ECHA
EUROPEAN CHEMICALS AGENCY

Tour de table

12th meeting of the ECHA Nanomaterials Expert Group (ECHA-NMEG-12) 6-7 November 2018, Helsinki, Finland

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. IUCLID reporting

MSCA - NL

The first step in any chemical evaluation is substance characterisation and identification. To facilitate this for nanomaterials, the Netherlands – together with the United States – is leading the OECD WPMN project "Physico-Chemical Decision Framework to Inform Decisions for Risk Assessment". This project is closely related to the project "Guiding Principles for Measurements and Reporting for nanomaterials: Physico-Chemical Parameters". The Decision Framework begins with guidance on the purpose for test methods in order to identify which methods are (or are not) appropriate to measure a given physico-chemical parameter. The "Guiding Principles" – lead by industry representatives in BIAC – provide guidance on improving the conduction of the studies, in addition to promoting consistent data reporting (including reporting details on sample preparation and measurement protocols) to maximise utility and comparability of the data.
Through the use of Decision Framework decision trees, a user is guided through specific questions to identify the most relevant purposes and related physico-chemical parameters to fill relevant knowledge gaps for characterisation, hazards or risks, for specific nanomaterial types. Once key physico-chemical parameter(s) are identified, and their relevance for specific (risk) endpoints established, the Decision Framework can further guide the user towards the best test methods by clearly defining the purpose for the measurement. The Guiding Principles provide a methodology for identifying methods that are fit-for-purpose based on the purpose description by the Decision Framework and a means to rank options based on common quality principles.
Case-studies showed the usefulness of the approaches, but also highlighted points of improvement. In September both projects were discussed in a workshop at OECD with stakeholders with regulatory, industrial and academic stakeholders. Both projects aim to have final reports ready in the spring of 2019.

2. Substance identity

MSCA - NL

The main goal of the EU project GRACIOUS (January 2018 until June 2021) is to generate a science-based framework to enable practical application of grouping and read-across of nanomaterials. The project has developed a draft framework (in line with existing approaches, e.g. DF4nano and the ECHA Guidance) that has been presented at a workshop at the OECD and discussed with regulatory (ECHA, EFSA, OECD delegations), industrial and academic stakeholders. The comments are used to adapt the framework and target further research. The project will continue to seek input from stakeholders to ensure that the framework effectively meets the needs of both regulators and industry. The GRACIOUS Framework will

be underpinned by scientific hypotheses identifying endpoints relevant to grouping and read-across. Application of the Framework will allow movement away from the case-by-case risk assessment paradigm, thereby improving the efficiency of risk analysis and decision making for safer design of quality nanomaterials. RIVM is a main partner in this project, as work package lead and playing a crucial role in the development of the Framework and engagement of stakeholders.

3. Phys-chem characterisation of nanomaterials

MSCA - NL

In May 2017 a project– led by the Netherlands – started to provide an overview of the existing knowledge on toxicokinetics of nanomaterials. After several meetings the document (ISO TR 22019) was further developed and finalised for adoption by ISO in their recent meeting in Kuala Lumpur (29 October – 2 November 2018). This Technical Report is expected to be finalised by the end of 2018. The document will subsequently be used as a basis for adaptation of the OECD test guideline document on performing toxicokinetic studies. This OECD project will also be led by the Netherlands with the UK as co-lead.

4. Hazard evaluation – human health

EFSA

The EFSA guidance for risk assessment has been published on 4 July 2018 after extensive public consultation. This guidance is now being implemented and applied. I pilot phase will offer troubleshooting on particular cases. https://www.efsa.europa.eu/en/efsajournal/pub/5327

ASO - PETA

The PETA International Science Consortium Ltd. has produced a series of webinars on alternative approaches for testing the toxicity of inhaled substances. The 17 pre-recorded webinars feature international experts from industry, government, and non-profit organizations presenting on in silico models, in vitro test systems, and integrated approaches to testing and assessment. Additional webinars will be added in the coming months. The webinars are available at https://www.piscltd.org.uk/inhalation-webinars/.

The PETA International Science Consortium, a member of the International Council on Animal Protection in OECD Programmes (ICAPO), is collaborating with Health Canada to develop an adverse outcome pathway (AOP) for lung fibrosis. The AOP entitled 'Secretion of inflammatory cytokines leading to lung fibrosis' is available on the AOPwiki (AOP 173: https://aopwiki.org/wiki/index.php/Aop:173). A manuscript on this work is currently under preparation.

The PETA International Science Consortium is funding the development of an advanced, three-dimensional in vitro system to predict the potential of manufactured nanomaterials to cause lung fibrosis in humans. The project is led by Professor Dr. Barbara Rothen-Rutishauser of the Adolphe Merkle Institute at the University of Fribourg and MatTek Corporation. The highlights of the project were presented this year at the 57th Society of Toxicology meeting and NanoTox 2018 – the 9th International Conference on Nanotoxicology. The final results are

expected to be submitted for publication by the end of 2018. As part of this project, MatTek Corporation has developed a model of the lower respiratory tract (EpiAlveolarTM); the model is currently available for beta-testing and should be commercially available in the coming year. The progression of this project can be followed on our website: http://www.piscltd.org.uk/nanoworkshop/.

In September 2016, the PETA International Science Consortium co-hosted a webinar series and workshop with the US NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), focusing on the use of alternative methods for acute inhalation toxicity testing. To implement recommendations from the workshop, four working groups were formed, each focussing on a specific area: 1) developing a database of existing acute inhalation toxicity data; 2) preparing a state-of-the-science review on mechanisms, dosimetry considerations, and assays for acute inhalation toxicity; 3) developing in silico models; and 4) conducting a proof-of-concept study to optimize an integrated approach comprised of in vitro and in silico methods. The most recent article published from this work is available here: https://www.ncbi.nlm.nih.gov/pubmed/29908304. The decision tree presented in the article is being used as the basis to design a testing strategy. A proof-of-concept study to demonstrate the utility of the non-animal testing strategy to predict the acute toxicity of inhaled substances is expected to commence in the coming months.

5. Hazard evaluation – environment

EFSA

EFSA launched a call for procurement for preparatory work on environmental risk assessment (offers expected by end September).

MSCA - UK

The following paper summarises the effort on bioaccumulation testing for nanomaterials, and especially in relation to developing the technical guidance document for the OECD. The paper includes ways of reducing the burden of testing with screening approaches, read-across and in vitro tiers.

Handy, R. D., Ahtiainen, J., Navas, J. M., Goss, G., Bleeker, E. A. J. and von der Kammer, F. (2018) Proposal for a tiered dietary bioaccumulation testing strategy for enginered nanomaterials using fish. Environmental Science: Nano, Doi: 10.1039/C7EN01139C

6. Read-across and grouping for nanomaterials

ECHA

The following OECD document/link presents a 'Case study on grouping and read-across for nanomaterials – Genotoxicity of nano-TiO2' developed by JRC and recently published. ECHA's Read-Across Assessment Framework (RAAF) was successfully applied for evaluating the confidence in the read-across argumentation of NMs. Some nanospecific issues were identified for further specification of the RAAF for NMS, in particular the concept of similarity which cannot be based only on structural similarity for NMs.

http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2018)28&docLanguage=En

7. Exposure assessment

N/A

8. Risk assessment

EFSA

communication: video to be considered for EUON: https://www.efsa.europa.eu/en/press/news/180704

ASO – PETA

The PETA International Science Consortium's Director was Guest Editor of a special June issue of Applied In Vitro Toxicology on 'Implementing Alternative Approaches for Inhalation Toxicity Testing'. The issue covered topics relevant to the risk management of nanomaterials and other substances including in vitro test methods, non-testing methods (e.g., quantitative structure activity relationships, grouping, or read-across), AOP development and dosimetry considerations. It is available to read here: https://www.liebertpub.com/toc/aivt/4/2.

9. Guidance or good practice documents for registrants and stakeholders

MSCA – UK

Progress is being made on the technical guidance document on bioaccumulation potential using a dietary exposure method for nanomaterials in fish. The document will next be considered at the meeting hosted by JRC on 12/13th December 2018.

MSCA - IT

In the framework of Malta Initiatives, Italy is proposing a new Guidance Document (GD) on a "Integrated in vitro approach for intestinal fate of orally ingested nanomaterials". The GD will be led by Istituto Superiore di Sanità (ISS) in cooperation with EcamRicert and IIT, JRC already supports this proposal.

The proposal was positively considered by most of the participants at the 2nd Face-to Face Meeting on Malta Initiatives (Berlin, April 2018).

Participants: Istituto Superiore di Sanità (ISS)
Contact: Dr Flavia Barone and Dr Isabella De Angelis (flavia.barone@iss.it; isabella.deangelis@iss.it)
Partner: EcamRicert and Istituto Italiano di teconologia (IIT).

ECHA

A presentation made during the NMEG-12 meeting will provide an update on Guidance to implement revised REACH annexes for nanomaterials.
A specific 'Workshop on supporting the implementation of the REACH information requirements for nanomaterials' is organised in ECHA on 8-9 November 2018, back-to-back with the NMEG-12 meeting.

10. Relevant new research projects or strategies on nanomaterials

MSCA – ES

Within the GUIDEnano Project we have developed a strategy to score the quality of studies of toxicity and ecotoxicity of nanomaterials.

MSCA – UK

Updates on the EU project, Nanofase which is primarily involved with collecting data on bioaccumulation of nanomaterials can be found at: http://www.nanofase.eu/.

Lead et al (2018) updates the 2008 review from this group on nanomaterials in the environment. The present review discusses new insights into fate and behavior, metrology, transformations, bioavailability, toxicity mechanisms and environmental impacts with a focus on terrestrial and aquatic systems.

Lead, J.R., Batley, G.E., Alvarez, P.J.J., Croteau, M-N., Handy, R.D., McLaughlin, M.J., Judy, J.D. and Schirmer, K. (2018). Nanomaterials in the environment: behavior, fate, bioavailability, and effects - An updated review. Environmental Toxicology and Chemistry, Vol 37(8), 2029-2063. DOI: 10.1002/etc.4147

ASO – PETA

The PETA International Science Consortium and Epithelix have announced an award to provide an opportunity for researchers worldwide to win three-dimensional reconstructed human respiratory tissues from Epithelix. The awardee will receive a $5,000 award redeemable for Epithelix MucilAirTM or SmallAirTM tissues. The award winner will be selected based on their proposal's scientific merit and potential to replace animal testing. More details on this award can be found here: https://www.piscltd.org.uk/epithelix-award/.

National Institute of Health (ISS)

RInnovaReNano: *Research and Responsible Innovation of Nanotechnologies: evaluation of safety and regulatory compliance, support the industrial development, accomplish an informative web-based platform to facilitate the access and the dissemination of the knowledge on nanotechnologies (November 2015-February 2018)*

In the framework of the RRI (Research Responsible Innovation), ISS carried out the RInnovaReNano project, funded by Lazio region and started in November 2015, in order to identify the nanomaterials (NMs) relevant for the regional and national companies. This project was accomplished in close cooperation with the Italian Association for Industrial Research (AIRI). The areas of investigation were related to chemicals, cosmetics, agri-food, biomed and pharma sectors.

The activities, in the contest of the project, have been devoted to transfer methodologies for nanomaterial risk assessment to the industry, through training initiatives such as workshops and conferences. One of the main goals was the advancement of scientific and technological awareness of the Lazio region companies involved in research and innovation of NMs and nanotechnology.

On 14th February 2018, ISS launched a National web-based platform (https://nanotecnologie.iss.it) to manage and facilitate the access of industry and scientific community to the knowledge of NMs and nanotechnology.

11. Experience from stakeholder or public dialogues

N/A

12. Any other scientific and technical issue

MSCA – DE

The German Environment Agency (UBA) held an Expert Workshop for the harmonized development of OECD TGs and GDs for Nanomaterials behaviour and fate in the environment at the 23rd-24th of August 2018. Aim of this core expert meeting was to technically discuss synergies and overlaps for the ongoing and planned TG/GDs development on solubility and dissolution, dispersion stability and transformation in the environment and to promote harmonisation of these activities by enhanced cooperation and communication. At the meeting project leading experts of the OECD TG No. 318, the (Draft) TG on Dissolution Rate in Aquatic Media (led by US), the (Draft) GD on Dissolution and Dispersion Stability in Environmental Media (led by DE), and the planned OECD TG on aquatic (environmental) transformation of NM (led by AT) were present or took part via video conference. Furthermore, the scope and timeline of the planned OECD TG on solubility and dissolution rate of NM in water and relevant synthetic biologically media (led by DK) was presented. Central results of the workshop were recommendations for a possible adjustment of the upcoming validation test for the draft TG on Dissolution Rate in Aquatic Media and the finalisation of the draft. It was also proposed to develop in longer term a standardised method for the determining dissolution rate for environmental media in a dynamic system in addition. For the draft GD on Dissolution and Dispersion Stability in Environmental Media it was noted which aspects need to be further addressed and who could deliver input: e.g. interpretation and presentation of data for risk assessment and test strategies, mid-term guidance for the determination of dissolution via dynamic method, hetero-agglomeration, derivation of attachment coefficient, data use for exposure modelling.

In summer 2018 UBA launched a new research project to accompany the development of a potentially new OECD Test Guideline for the determination of bioaccumulation in Hyalella azteca. Within the CEFIC-LRI Project ECO 40 (Investigations on the bioconcentrations of xenobiotics in the freshwater amphipod Hyalella azteca and inter-laboratory comparison of a new BCF test protocol) a test protocol for testing of bioaccumulation in crustacea Hyalella azteca was developed on the basis of five lipophilic substances and a validation ring test will be performed. The UBA project will investigate the applicability, resilience, and limitation of this non-vertebrate test method for highly lipophilic

organic substances and nanomaterials. If the method is applicable, a proposal will be prepared on how the method can be applied to these substances and, if relevant, which adaptations are needed. A draft test guideline will be developed. https://www.umweltbundesamt.de/en/topics/chemicals/nanotechnology/research-development-projects

ECHA

OECD GD on aquatic and sediment toxicity testing of NM. Second version was under commenting until end of October.
This document is a relevant and useful update for the preparation and testing of nanomaterials in aquatic and sediment toxicity environment or their behaviours in test media.

13. General

N/A

14. EUON

ECHA

A presentation made during the NMEG-12 meeting will provide an update on the development of the EUON.