Tour de table

15th meeting of the ECHA Nanomaterials Expert Group (ECHA-NMEG-15)
3 May 2022, Helsinki, Finland (remote meeting)

The representatives from the Member States, the Commission, the accredited stakeholder organisations from industry and NGOs, and ECHA are encouraged to summarize **briefly** below any **highlights/progresses** since the previous meeting in areas relevant for the work of the NMEG. The aim is to share information within the NMEG, and possibly identify **topics for future discussions**. NB: only non-confidential information should be shared.

1. Registration & IUCLID reporting

ECHA
By 8 April 2022, 600 registration dossiers covering nanomaterials were successfully submitted, resulting in a total of 149 substances covering nanoforms for which registration dossiers have been submitted following the updated REACH requirements.

2. Substance identity and characterisation of nanoforms (Annex VI)

ECHA
The **nanomaterials nomenclature** draft document (discussed at the previous meeting NMEG-14), along with the relevant examples, has been finalised. The draft will be shared with NMEG members before the NMEG-15 and members are invited to provide comments by **31 May 2022**.

ECHA has been in contact with several registrants to support and advise them on correct reporting of nanoforms. This concerns especially incorrect reporting of set of nanoforms as single nanoform.

3. Phys-chem characterisation of nanomaterials (Annex VII)

ECHA
ECHA has included in the updated Appendix R7-1 for nanoforms applicable to Chapter R7a Endpoint specific guidance recommendations for the determination of Dustiness (new information requirements for nanoforms).

4. Hazard evaluation – human health

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5. Hazard evaluation – environment

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6. Read-across and grouping for nanomaterials

ECHA
The OECD Working Party on Hazard Assessment is working on an update of the Guidance on Grouping of Chemicals, Series on Testing & Assessment No. 194, ENV/JM/MONO(2014)4.
Under the OECD WPMN an SGTA Ad hoc group has been set up for contributing an updated chapter 6.9 to this OECD Guidance (in the current version: “Initial considerations applicable to manufactured nanomaterials”).

A first draft version was circulated by the drafting team in March 2022 for commenting.

MSCA-NL
In September 2021 the European GRACIOUS project (www.h2020gracious.eu) has ended. The project has developed a highly innovative science-based framework that supports the assessment of risk posed by the ever-increasing array of nanomaterials on the market and under development. The framework streamlines the process for assessing their risk by logically grouping nanomaterials thereby allowing extrapolation between (read-across) nanomaterials and reducing the need to assess exposure to and toxicity on a case-by-case basis. To facilitate the use of the Framework, an extensive guidance document (https://doi.org/10.5281/zenodo.5534466) was published, together with a guidance in a nutshell (https://doi.org/10.5281/zenodo.5534105) that provides a brief introduction. Further details on the different aspects of the framework are published in scientific literature (www.h2020gracious.eu/library/publications). Output from the project forms an important foundation in the currently ongoing update of the section on nanomaterials in the OECD Guidance on Grouping.

7. Exposure assessment (e.g. exposure measurement, exposure mitigation)

MSCA-NL
Initiated by RIVM, an international team of experts in the field of occupational risk assessment for nanomaterials explored the possibilities to derive health-based nano reference values (HNRVs) for the workplace. Discussions involved experts from the Netherlands (RIVM and University of Amsterdam), Denmark (NRCWE), Spain (LEITAT), United Kingdom (HSE), USA (NIOSH), and Switzerland (SCOEH). In addition, written feedback was provided by experts from UK (HSE), USA (NIOSH), Spain (INSHT), Switzerland (SUVA), Germany (BAuA and DGUV/IFA), Norway (NLIA) and Belgium (VITO). The discussion sessions resulted in a proposal for categorization of nanomaterials in six categories: (1) WHO-fibre-like high-aspect ratio nanomaterials (HARNs), (2) other non-spheroidal nanomaterials, (3) readily soluble spheroidal nanomaterials, (4) biopersistent spheroidal nanomaterials with unknown toxicity and (5) biopersistent spheroidal nanomaterials with and (6) without substance specific toxicity. Details on the categorisation and recommendations for deriving HNRVs are described in an open access scientific paper (https://doi.org/10.1016/j.impact.2022.100396).

8. Risk assessment

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9. Guidance or good practice documents for registrants and stakeholders

ECHA
Two updated guidance documents were published recently:
- The **registration** guidance ('Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification', version 2.0) was published in January 2022 (https://echa.europa.eu/documents/10162/17250/how_to_register_nano_en.pdf/f8c046ec-f60b-4349-492b-e915fd9e3ca0?t=1643716680095).
- The **human health** guidances (IR&CSA Appendix R7-1 for nanoforms applicable to Chapter R7a and R7c Endpoint specific guidances, Version 3.0) were published in October 2021 (https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment).

Regarding the Guidance appendices R7 a, b and c under revisions for **Physico-chemical** and **Environment** endpoints for nanomaterials, the update process started in May 2021. R7a appendix is updated on PC and ENV endpoints, including granulometry, solubility, dissolution rate in water and environmental media, n-octanol/water partition coefficient and adsorption/desorption. A new section was added on Dustiness as this is a new nano-specific standard information requirement. Both R7b and R7c appendices are also under update. The PEG consultation for R7a was held 22 and 23 March 2022, and PEG cross check and Committees consultation is planned in May and June. R7b and R7c appendicesx are is foreseen to be revised and sent for consultation by end of 2022 (drafts will be available on ECHA website at that stage).

MSCA-NL
The OECD WNT project "Development of new Test Guideline on toxicokinetics to accommodate testing of nanoparticles" is led by the Netherlands (RIVM) and co-led by the UK (PHE). Korea and Australia are contributing by providing studies, and the EU contributes via accommodating work in the H2020 project NanoHarmony (https://www.nanoharmony.eu/). The OECD project aims to develop a new TG on in vivo toxicokinetic testing of nanoparticles following the inhalation and oral route. The current OECD TG 417 on toxicokinetics was identified as not applicable to nanomaterials. A literature overview was compiled for the model substances titanium dioxide, cerium dioxide, and silicon dioxide. This overview identified some knowledge gaps for the appropriate design of a toxicokinetics study. These can partly be addressed with recently finalised study from EU projects (e.g. PATROLS, https://www.patrols-h2020.eu/), and some limited experimental work in NanoHarmony. An important starting point in the development of the new test guideline is the dissolution rate of nanomaterials that may help to estimate the necessary test duration to enable monitoring the distribution of a nanomaterial inside an organism. Test development for dissolution rate is ongoing in OECD and supported by EU projects Gov4Nano (http://www.gov4nano.eu/) and NanoHarmony. Another important issue in toxicokinetics is the ability to measure nanomaterial inside an organism without (large) interference from tissues or other substances. UK is developing an OECD Guidance Document, also supported by the NanoHarmony project. Within NanoHarmony close collaborations between the different projects are optimised to ensure exchange of information and optimal use of each other's expertise.

10. Relevant new research projects or strategies on nanomaterials

MSCA-BE
A report on the nanomaterials put on the Belgian market is published every year on the website of our registry (https://www.health.belgium.be/en/environment/chemical-substances/nanomaterials/register). At the moment, annual reports from 2016 to 2020 are available. The annual report on 2021 data will be available within a few weeks.

BE CA is continuously working on the improvement of our nanoregistry. Belgium mandated an external study on the functioning of the nanoregistry database and its compliance with the objectives described in the Royal Decree of the 27 May 2014 on the put of the Belgian market of nanomaterials. We are going through the results at the moment and will take the necessary measures to ensure an improvement of the quality of the registered data.
Register | FPS Public Health (belgium.be)

FPS Economy – National Standards – Nanometrology laboratory

The Belgian National Metrology Institute SMD of the FPS Economy has a laboratory dedicated to nanometrology. The laboratory is active on the development and validation of instruments for the metrological characterization of nanomaterials.

Research projects:
The nanometrology laboratory has participated in 2 projects of the European Metrology Programme for Innovation and Research (EMPIR):
- nPSize (2018-2021): Improved traceability chain of nanoparticle size measurements. This project aimed to develop methods, reference materials and modelling to improve the traceability chain, comparability, and compatibility of nanoparticle size measurements.
- EMUE (2018-2021): Examples of Measurement Uncertainty Evaluation. This project aimed to provide a comprehensive set of worked examples illustrating how the principles of measurement uncertainty can support and give added value to normative and related practices. In particular the goal of SMD was to provide metrological traceability for nanoscale measurements and support instrument' users with comprehensive guidance on uncertainty estimation.
Publication of a compendium of examples: Good Practice in evaluating measurement uncertainty
http://empir.npl.co.uk/emue/wp-content/uploads/sites/49/2021/07/Compendium_M36.pdf

The laboratory participates in 2 new EMPIR Projects:
- POLight (2021-2024): Pushing boundaries of nano-dimensional metrology by light. The goal of SMD in this project is to evaluate the uncertainties related to size distribution measurement of nanoparticles using FFF-MALS to improve the comparability with other methods.
- PlasticTrace (will start in 2022): Metrological traceability of measurement data from nano to small-microplastics for a greener environment and food safety. SMD will contribute to the preparation and characterisation of nanoplastic samples using Atomic Force Microscopy and Field Flow Fractionation – Multi-Angle Light Scattering techniques.

Publications:
- Petry, J., De Boeck, B., Sebaihi, N., Coenegrachts, M., Caebergs, T., & Dobre, M. (2021). Uncertainty evaluation in Atomic Force Microscopy measurement of nanoparticles based on statistical mixed model in a Bayesian framework. Measurement Science and Technology. https://doi.org/10.1088/1361-6501/abe47f
- Alasonati, E., Caebergs, T., Pétry, J., Sebaïhi, N., Fisicaro, P., & Feltin, N. (2021). Size measurement of silica nanoparticles by Asymmetric Flow Field-Flow Fractionation coupled to Multi-Angle Light Scattering: A comparison exercise between two metrological institutes. Journal of Chromatography A, 1638, 461859. https://doi.org/10.1016/j.chroma.2020.461859

Normalization:
The laboratory is active as expert in ISO/TC229 – CEN/TC352 Nanotechnologies and ISO/TC201 Surface chemical analysis. The laboratory is involved in several WG dedicated to the labelling of manufactured nano-objects and the determination of aggregation/agglomeration state of nano-objects.

The laboratory also participates to Versailles Project on Advanced Materials and Standards (VAMAS) pre-normalization studies:

- VAMAS/TWA2 Surface chemical analysis: round robin test for guidelines for shape and size analysis of nanoparticles by atomic force microscopy.
VAMAS/TWA34 Nanoparticle Populations: Measurement of particle size, shape distribution and relative number concentration of titania and silica nanoparticles

VITO:

1. Project for Department Omgeving regarding Optimization of Animal Free Methods for Inhalation Toxicology.
Within this project we are performing three case studies with three different compounds: Nano TiO2, nano/microplastics and a pharmaceutical compound.
With these results we will generate data, reports and papers which will be demo-cases to convince stakeholders to use alternative *in-vitro* test methods for inhalation toxicology to reduce the number of test-animals.
We used the dry powder generator PreciseInhale to expose A549 cells to nano TiO2 in two different Air Liquid Interface Aerosol Exposure Platforms (Vitrocell 6/4 and Navetta).
Biological readouts: cell viability, cytotoxicity, protein secretion of inflammatory markers, gene expression of oxidative markers, detection of potential innate immune responses.
For the nano/microplastics case we use the CLOUD 12 (Vitrocell) Air Liquid Interface Aerosol Exposure Platform and commercially available plastic particles (e.g. (non)functionalized polystyrene particles of different sizes) and determine cytotoxicity.

2. Ag-Mask project in collaboration with Sciensano
With Sciensano we are currently working on the Ag-mask project. The AgMask project evaluates the types, efficiency and potential health risks of silver-based biocides that gives antimicrobial properties to face masks. Also nano-TiO2 is included in this study. VITO is responsible for performing breathing simulation tests on masks, particle sampling of inhaled air and chemical analysis of samples.
Please find a link to the project below:
https://www.sciensano.be/en/projects/evaluation-types-efficient-use-and-health-risks-application-silver-based-biocides-provide
Sciensano is coordinating the project so I think Jan or Eveline will give some more input.

3. VITO is also participating as a partner in the H2020 CARMOF project https://carmof.eu/.
Within the project VITO's HEALTH department is responsible for the nanosafety evaluation and regulatory requirements in the industrial production lines.
International legislation and regulatory recommendations on the manufacture of the nanoparticle containing products will be reviewed to identify trading barriers in different geographical regions based on the health impact (e.g. product labelling or a ban on the manufacture or use). Exposure scenarios were developed to determine safety of workers and the environment. Nano aerosol exposure assessment was performed in occupational settings where a nano-aerosol inhalation risk was present. Also eye and skin irritation/corrosion testing of CARMOF test items was performed at VITO.

11. Experience from stakeholder or public dialogues

MSCA-NL
The European Gov4Nano project organised a second Trans-Regulatory Risk Analysis Summit (RRAS) on 24-26th of January 2022. The online meeting aimed to raise awareness for (new) challenges for risk analysis of nanomaterials posed by the goals and ambitions of the Green Deal (GD) and underlying relevant

strategies from a trans-regulatory perspective. Emphasis lay on the potential impact of the Chemical Strategy for Sustainability (CSS). Moreover, specific topics from the CSS, e.g. one substance, one assessment, and new toxicological endpoints to be addressed (like endocrine disruption) were discussed. Major outcomes include the continuous need for (1) a structural way of trans-regulatory sharing of lessons (including those learned in the nanosafety community), knowledge and information to address the goals and ambitions of the CSS, (2) prioritisations in the 87 actions of the CSS and frequent updates of regulatory and research roadmaps for nanomaterials, and (3) promotion of harmonization to enable risk (and sustainability) governance to deal with the ambitious policy goals and dynamic character of a transition, in which sharing state-of-the art information is critical. A report of the RRAS will be published at the Gov4Nano website (www.gov4nano.eu; June 2022).

MSCA-DE
From December 2019 until June 2020, UBA executed a series of thematic conferences to initiate international stakeholder exchange on challenges of advanced materials for chemical safety and sustainability. At the conferences the heterogeneity of the field, approaches to cluster the broad field but also proposals to priorities advanced materials based on concerns regarding safety, insufficient regulation or impacts for sustainability were discussed. Examples of advanced materials were presented which were already identified to pose challenges to current risk assessment tools, chemical regulations or might hamper circular economy of products. In the final conferences, considerations and options for actions on advanced materials were discussed from different stakeholder perspectives.
The final report describing the execution and outcomes of the thematic conference is now available at: https://www.umweltbundesamt.de/en/publikationen/thematic-conferences-advanced-materials

12. Any other scientific and technical issue

MSCA-NL
In collaboration with BfR, BAuA and UBA RIVM developed a novel 'Early WArning, pRioritisation and actioN system' (EWARN) to systematically identify emerging safety and sustainability issues of advanced nanomaterials. This system can be applied by regulators, risk assessors, as well as innovators. Details of how this system works are described in a brochure (https://doi.org/10.21945/brochure-advanced-materials). The system aims to provide an anticipatory risk governance approach and to proactively avoid the occurrence of potential unexpected risks of advanced (nano)materials. Addressing safety and sustainability issues early in the innovation chain can support innovation by preventing problems later on. The brochure of the proposed EWARN system can be regarded as a thought starter. The main purpose of this brochure is to receive input on the structure and content of the proposed EWARN system for advanced nanomaterials. The input and feedback will be used to further improve the EWARN system in the coming year, facilitate discussions at an EU-level, and to bring the system to the OECD WPMN Steering Group on advanced (nano)materials.

In January 2021 the new EU project SUNSHINE (https://www.h2020sunshine.eu/) has started. SUNSHINE is the acronym for Safe and sUstainable by desigN Strategies for HIgh performance multi-component NanomatErials. The main goal of this project is to develop and implement Safe & Sustainable by Design (S&SbD) strategies for products enabled by multi-component (advanced) nanomaterials (MCNM), including high aspect-ratio nanomaterials (HARNs). Currently, work on the operationalisation of safe-and-

sustainable-by-design (SSbD) for multi-component materials (MCNMs) is ongoing. An industry user committee was set-up consisting of experts in human and environmental toxicology, material scientists, safe-by-design, sustainability and regulatory. This user committee supports the five case studies in the operationalisation of SSbD. A methodology on how to integrate safety and sustainability throughout the innovation process is now being developed and tested in the case studies. RIVM is coordinating the work package on regulatory preparedness that performed an analysis on how to define multicomponent nanomaterials from a regulatory (REACH only) viewpoint. An overview was also made of the different types of MCNMs and a matrix was developed with the different characteristics of MCNMs. RIVM is also involved in adapting grouping and read-across approaches to multi-component nanomaterials. Properties related to the new or enhanced functionality of multi-component nanomaterials are considered for their potential impact on risk and how this information can be used in risk assessment and grouping and read-across approaches.

MSCA-DE

The German higher federal authorities Federal Institute for Occupational Safety and Health (BAuA), the German Federal Institute for Risk Assessment (BfR) and the German Environment Agency (UBA) have issued a joint paper with recommendations for the responsible use and appropriate governance of advanced materials.

This includes, among other things, an early warning system to identify materials that give cause for concern. The authorities also see the need to review and, if necessary, to adapt existing laws, regulations and assessment methods in a timely manner. Only in this way can the legal framework keep pace with technical innovation.

This joint perspective also takes up the on current discussions about concepts for safe and sustainable design ("Safe and Sustainable by Design") of chemical substances, materials and products. In doing so, it offers recommendations regarding what needs to be considered in order to apply these concepts to advanced materials.

In view of the interdisciplinary nature of the subject and the diversity of the interest groups concerned, the paper emphasises the importance of establishing dialogue mechanisms. In addition, future research needs are also determined. In particular, preliminary research should be intensified in order to support safe and sustainable early-stage development of material innovations. Research accompanying regulation is also required, examining the need for specific regulatory measures and developing adapted test and assessment methods.

The paper, which summarises current activities, considerations and recommendations of BAuA, BfR and UBA, is intended to serve as a basis for discussion at national, European and OECD level. It picks up the discussions that were held in a series of three international thematic conferences organised by the UBA on advanced materials and their challenges.

It can be found at the webpage of UBA: https://www.umweltbundesamt.de/en/publikationen/risk-governance-of-advanced-materials

13. Classification and labelling

ECHA

MWC(N)T (SID description of the substance: Multi-Walled Carbon Tubes (synthetic graphite in tubular shape) with a geometric tube diameter range ≥ 30 nm to < 3 µm and a length ≥ 5 µm and aspect ratio > 3:1, including Multi-Walled Carbon Nanotubes; MWC(N)T) by DE for STOT RE 1 and Carc 1B; H350i, was subjected to Consultation from 5 July to 3 September, 2021. Following discussion in the RAC CLH WG in January 2022 in their opinion adopted at the RAC plenary in March 2022 RAC concluded that MWC(N)T should be classified as STOT RE 1

(lungs) (inhalation), with specific concentration limits of C > 1 % for STOT RE 1 and 0.1% < C < 1 % for STOT RE 2, and Carc 1B; H350i. The CLH opinion, proposal and comments received during the Consultation of the CLH report can be accessed from MWC(N)T.

The CLH proposal for Silver (EC / List no: 231-131-3 CAS no: 7440-22-4) submitted by SE included data was subjected to Consultation from 19 October to 18 December 2020. A further targeted consultation of documents relevant to selected endpoints ended in July 2021. The proposal was for silver, including nanosilver to be classified as Skin Sens 1, Muta 2 and Repr 1B; H360FD, aquatic acute 1 and aquatic chronic 1. It was further proposed that the aquatic classifications for bulk silver would be accompanied by M-factors of 10 for both aquatic acute and chronic classifications and that nanosilver be accompanied by M=1000 for aquatic acute and M=100 for the aquatic chronic classifications. The proposals were discussed in the RAC plenary in November 2021 and March 2022 as well as in the RAC CLH WG meetings in January and April 2022. It is anticipated that the opinion will be adopted at the RAC plenary in June 2022. The CLH opinion, proposal and comments received during the Consultation of the CLH report can be accessed from Silver.

MSCA-SE
Silver: Sweden proposed, amongst other, Skin Sens. 1, Muta. 2 and Repr. 1B H360FD classification for elemental silver including nanoforms. Discussion are ongoing at RAC.

14. EUON

ECHA
The following studies have been concluded (reports to be published by end 2022):
- Market study of the EU market on nanomaterials, including substances, products, uses, volumes and key operators.
- Study on (bio)degradation and safe by design for nanomaterials.

15. Suggestion of discussion topic for next NMEG meeting (NMEG-16)

MSCA-NL
EU Chemicals Strategy for Sustainability: how are nanomaterials included in the strategy?

16.None of the above

MSCA-NL
The Netherlands volunteered to initiate pilot inspections on REACH registrations of nanomaterials. The main aim is to determine whether EU-wide enforcement action should be put in place to tackle the low level of information updates in dossiers for substances in nanoforms. ECHA will provide support together with the REACH competent authority in the Netherlands. Based on a list provided by ECHA, companies will be selected to gain insight in the type of information companies use in their considerations to register the substances with nanoforms or not. With the project the inspectors aim to build up knowledge and expertise on the (low number of) registrations of nanomaterials. France also showed interest in performing such pilot inspections. Depending on the results of the experiences in these pilot inspections, the ECHA Forum may discuss potential further action related to nanomaterials at a later stage.