regulation of NM. In 2013, three different activities were initiated to: (i) amend REACH annexes to include NM; (ii) revise the EU Commission's (COM) recommendation (EU 2011/696) on the definition of NM; and, (iii) evaluate the need to increase transparency and ensure regulatory oversight for nanomaterial (e.g. traceability and an EU-register).

To date:

It has been decided that a European Observatory for nanomaterials (EUON) will be managed by ECHA and be fully operational by 2019. The Observatory will compile readily available information which will be available to regulators and stakeholders with an aim to meet the needs of consumers.

Work on the revision of the EU recommended definition for NM has been delayed but a public consultation is expected to be launched before summer 2017. Endorsement is expected shortly thereafter followed by implementation into different regulations e.g. REACH (EC 1907/2006), biocides (EU 528/2012), cosmetics (EC 1223/2009) and novel foods regulation (EU 2283/2015).

Work on the adaption of REACH annexes has been delayed and they will not be applicable for the last REACH registration by 31 May 2018. At present a non-paper has been presented

to the REACH committee which is a formal voting body. It is necessary that a Commission proposal is also supported by an Impact Assessment. However, a recent decision by the Board of Appeal ruling that REACH has no obligations to identify nanoforms, requires that both the Impact Assessment and REACH annexes be further adapted. An EU Commission proposal is promised by summer 2017.

For additional information, see the slides from the presentation at the following link
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Ensuring the Safety of NM. From Science to Regulation: Reflections on Uncertainty, Regulation and Innovation

David Azoulay, Center for International Environmental Law (CIEL)

David Azoulay began by introducing CIEL's involvement in the regulatory issue of nanomaterials. CIEL has been working on nano since around 2007 and published their first paper in 2009. CIEL is a member of the European Commission Competent Authorities subgroup on Nanomaterials (CASG nano), head of the NGO OECD Working Party on Manufactured Nanomaterials (WPMN) delegation and chair of the IPEN nano working group, which is a group of NGO's from the five continents working on nano issues.

Subsequently, he briefly described the regulatory activity in the past ten years, the question of the definition of nanomaterials, transparency and public registers, discussions on REACH and sectoral regulations (e.g., cosmetics, biocides, food). David Azoulay concluded that the effect of these activities has been limited and that there is very little effective and enforced regulation in place in the EU. As an example of this, he stated that no one has the answers to the questions of: What is being produced? How much of it is being produced? Where does it go?

> "If you cannot answer these questions, developing effective and enforceable regulation can be very difficult and very challenging."

David Azoulay pointed out that there are currently no reliable sets of exposure data for the vast majority of nanomaterials. He labelled the last decade's discussions about obtaining

this information via a mandatory EU registry as "a decade of denial", with discussions centred on costs and its potential impact on innovation.

On the question of hazards, he stated that important progress has been made, for instance in NANoREG, but that large data gaps remain.

> "We have to come to terms with the idea that there is no such thing as scientific certainty. We will have to deal with some level of uncertainty for some time to come, whether it is about the materials currently in the market or the materials that will be coming on the market very soon. Waiting for certainty to take action therefore means that we will never take appropriate actions and we have to be ready to act, in a precautionary way, based on available information."

In Europe, David Azoulay noted, we do have a system that should allow us to collect this information i.e., REACH, but the past eight years have shown that it is not efficient when it comes to nanomaterials.

The first nanospecific regulation to be adopted was the cosmetics regulation.

> "From a legal standpoint, it was a really innovative piece of legislation and it was a negotiated compromise. // The problem is, that when it comes to nanomaterial, there has been no political will to enforce it or there has been obstacles to the enforcement."

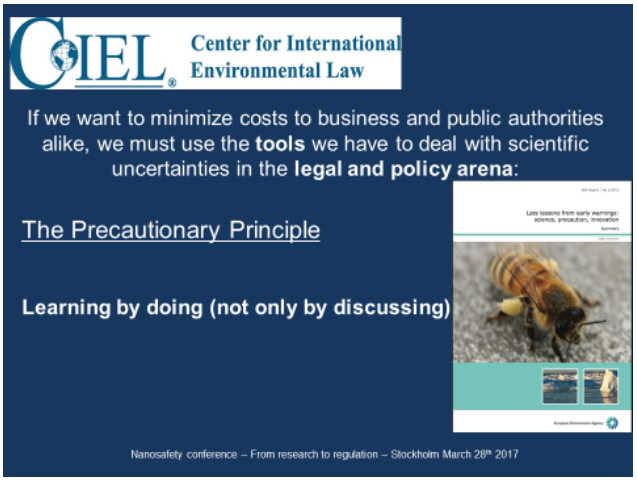
As an example, he mentioned the obligation for the commission to publish a list of all nanomaterials that are currently used in cosmetics. The list was supposed to be published in 2014. CIEL has made several official requests to the commission in order to clarify when the list will become public. However, this is still not known.

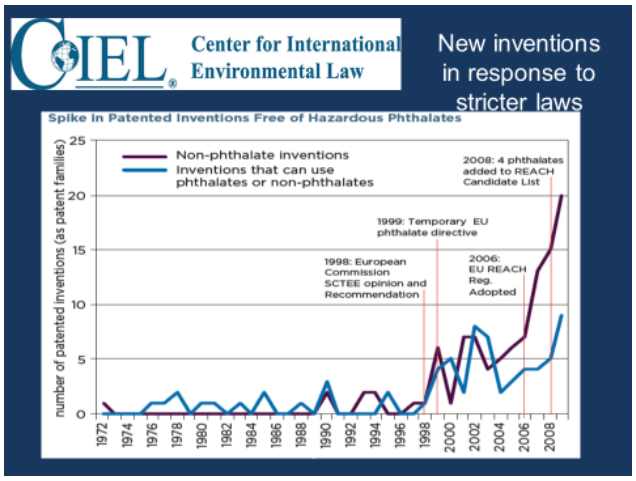
Regarding the legislation on novel food and food information to consumers, there are also problems with the enforcement, according to David Azoulay. For the biocide regulation, which also contains nanospecific provisions, he said that the jury is still out because the implementation is just at its beginning.

Concerning the issues above, David Azoulay highlighted some of their common features in the following way: there are technical challenges, scientific uncertainty has to be balanced with legal uncertainty, and safety is systematically undermined by the reluctance to negatively impact innovation.

> "The silver lining in dealing with these kinds of uncertainties is that we have tools to deal with scientific uncertainty. // It is called the precautionary principle. It is

sometimes challenging to implement but the NGO position is that we should learn by doing."





Is the precautionary principle an obstacle to innovation? CIEL has investigated this question by doing case studies on what happens to a product when it becomes regulated. David Azoulay showed an example of a case study on phthalates that are endocrine disrupting chemicals and have been regulated gradually over the past years. To study the impact of regulation, CIEL investigated the number of patents filed on phthalate alternatives, or products that could be used without phthalates, and compared the timing of filing of those patents with the timing of new regulations. He concluded that in this case, new inventions were spurred in response to stricter regulations, as illustrated in the figure to the right above.

> "Innovation is indeed changed by regulation but there is a re-direction of innovative efforts to a more socially approved area rather than an absolute decline."

David Azoulay's final remarks on innovation were:

> "Innovation needs to be guided to benefit all society. // How do we balance the social needs and the need for coming out with new products that provide a lot of customer satisfaction? In that context of enduring uncertainties, precaution-based regulation is our best instrument to do so."

> "Remember that when we are avoiding costs of action, costs of regulation – if we don't regulate, those costs will not disappear, they will just be shifted to other parts of society.// Reducing cost is important, as long as we look at all the costs and all the potential benefits."

For additional information, see the slides from the presentation at the following link
http://swetox.se/en/presentations-from-swenanosafes-first-annual-conference/

Comments:

Björn Johansson (IKEA):

> "I would actually like to have more regulations because it would help us. From IKEA's side, we set up IKEA requirements on our suppliers and just [need] getting the help from the regulators concerning what to do here, because I am just in favour of everything you have said here today."

David Azoulay:

> "I think this really exemplifies one of the issues we have in the EU. In the EU, law making on chemicals, when we talk about industry, the only industry we have are chemical producers – where are the downstream users? Industry is a very diverse community with very different types of interests. We have heard from IKEA and others, of course they want regulation because they are on the frontline, consumers are seeing their brand and if something happens, they are going to be the one's impacted not BASF, not Dupont, not Bayer [chemical producers], because the product chain is such.
>
> In response to your very encouraging comments, I would say to IKEA and other downstream users: come and speak with us, participate in the actual law making and don't let chemical producers speak on your behalf. They are your producers but they sometimes have diverging interests so we need you to give the view of the downstream users."

The Importance of Nanomaterial Characterization (cancelled)

Andrea Fornara, RISE Research Institutes of Sweden, RISE Bioscience and Materials/Chemistry, Materials and Surfaces Unit

Abstract

Nanotechnology as Key Enabling Technology is empowering profound changes in material performances and new possibilities to tackle several challenges: from medicine to energy, from transport to construction. At the same time safety aspects for human health, environment and society have to be investigated and risks should be mitigated. In both cases the physico-chemical characterization of nanomaterials is a key component to understand and predict the material performances and the interaction with the surroundings.

In order to obtain reliable information about the material, the characterization should be conducted in a proper way, according to best practice, following existing Standard Operating Procedures (SOPs), ISO or other standards and in agreement with established guidelines (i.e. OECD).

In order to rely on characterization data, the quality of such data should be guaranteed via established standards, guidelines and via reliable and even accredited labs and institutions that have performed reproducibility and reliability checks and round-robin tests. Within the NANoREG project, several methods have been checked to assure their usefulness and quality. They can be used in more complex nanosafety assessment to understand first the intrinsic physico-chemical characteristics and second the interaction between nanomaterials and the environment or biological entities, for example in degradation studies.

Development of Nanospecific Physiologically-based Pharmacokinetic Models

Gunnar Johanson, Institute of Environmental Medicine, Karolinska Institutet

Abstract

Physiologically-based pharmacokinetic (PBPK) modelling is useful to understand, explain and predict the uptake and disposition of chemicals in the body in relation to physicochemical properties from various aspects, including dose-effect relationships and dose, route and species extrapolations, and biological exposure monitoring.

The aim of this project was to develop a general PBPK model for nanoparticle (NP) uptake and biodistribution/biokinetics in a stepwise approach: (1) start with biodistribution/ biokinetics in rat for intravenous doses of well-defined NPs, (2) expand to a general intravenous model for rat (covering different NP doses, sizes, and composition), (3) expand to other routes (oral, inhalation, skin), and (4) expand to other species, in particular humans.

Our thus developed nano PBPK model captures the experimentally observed biokinetics of five NP types (pegylated and uncoated polyacrylamide, gold nanorods, titanium dioxide, cerium dioxide) given *i.v.* to rats. The model is the first to include phagocytosis and influence of corona on NP tissue partitioning. The simulations suggest that the biokinetics are strongly dose, size and route dependent. The model contains many fitted parameters for which experimental validation is needed. To this end, more well-designed biodistribution studies are required.

The project was funded by Forte and NANoREG.

For additional information, see the slides from the presentation at the following link
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Airborne Exposure – Measures and Risks (cancelled)

Jenny Rissler, Ergonomics and Aerosol Technology, Lund University; RISE Bioscience and Materials

Abstract

Jenny Rissler[1,2], Joakim Pagels[1], Maria Hedmer[3], Maria Messing[4], Linus Ludvigsson[4], Karin Loven[1], Christina Isaxon[1], Christian Svensson[1], Anders Gudmundsson[1] (1) Ergonomics and Aerosol Technology, Lund University (2) RISE Bioscience and Materials (3) Occupational and Environmental Medicine, Lund University (4) Solid State Physics, Lund University

Due to the increased industrial use of novel-manufactured nanomaterials there have been growing concerns of the health risks related to unintentional exposure of engineered nanoparticles. One important exposure route that has been pin pointed, is that by inhalation of airborne particles. An environment where there are obvious risks of airborne exposure is workplaces, e.g. during synthesis, refinement, and manufacturing.

There are many challenges when it comes to airborne nanoparticle exposure. One is that of efficient, accurate and relevant methods for exposure assessments. Another is that of stable particle generation with high enough particle output for toxicological testing (*in vitro* and *in vivo*), as well as relevant and detailed enough characterization of the particles. As a part of the NANoREG project we performed workplace exposure studies using traditional techniques, introduced and applied novel characterization techniques and methods. We also performed laboratory tests of *in situ* characterization techniques and suggested methods for generation and characterization of particles in toxicological studies.

Inhalation Toxicity Testing in Vitro using Air-Liquid Interface Exposure – Dry generation of CeO_2 nanoparticles and deposition onto a co-culture of A549 and THP-1 cells in air-liquid interface – dosimetry considerations and comparison to submerged exposure

Hanna Karlsson, Institute of Environmental Medicine, Karolinska Institutet

Abstract

Francesca Cappellini[1], Sebastiano Di Bucchianico[1], Siiri Latvala[2], Maria Malmlöf[1,3], Maria Kippler[1], Karine Elihn[2], Inger Odnevall Wallinder[4], Per Gerde[1,3] and Hanna L. Karlsson[1]

(1) Institute of Environmental Medicine, Karolinska Institutet, (2) Department of Environmental Science and Analytical Chemistry, Stockholm University, (3) Inhalation Sciences and (4) Division of Surface and Corrosion Science, KTH Royal Institute of Technology.

Few studies to date have generated a dry aerosol from a powder of nanoparticles (NPs) and compared the response from the same powder in submerged and air-liquid interface (ALI) conditions. The aim of this study, performed within the frame of NANoREG, was to investigate the cytotoxic and inflammatory potential of CeO_2 NPs (NM212) in a co-culture of A549 lung epithelial and THP-1 monocytic cell lines. Thus, exposure in submerged and ALI conditions was compared and the cellular dose in each exposure setting was analyzed using ICP-MS in order to enable proper dosimetry comparisons. An aerosol of CeO_2 NPs was generated by using the PreciseInhale® system. Even deposition of NPs (sizes 50-200 nm) in the cell exposure unit Xpose*ALI*® was observed using SEM imaging. CeO_2 depositions of 0.5, 1, 2 and 5 μg/cm^2 were obtained onto the co-cultures following ALI exposure. In submerged cultures, 2, 10, 20, 30 and 40 μg CeO_2/cm^2 were applied resulting in measured cell doses of 1, 5, 9, 15 and 22 μg/cm^2, respectively. Regarding cytotoxicity, there was no effect on mitochondrial activity in any of the exposures but a slight increase in LDH release in the highest ALI dose (5 μg/cm^2). This was not observed in the submerged exposure. Furthermore, there was no increased inflammatory cytokines release (IL-1β, IL-6, TNFα, MCP-1) in any of the CeO_2 exposed cultures, although a statistically non-significant increase of TNFα was observed in the highest submerged doses. Taken together, we demonstrated the applicability of the PreciseInhale® system for generation and deposition of dry aerosols, allowing for proper comparison of ALI and submerged exposure. The tested CeO_2 NPs showed, however, low cytotoxicity and inflammatory potential following exposure of A549 and THP-1 co-cultures in both exposure systems.

For additional information, see the slides from the presentation at the following link
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Expert Stakeholders' Understanding of Risks and Benefits of Nanotechnology: Challenges for Regulation

Åsa Boholm, School of Global Studies, Gothenburg University

Abstract

Main Author: Åsa Boholm [1], Co-author: Simon Larsson [2]

(1) School of Global Studies, Gothenburg University, (2) Gothenburg Research Institute, Gothenburg University

Swedish expert stakeholders' attitudes towards nanomaterials and nanotechnology

Nanotechnology innovation is growing fast on a global scale. Areas of application include electronics, food, textiles, health care, drugs, diagnostics, coatings, as well as cosmetics. While benefits of nanotechnology may be regarded as an established fact, risks to the environment and to humans is a concern engaging different societal actors. Risk assessments of nanomaterials is surrounded by considerable uncertainty; thus, regulatory bodies ask for robust scientific risk assessment that can serve as decision support for policy and steering. The establishment of trustworthy, legitimate and efficient governance frameworks for the regulation of nanomaterials will demand inter-institutional and inter-organizational collaboration. Hence, concerns about nanotechnology engage expert stakeholders representing different organisations.

This study explores the views of Swedish expert stakeholders on a number of issues and challenges regarding nanotechnology innovation. A web based questionnaire has been administered to some 240 expert stakeholders representing regulatory bodies, industry, funding agencies and NGOs (e.g. industry associations, consumer organisations, environmental organisations, and trade unions). The study investigates stakeholders' understanding of risks and benefits of nanomaterials and nanotechnology. It also addresses stakeholder's preferences for, and ideas about, what regulatory tools are appropriate for nanomaterials, as well as their more general ideas about need for public involvement and/or scientific knowledge in regulatory processes. The study contributes to a scholarly debate on how risk perception correlates with assumed benefits and how preferences for regulation varies with stakeholder's attitudes.

For additional information, see the slides from the presentation at the following link
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Environmental Nanosafety Research: Where do we stand, where do we (need to) go?

Thomas Backhaus, Department of Biological and Environmental Sciences, University of Gothenburg

For additional information, see the slides from the presentation at the following link
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Is Nanotechnology Good for the Environment? A Life Cycle Perspective

Rickard Arvidsson, Environmental Systems Analysis, Chalmers University of Technology

Abstract

One way to consider environmental impacts from nanotechnology is to quantify emissions and resource use of nanomaterial-containing products in a life cycle perspective. A number of such studies (<100) have been conducted so far. These generally show that many nanomaterials (e.g. carbon nanotubes) have high impacts per kg compared to conventional materials (e.g. steel). However, when products containing nanomaterials are compared to conventional products, the picture becomes diverse. In some cases, a nanomaterial can reduce impacts of the product as a whole. One example studied in the Mistra Environmental Nanosafety project is graphene as replacement for indium tin oxide in transparent electrodes, where graphene was shown to be superior both regarding energy use and use of scarce metals. In other cases, nanomaterial products do not reduce impacts compared to conventional products. One example of this is titanium dioxide nanomaterial coatings to window glass. Such coatings make the windows self-cleaning and able to degrade some air pollutants. However, the production of the coating has impacts and may influence heat balances in buildings. Net life cycle impacts tend to be similar between nano-coated glass and conventional glass. Overall, the literature on life cycle assessment of nanotechnology shows that generalisations of nanotechnology's environmental impacts are difficult to make. Preferably, each nanotechnology should be evaluated separately using life cycle assessment.

I. Voices from Industry, Retail and Authority

Michael Persson (AkzoNobel), Björn Johansson (IKEA) and Monica Tammela (Medical Products Agency, Sweden)

Question 1: What have you learned today?

Björn Johansson:

"I have learned a lot of things but my time plan is a bit shorter than this [current regulatory] time plan. // We do not want to wait ten years for some regulation to pop up, because we like to do things well in advance. // The frustration is that it started so late because for me it is quite obvious, if you look at REACH for example, if you place something [chemical, nanomaterial] on the market it should be safe. I don't think that is always the situation with nanomaterials."

Björn Johansson, Michael Persson and Monica Tammela

Michael Persson:

"A reflection from the discussions of today, is [about] the definition. I can understand the problems some companies and industry face when they look at that definition. [But] for us it is not a problem, independent of how you change the definition, all our products in the silica area will be [a nanomaterial] according to the definition. //

The reason why we are here and [collaborate] with Mistra and so on is that we think we can learn a lot from this type of research, be proactive, get early warnings and to see that we are moving in the right direction. Because we are also looking at new concepts and new modifications and it is essential that we don't make our particles hazardous (colloidal silica are classified to be non-hazardous). So I don't understand the discussions that there are companies that don't connect innovation with safety assessment and sustainability. They are connected and otherwise you are taking unnecessary risks in the potential business. You can make a lot of mistakes if you don't reflect quite early [in the process of innovation].

[For smaller companies] we see a role for Swetox to play to [provide] the competence they need and can't afford to hire themselves. We [AkzoNobel] have our own toxicologists and experts and even if we have good experts internally, I don't mind to have a second opinion from Bengt Fadeel, Roland Grafström and others, because we can't afford to make any mistakes in this area. // We need good regulation now but on EU level, otherwise it will be complicated and costly."

Monica Tammela:

"I would like to highlight one sentence that I noticed during the speeches here today and that is that we can foresee publicly available no-effect studies. Because I really long for that. Nowadays it is only the worse-effect studies we notice and can take care of. If it [would be] possible to make all data available, both for companies, scientific committees and authorities, the regulation and the compliance would become much faster I think."

Question 2: Tell us about one typical case in your organisation when you come into contact with nanomaterials and the questions that arise.

Michael Persson (MP):

MP is an innovation manager and presented a case based on paints. AkzoNobel produces silica particles for paints or similar products. MP described the type of challenges they encounter during the development of paints. There has been a shift from solvent-born paints to water-born paints. This has in turn resulted in issues that have to be solved with the water-born paints, which have only been developed for a relatively short time. MP referred to a master thesis from Chalmers and stated that if you for example can increase the performance of the paint, environmental costs may be reduced due to less need for repainting and cleaning.

"Therefore, performance is everything when toxicity and all other aspects are the same or better."

MP said that AkzoNobel uses eco-efficiency assessments, including life cycle analysis.

"It gives you very good guidelines in what direction you should move."

"We always do that analysis; it is a pre-requisite for any investment. We also have targets to increase the share of eco-premium products every year."

Finally, MP pointed out that AkzoNobel has a long term perspective on safety and sustainability:

> "It is a matter of minimising the risk and maximising the business potential, create more value from fewer resources."

Björn Johansson (BJ):

> "A key point from our customers is that our products are safe. // Not possibly safe, not probably safe, but safe."

BJ described the problems that arise for IKEA in relation to the product chain – from the producer of a nanomaterial to the finished IKEA product.

> "The further we go to the right [in an illustration of the product chain from the finished product toward the producer of the nanomaterial], the more and more it becomes sort of a black box, less and less information about what is going on."

BJ pointed out that not only product safety but safety issues during production and environmental safety are important issues for IKEA.

> "We have 10 000 products, we have 1 000 suppliers in fifty countries, so this is not just a Swedish issue for us. We have to make sure that it is okay depending on where we do the production."

> "We try to have responsibility for the whole [product] chain. // We have a really good communication with our suppliers and our sub-suppliers, for instance coating-manufacturers // but then further down it is sort of becoming a black box, we don't know what is inside what, what type of materials we need to take action on. Because you are talking about implementation of regulation ten years from now, maybe, but from IKEA's side, if we see something that is a concern for our customers, that is a serious concern during production, we can take action much faster and work pro-actively, which we try to do. Given the right tools, and that is what I am looking for here // then we can take our own action."

Thus, the hurdles for IKEA are about obtaining the safety information from suppliers further down the product chain. IKEA has to make a risk assessment for each new material. In the worst case scenario concerning a nanomaterial, the suppliers are not prepared for the questions and the information given often does not help in doing the risk assessment. Either there is no information down the product chain or the information is not shared. Hence, the product cannot be sold because IKEA is responsible for the safety of the product.

"If we find something that is 'out of the box interesting', we can launch our own investigation into the type of material."

Question 3, to Monica Tammela. What has happened within the regulation on nanomaterials in cosmetics since it was adopted?

Monica Tammela (MT):

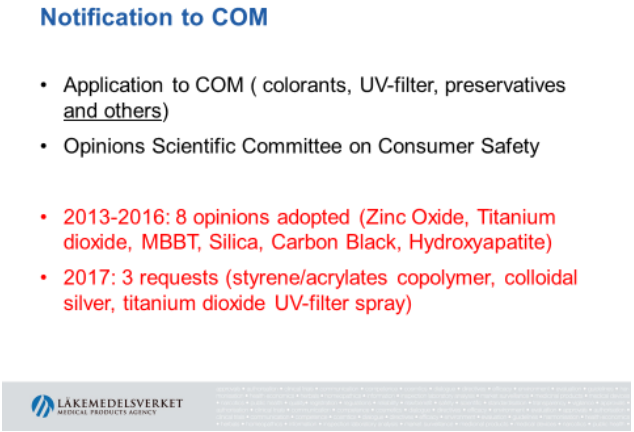
"[The regulation] was adopted already in 2009, so we have had some time to 'learn by doing'."

"The definition used in cosmetics is not the full recommendation. You have to note that it is only for insoluble or biopersistent material and it should be intentionally manufactured. So there is no requirements on liposomes // or other nanomaterials that dissolve when they come in contact with the body."

The products concerned include sun screens, colours and some other materials, for example silica. Every manufacturer has to make an application to the Commission six months before marketing a product containing nanomaterials. If the Commission has concerns about the safety of a material, it should ask for an opinion of the Scientific Committee on Consumer Safety that in turn should conclude on the safe use of the material in cosmetics.

"From 2013 to 2016, there has been eight opinions adopted."

Several opinions have also been revised. In 2017, there are three requests of opinions for other nanomaterials. For more information, see figure to the right.



In addition, the Scientific Committee on Consumer Safety in 2015 revised the notes of guidance for the testing of cosmetic substances and their safety evaluation, adding more guidance on nanomaterials. Previously, the Committee also has produced a number of other guidance documents.

"Most questions I think has been regarding the characterisation of the material, both characterisation of the material used in the products but also the characterisation of the materials used in the old toxicity testing."

MT pointed out that one advantage with cosmetics is that the products have to be labelled with '(nano)' and the labelling is rather well complied with, according to a market surveillance. Every company also has to indicate if there is nanomaterial in their product. But as discussed earlier by David Azoulay, many substances were wrongly indicated as nanomaterials.

> "We hope that this is now corrected."

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On NANoREG, MT commented:

> "I hope that the NANoREG tool box can help both companies to collect the necessary data and the scientific committee and authorities to evaluate the information sent to the commission".

Comments on the balance of innovation and regulation:

Michael Persson:

> "I don't see a big conflict regarding IP but during the patenting phase in most cases, when it is confidential, then it can be an issue, but that is a matter of 18 months I think. After 18 months the patent application will become public."

Björn Johansson:

> "From the outside, it is a complex situation. We cannot compromise with our customers. We work case by case and if we see the good will of the company, that they will proceed and try to get the [safety] information out there, we will continue with them. // We want to find the 'good' suppliers."

BJ also said that IKEA challenge their suppliers with requirements and that many companies manage that. He pointed out that with nanomaterials, there should be some challenges given to the industry and also confidence in the industry solving the challenges.

> "One of the reasons we want regulations and set up requirements is to be able to use nanomaterials."

IKEA would like to know which nanomaterials the company can safely use. To test what is in the materials, IKEA use external consultants and laboratories.

II. Needs, Challenges and Suggestions for the Future

Thomas Backhaus (University of Gothenburg), Åke Bergman (Swetox), Bengt Fadeel (Karolinska Institutet), Roland Grafström (Karolinska Institutet), Åsalie Hartmanis (SwedNanoTech), Eva Hellsten (Senior Advisor, Swetox), Therese Jacobsson (Swedish Society for Nature Conservation), Björn Johansson (IKEA), Gregory Moore (Swedish Chemicals Agency), Michael Persson (AkzoNobel), Monica Tammela (Medical Products Agency, Sweden), Tom van Teunenbroek (Ministry of Infrastructure and Environment, the Netherlands)

Eva Krutmeijer, Åke Bergman, Bengt Fadeel, Björn Johansson, Åsalie Hartmanis, Gregory Moore, Michael Persson, Monica Tammela, Therese Jacobsson, Tom van Teunenbroek and Roland Grafström.

In this section, statements made, issues raised and suggestions for the future voiced during the second panel discussion are summarized in bullet points. Each bullet point refers to a point made from the individuals that took part in the discussion and illustrates current aspects on and challenges within the field of nanosafety.

Statements

- It is not the role of academia to do routine safety assessments of products for the industry, independent on where you are on the value chain. Industry needs to be pro-active in getting the safety information.
- The lack of safety assessments shows the lack of legislation in this area, because the idea with REACH is to provide safety data sheets.
- Those placing a product on the market should be aware that they are responsible for providing safety information about the product.
- It should be in the interest of companies to prove that the products or processes are safe.
- The Swedish National Platform for Nanosafety is now in place to provide a forum for communication and exchange of knowledge between different stakeholders.

The largest environmental NGO in Sweden, the Swedish Society for Nature Conservation (Naturskyddsföreningen), stressed the mandate there is from their organisation to demand regulations that safeguard health and the environment and that it is important to make sure that the public has confidence in the regulatory process.

Issues raised

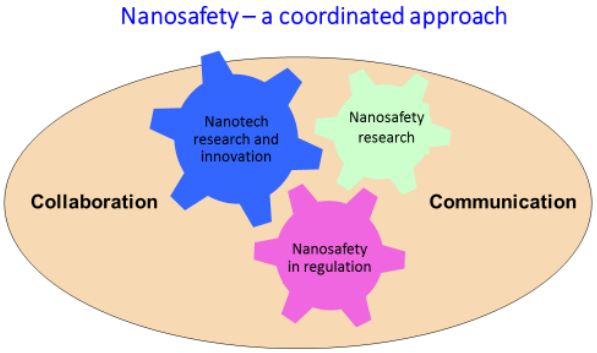
- There is a growing frustration that the different regulatory processes are taking so long.
- There are no answers from the European Commission on why the regulatory processes are taking so long.
- It is important to be aware that the EU is not a thing in Brussels, it is *us – we* in the member states have to do something.
- There is an urgency to move in order to keep public trust in the abilities of authorities and politicians to safeguard public health and the environment.
- Where do we get transparent, independent and publically communicable safety assessments? Who is producing them and how do we make them available?
- Regarding the concept of safe by design, it is an issue that large companies may not consider the toxicity of new materials until they are going to market them. Then the companies may limit toxicity assessments to the regulatory requirements. Thus, there is no interest in safety considerations early in the development of materials.

Suggestions for the future

- SweNanoSafe could arrange a workshop with all actors, including manufacturers and authorities, involving representatives from governments that are responsible for research, industry and the environment in the EU. The result of such a workshop could contribute to EU policy making in this area.
- It would be a step forward if the funding agencies put demands on risk assessment, safe by design etc. as a prerequisite for funding.
- Increase data sharing as much as possible, not only from scientists but also from companies.
- It is important also to publish no-effect data. Create an online publishing site for no-effect data.
- The industry could take initiative to create a certificate-type of system to ensure product safety. This could complement formal regulation that is not yet in place.
- Create a system for classifying nanomaterials and nanotechnologies according to the current knowledge: a 'green basket' for safe to use, a 'red basket' for materials with large safety issues and a 'grey basket' for the materials in between.
- One could try to use the innovation system to deliver products that go beyond any possible regulation.
- We should use the advantage of being a small country and work together, creating a 'pilot platform' for innovation in nanomaterials.
- Could the way ChemSec works with small and medium-sized companies be a useful approach to promote nanosafety?
- First, the way forward is to understand the mode of action of nanomaterials. However, there is a need for more QSAR studies of high quality in order to elucidate the mode of action. Secondly, there is a need to elucidate ways to speed up risk assessment with novel techniques.
- To get the mode of action will take 'forever' – we also have to use other levels of experimental work that gives us certainty to an extent that we can take action.
- Don't go forward in generating new or novel projects without involving modellers in what type of experimental data that needs to be generated.
- Start using the precautionary principle to actually start regulating.

Reflections on the conference from a policy perspective

Eva Hellsten, Senior advisor SweNanoSafe, Swetox



Eva Hellsten began by stating that it had been extremely interesting to learn about all the scientific progress made.

> "On the other hand, we have also heard the need for more knowledge and the lack of progress in regulation, I would say, with a few exceptions. The question I am asking is how well progress meets the needs?"

In chemicals policy, Eva Hellsten pointed out, decisions are always taken under a certain amount of scientific uncertainty, but are we still too far off with the nanomaterials? Although there had been no clear answer to this question during the day, Eva Hellsten said that the conference had given an idea of where we stand today and shown important contributions to close the knowledge gaps.

> "I congratulate NANoREG for bringing together this huge and challenging project."

She also said that the project has provided a logical and structured approach to the risk assessment of nanomaterials in a regulatory context and that she was eager to see how the finalisation of the project together with the white paper will impact both policy making and risk assessments.

A broader policy perspective

Eva Hellsten said that:

> "Nanosafety became a policy issue in EU around 2005 and it was exactly at the time when REACH was in its final negotiation and up for adoption. It was unfortunate that the timing was so bad that it was not possible at all to take any consideration to nanomaterials."

Instead, the Commission produced an action plan (Nanotechnology Action Plan 2005-2010) with the aim to support the long term safe and sustainable development of nanotechnology by integrating nanotechnology R&D (Research and Development), nanosafety research and regulatory activities.

> "The action plan allowed for putting aside a budget in the framework programmes to follow through".

The Nanosafety Cluster was formed to improve coordination and communication among researchers. There was also an inter-service Commission group working together on nanotechnology that included DGs research, industry, environment, consumer health and worker protection. Similar groups were also set up in several member states. In parallel, the OECD WPMN was initiated with focus to review regulatory test guidelines regarding nanomaterials.

Eva Hellsten further stated that from a regulatory and policy perspective, there has been two major scientific achievements that she wanted to highlight. These had been addressed during the conference, mainly in NANoREG but also in the other projects. One was the understanding of the specific needs to use well characterised nanomaterials for testing purposes and well defined testing conditions. Previously, nanomaterials testing results on different types of hazards could often be unreliable and were often disputed.

> "The other scientific achievement that I find extremely important is perhaps an opening to move away from the traditional paradigm for risk assessment to work on a 'case by case' basis. As Tom and others have pointed out, for nanomaterials the process would be too costly and too slow. So it was highly interesting to hear about newer and modern efficient test methods like high throughput, QSAR, read across and several other possibilities that we have heard of today. Such scientific developments should be essential for legislation."

On the regulatory side, Eva Hellsten concluded that there is frustration when it comes to REACH and to activities at the EU political level. In the EU Regulatory Reviews (2008 and 2012) the Commission stated that "modifications may be required".

> "We can only hope that something will be done with the REACH annexes to move things ahead, as Gregory Moore also mentioned, perhaps summer this year".

Eva Hellsten pointed out that the slowness in legislation is not new. However, it is worrying when it comes to REACH because REACH is the key legislation that enables us to request information on hazards and risks from the manufacturers and importers.

> "Looking at the past, although it was known that asbestos can cause mesothelioma and this was scientifically proven in 1976, it took some additional 25 years to get a complete ban of asbestos fibres, at enormous suffering and costs".

Eva Hellsten said that this should not be taken as an excuse for the current slowness. However, she emphasised, we must be aware that nanomaterials are more complex from a scientific perspective than other chemicals.

> "We need to see a safe and sustainable future for nanotechnology as it can bring many good things to both us humans and the environment. With nanomaterials, we have a golden opportunity today, as nanotechnology mainly lies ahead of us. If we, as many have stressed today, work together and integrate safety early in the innovation process and investigate critical issues about safety, I am sure that we will be able to meet high health and environment standards at reasonable costs."

Eva Hellsten also highlighted the perspective put forward by NGO's that policy makers cannot afford not to do anything.

Finally, she concluded, that to support this we need collaborations within and between groups of stakeholders and this is the purpose of the Swedish National Nanosafety Platform.

> "I hope we can join forces and really push things ahead. We have heard many excellent ideas today."

Closing of the conference

Åke Bergman, Head of Swetox and Chair SweNanoSafe Steering Committee

Åke Bergman highlighted the function of the Swedish National Platform for Nanosafety, including the Cooperation Council and the Expert Panel. To ensure a continuous communication and knowledge exchange on nanosafety issues, the next step for the Cooperation Council is to recruit representatives from the area of industry and businesses, from academia (on a strategic level) and NGO's. He stressed that in promoting the discussion on nanosafety, several of us may have to leave the comfort zone and importantly, ask basic questions if we are not familiar with a certain terminology. This type of questions may help clarify issues for many others.

In addition, Åke Bergman stated that SweNanoSafe's Expert Panel is established and that he is very much looking forward to the continuation of the work within the platform. Several of the panel members participated in the conference.

He further asked the audience to remember and reflect on the question of identifying hurdles to a safe use and handling of nanomaterials. He stressed the importance of data sharing and to promote proactivity, which in turn he believes will promote innovation.

> "In my view, it is absolutely wrong that there should be confidential information on safety within the industry, while we are publishing and reviewing the publications that we are contributing with on the academic side."

Åke Bergman also emphasized the need for collaboration and cooperation, not least to prevent the spreading of misinformation.

Finally, he expressed his gratitude to the organisers of the conference, to the speakers for their excellent contributions and to the audience for taking part in the event.

Annex I. List of participants

First name	Last name	Organisation
Ernesto	Alfaro-Moreno	Swetox Södertälje
Rickard	Arvidsson	Chalmers University of Technology (SweNanoSafe Expert Panel)
David	Azoulay	CIEL - Center for International Environmental Law
Thomas	Backhaus	University of Gothenburg
Josefin	Backman	Swedish Medical Products Agency
Marie	Beckman	SweNanoSafe - Swetox Södertälje
Kim	Berglund	Svenska Målareförbundet
Åke	Bergman	Swetox Södertälje
Anna	Billme	Scania CV AB
Åsa	Boholm	Gothenburg University
Gustaf	Bäck	Swedish Work Environment Authority
Ulrika	Carlander	SweNanoSafe – Swetox Södertälje
Cecilia	Clemedson	AdvocoTox AB
Ian	Cotgreave	Swetox Södertäle
Susana	Cristobal	Linköping University
Hugues	Crutzen	European Commission - Joint Research Centre
Elina	Drakvik	SweNanoSafe - Swetox Södertälje
Willem	Duis	IVL Svenska Miljöinstitutet
Karine	Elihn	Stockholms universitet, ACES
Anne	Engardt	ScaniaCV
Caroline	Enmyren	Stora Enso
Bengt	Fadeel	Karolinska Institutet (SweNanoSafe Expert Panel)
Anna	Furberg	Chalmers University of Technology
Jonas	Förare	Swetox Södertälje
Aidin	Geranmayeh	Sweco Environment AB
Anda	Gliga	Karolinska Institutet
Roland	Grafström	Karolinska Institutet
Åsa	Gustafsson	Swetox Södertälje/FOI
Tomas	Gärdström	Swedish Ministry of Enterprise and Innovation
Mats	Hagwall	Henkel Norden AB
Ulf	Haraldsson	SIS, Swedish Standards Institute
Åsalie	Hartmanis	SwedNanoTech
Lena	Hellmér	Swedish Chemicals Agency

First name	Last name	Organisation
Heike	Hellmold	SweNanoSafe - Swetox Södertälje
Eva	Hellsten	SweNanoSafe - Swetox Södertälje
Carina	Hemstrand	H&M
Linda	Hussami	KTH Royal Institute of Technology
Therese	Jacobson	Swedish Society for Nature Conservation (Naturskyddsföreningen)
Gunnar	Johanson	IMM, Karolinska Institutet
Björn	Johansson	IKEA of Sweden
Emma	Johansson	Processum
Boel	Jönsson	Kemivärlden Biotech Kemisk Tidskrift
Eva	Klasson Wehler	Stockholm University
Pekka	Kohonen	Karolinska Institutet
Janna	Kokko	Statens medicinsk-etiska råd, Smer
Eva	Krutmeijer	EKKO AB
Monica	Kåredal	Arbets- och miljömedicin Syd
Ekatherine	Lagovardos	SweNanoSafe - Swetox Södertälje
Simon	Larsson	University of Gothenburg, GRI
Carolina	Lavén	Stora Enso
Ewa	Lie	RISE
Monica	Lindh de Montoya	Gothenburg Research Center (GRI)
Maria	Lindqvist	Karolinska Institutet
Cecilia	Mattsson	Swedish Environmental Protection Agency
Olga	Matzén	H&M HENNES&MAURITZ GBC AB
Klara	Midander	Karolinska Institutet
Sverker	Molander	Chalmers University of Technology
Gregory	Moore	Swedish Chemicals Agency (SweNanoSafe Expert Panel)
Ann Britt	Nilseng	BillerudKorsnäs
Annika	Nilsson	Lund University, Faculty of Law
Maj-Inger	Nilsson	MINEK Consultancy
Penny	Nymark	Karolinska Institutet
Lena	Palmberg	Karolinska Institutet
Michael	Persson	Akzo Nobel PPC
Tuija	Pihlström	National Food Agency in Sweden
Michael	Reineskog	IKEM
Déborah	Rupert	Biolin Scientific AB
Axel	Rydevik	National Food Agency in Sweden

First name	Last name	Organisation
Anne	Samuelsson	IVL-Svenska Miljöinstitutet AB
Anabela	Stan	Labmedicin Arbets- och Miljömedicin Syd
Anna	Stattin	Swedish Board for Accreditation and Conformity Assessment
Joachim	Sturve	University of Gothenburg (SweNanoSafe Expert Panel)
Jouni	Surakka	Swedish Work Environment Authority
Karin	Svens	TKT - Toxicology Knowledge Team
Kettil	Svensson	National Food Agency in Sweden
Monica	Tammela	Swedish Medical Products Agency
Muhammet	Toprak	KTH Royal Institute of Technology
Fredrik	Waern	AstraZeneca
Tom	van Teunenbroek	Ministry of Infrastructure and the Environment, the Netherlands
Jane	Wigren	SundaHus
Jon	Wingborg	SIO Grafen
Carmen	Vogt	KTH Royal Institute of Technology
Walter	Zobl	Swetox Södertälje
Eva	Ålander	RISE Bioeconomy