Harmonisation and standardisation of testing methods

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OECD Working Party on Manufactured Nanomaterials (WPMN) and NMBP-13 & 34

INISS-nano February 16, 2023

BETTER POLICIES FOR BET

Content

- Introduction: OECD and harmonisation & standardisation
- European research in context of Harmonisation and standardisation
- Future outlook: needs in research and governance of harmonisation and standardisation

Organisation of Economic Co-operation and Development (OECD)

Inter**governmental** organisation

- 37 Member countries representatives and Europe Commission
- Industry representation (Business and Industry Advisory Committee, BIAC)
- Animal welfare organisations (ICAPO)
- Green NGOs
- Other Partners (i.e Malaysia, Thailand, South Africa)
- International Organisations (i.e. WHO, UNITAR, UNEP, ISO TC 229)

OECD Working Party on Manufactured Nanomaterials

Testing and Assessment (EU)

Continue assessing the need for developing TGs/GDs for Nanomaterials and Advanced Materials; Further Guidance for hazard testing & assessment

Exposure Measurements and Exposure Mitigation (US)

Guidance on release and exposure testing & assessment

Risk Assessment and Regulatory Programmes (CA)

Reviewing needs and priorities

Advanced Materials (GER and NL)

Safer and Sustainable Innovation Approach (SIA; for more Sustainable Nanomaterials and Nano-enabled Products (leads NL, CA and BIAC)

- Working Description Sus and SSbD
- Identify solutions for its implementation

Developing quality standards for the safe assessment of chemicals (including Nanomaterials)

- The **OECD Guidelines for the testing of chemicals** are a collection of internationally agreed testing methods used by governments, industry and independent laboratories to assess the safety of chemicals.
  - OECD Test Guidelines are covered by the **M**utual **A**cceptance of **D**ata System ("*tested once, data accepted everywhere*")

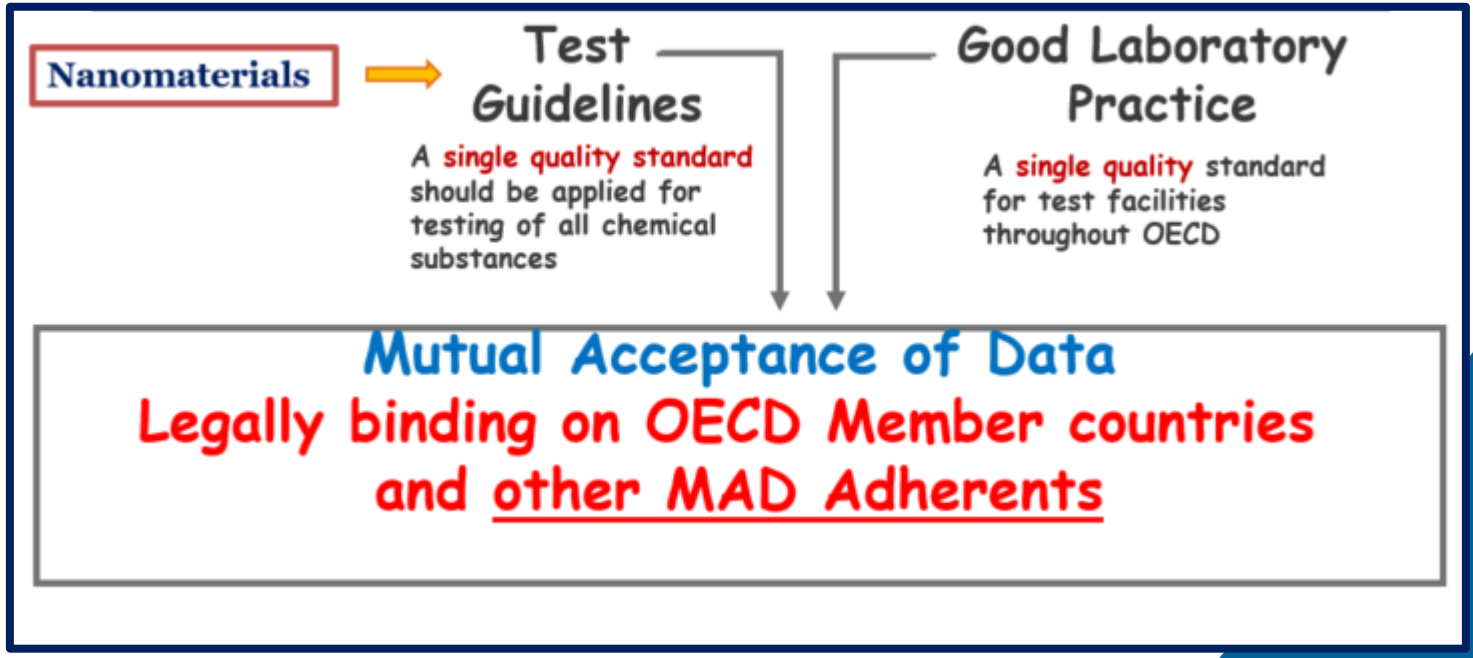
- To support the adequate conduct of Guideline studies, Guidance Documents are developed.
  - GDs provide more detailed explanations on selected aspects of testing
  - GDs provide flexibility to adapt guidance to specific tests or tested chemicals

THE MUTUAL ACCEPTANCE OF DATA SYSTEM

Data generated using **OECD Test Guidelines (TG)** under **Good Laboratory Practices (GLP)** are accepted across member countries and MAD adhering countries having the same data requirement

"tested once, accepted everywhere."

Saving Costs in Chemicals Management
https://oe.cd/chemicals-costs



To keep in mind

- Test Guidelines and Guidance Documents **respond to a regulatory need**
- Support the **uptake of new and/or complex met**hods by relevant and sufficient guidance on testing and interpretation of data, and the reporting via templates
- Harmonised testing methodologies that are:
  - **Robust** and **reliable** for governments to base their decisions
  - Mindful of **animal welfare** considerations, “3Rs principles”
  - Mindful of economic implications of testing
- As broadly accessible as possible
- OECD Member countries are the ones that agree by consensus the final TGs and GDs.

OECD Test Guidelines and Guidance Documents on Nanomaterials

Section 1: Physical Chemical Properties

- TG 124 Determination of the (Volume) Specific Surface Area of MNs (EU-JRC)
- TG 125 Particle Size and Size distribution of MNs (GER)

- WNT 1.5_GD on Determination of solubility and dissolution rate of NMs in water and relevant synthetic biological media (DNK/GER)
- WNT 1.6_ GD on Identification and quantification of the surface chemistry and coatings on nano- and microscale materials (DNK/GER)
- WNT 1.8_TG on Determination of the Hydrophobicity Index of MNs through an Affinity Measurement (EU)
- WNT 1.9_TG on Determination of the Dustiness of MNs (DNK/ FRA)
- WNT 1.10 GD Determination of concentrations of nanoparticles in biological samples for (eco)toxicity studies (UK)

Section 2: Effects on Biotic Systems

- Study Report on a test for removal in wastewater treatment plants of gold manufactured nanomaterial (US)

- WNT 2.71 Additional guidance on the use of TG 201, 202, on Aquatic Toxicity Testing of Nanomaterials (France/Spain)

Section 3: Env. Fate and Behaviour

- GD 317 on Aquatic Toxicity Testing of Nanomaterials (US)
- GD 342 on testing Nanomaterials using OECD TG No. 312 "Leaching in soil columns" (CAN/GER)
- TG 318: Dispersion stability in simulated environmental media (GER)
- Guidance document No. 318: Solubility and dissolution rate (GER)

- WNT 3.10_TG on dissolution rate of NMs in aquatic environment (GER)
- WNT 3.11 _TG for nanomaterial removal from wastewater (US)
- WNT 3.12_GD on assessing the apparent accumulation potential for NMs (Spain)
- WNT 3.14_GD to support implementation of TG 312 for NMs Safety Testing (CAN/GER)
- WNT 3.16_GD Environmental abiotic transformation of NMs (AT) and TG (GER)
- WPMN_Scoping review for a tiered approach for reliable bioaccumulation assessment of MNs in environmental organisms minimising use of higher tier vertebrate tests (UK)

Section 4: Health Effects

- Updated TG 412 Subacute Inhalation Toxicity: 28-Day Study (Nano) (NL/US)
- Updated TG 413: Subchronic Inhalation Toxicity: 90-day Study (Nano) (NL/US)
- Revised GD 39 on Inhalation Toxicity (NL/US)
- Study Report and Preliminary Guidance on the Adaptation of the *In Vitro* micronucleus assay (OECD TG 487) for Testing of MNs (GER/UK)

- WNT 4.133_Applicability of the key event based Test Guideline 442D for *in vitro* skin sensitisation testing of NMs (Switzerland)
- WNT 4.146_TG on toxicokinetics to accommodate testing of nano-particles (NED/ UK)
- WNT 4.158_GD on IATA for intestinal fate of orally ingested nanomaterials(Italy)

Visit our website: oe.cd/nanomet

Testing and Assessment: current priorities

1. Revision of the Guidance on Sample Preparation and Dosimetry (GSPD

2. OECD Guidance on Grouping of Chemicals (GD 194) includes section 6.9. addressing “Initial considerations applicable to manufactured nanomaterials”

3. Reviewing remaining needs on TG/ GD for Nanomaterials and Advanced Materials considerations

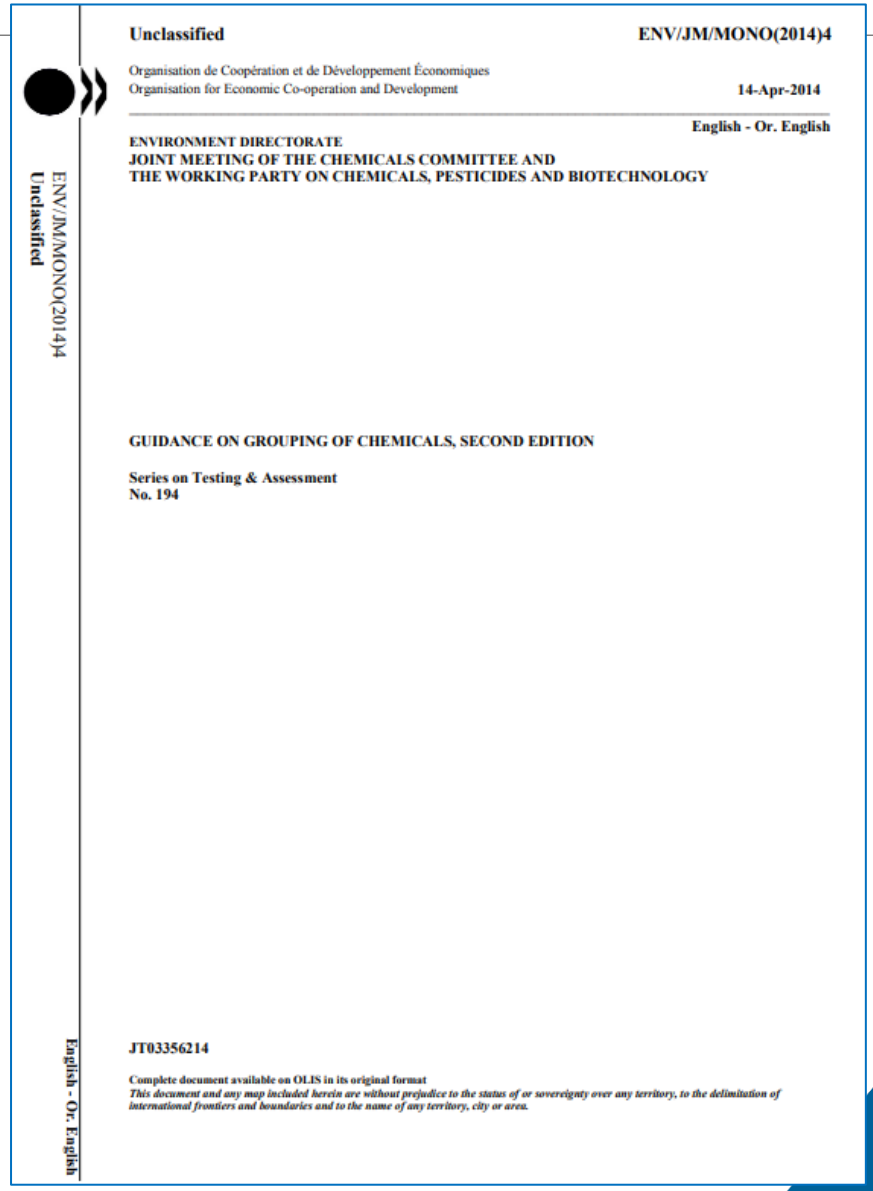
GSPD: Different Sections

- General Introduction
- Terminology
- Considerations on Appropriate Dose-Metrics
- Common Issues Regarding Sample Preparation and Dosimetry
- Specific Considerations
  - **A. Physical-Chemical Properties**
  - **B. Guidance on Preparation Samples of Nanomaterial in Exposure Media for Ecotox Studies**
  - **C. Guidance on Preparing Nanomaterial Samples for Degradation , Transformation and Accumulation Studies**
  - **D. Health Effects, Preparation of a Test Substance and Dosimetry**

Grouping of Chemicals (GD 194) section 6.9. addressing “Initial considerations applicable to MNs”

- Last update in **2014**

- Section 6.9 : Placeholder nanomaterials ***“Initial considerations applicable to manufactured nanomaterials”***



https://doi.org/10.1787/9789264274679-en

EU Call NMBP 13 and 34

The 

Initiative – A European Action to Develop OECD Test Guidelines for Nanomaterials

Call NMBP 13 - Risk Governance of nanotechnology (RIA)

Call NMBP 34 – In support of documentary standards (CSA)

European Union's Horizon 2020 research and innovation programme grant

The EU NMBP 13 Projects Risk Governance of nanotechnology (RIA): Focus on research related to MI

NANORIGO

Review of available guidelines, SOPs with subsequent recommendations and conclusions for the sections of Material, Exposure, Hazard - Human, Hazard – Environment, Risk

RISK GONE

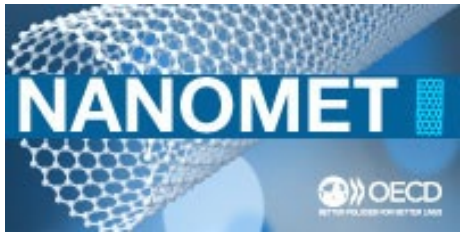
Adaptation of available and development of new TGs/GDs mainly related to nanomaterial properties/biological endpoints at the OECD stage - Pre Project Proposal

Gov4Nano meeting the needs of nanotechnology

Adaptation of available and development of new TGs now mainly at the OECD stage: WNT Projects
and
task to coordinate the scientific developments towards OECD TG/GDs between each other and with the OECD secretariat

European Union's Horizon 2020 research and innovation programme grant

EU NMBP 34 Projects
In support of documentary standards (CSA)



Coordinates OECD-EU activities that support TG/GD
- Ensuring actions fulfil OECD requirements
- Informing and engaging Member countries and organisations
- Interactive exchange and collaboration with related EU projects

NanoHarmony

Supporting development of TGs/GDs
Coordinate the scientific activities also beyond NanoHarmony
Facilitate information exchange between research and OECD
……

RISK GONE

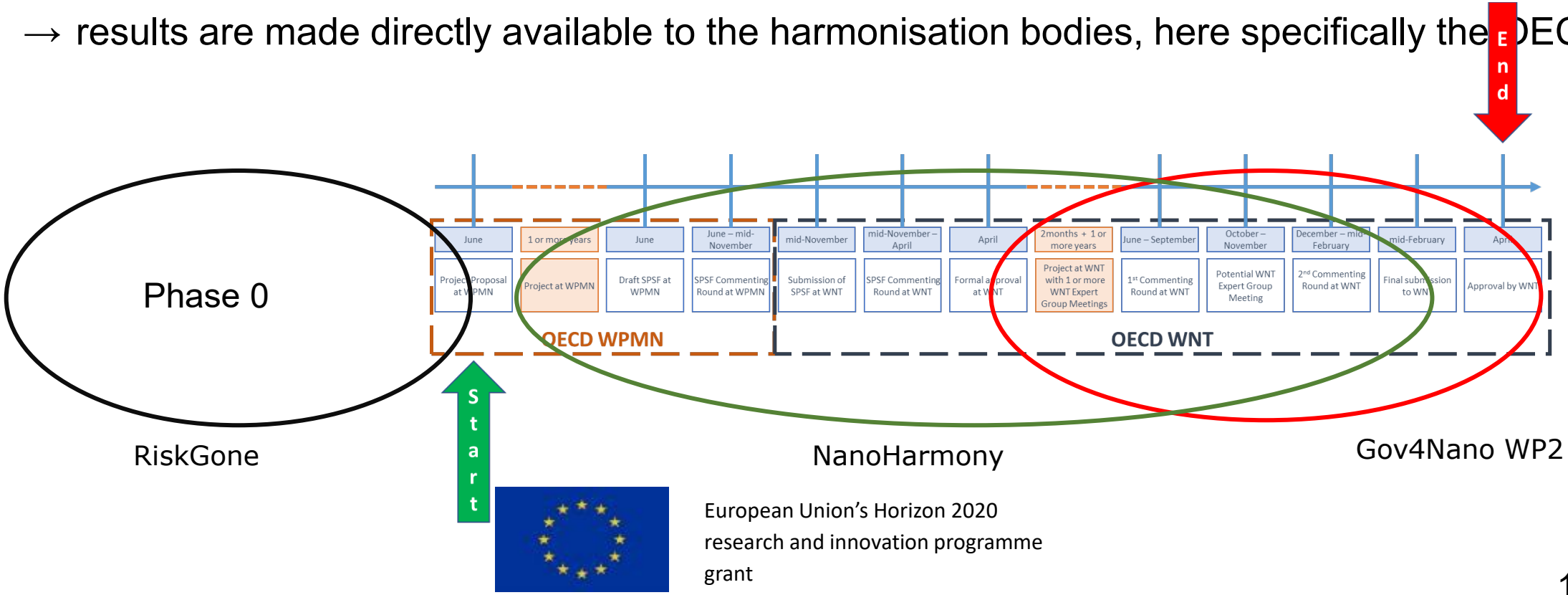
Gov4Nano
meeting the needs of nanotechnology

European Union's Horizon 2020 research and innovation programme grant

Research & Development towards guidance & guidelines for testing of nanomaterials

- Focus on relevant endpoints for the regulatory safety assessment of nanomaterials in Europe
- Fill remaining gaps that hamper test method development for several nano-related REACH endpoints

  → results are made directly available to the harmonisation bodies, here specifically the OECD



European Union's Horizon 2020 research and innovation programme grant

Supporting Risk Governance

Nano-Risk Governance

- Any evaluation or decision making process relies on a sound scientific basis:
  - Tools to support the process of Risk Assessment and Risk Management (Risk Governance)
  - Tools rely on availability of data on environmental and human safety for nanomaterials (FAIR data)

➢ Harmonised Test Guidelines and Guidance Documents to generate reliable data

> Standardisation organisations like OECD

> Malta Initiative supports adaptation of TGs/GDs for nanomaterials

- Developing knowledge and data to improve TGs/GDs
- Recommendations on improvements for practical application

European Union's Horizon 2020 research and innovation programme grant

Ongoing TG Developments

Section 1 Physical Chemical Properties	Section 2 Effects on Biotic Systems	Section 3 Env. Fate and Behaviour	Section 4 Health Effects
TG on determination of the (volume) specific surface area of manufactured nanomaterials **(EU) WNT 1.3** Completed 2022	Recommendations for guidance on adaptations needed when using OECD TG 201, 202 and 203 for the determination of the Ecotoxicity of MNs **(FR/ES) WPMN**	TG on dissolution rate of nanomaterials in aquatic environment **(DE) WNT 3.10**	GD on the adaptation of *in vitro* mammalian cell based …icity TGs for testing of …ed nanomateria… Completed 2022
TG on particle s… …ize distribution of manufactured nanomaterials **(DE) WNT 1.4**		TG for nanomaterial removal from wastewater **(US) WNT 3.11**	Applicability of the key event based TG 442D for *in vitro* skin sensitisation testing of nanomaterials **(CH) WNT 4.133**
GD on determination of solubility and dissolution rate of nanomaterials in water and relevant synthetic biological media **(DK/DE) WNT 1.5**		GD on assessing the apparent accumulation potential for nanomaterials **(UK/ES) WNT 3.12**	TG on toxicokinetics to accommodate testing of nanoparticles **(NL/UK) WNT 4.146**
GD on identification and quantification of the surface chemistry and coatings on nano- and microscale materials **(DK/DE) WNT 1.6**		GD to support implementation of TG 312 for nanomaterial safety testing **(CA/DE) WN T 3.14**	Integrated *in vitro* approach for intestinal fate of orally ingested nanomaterials **(IT) WPMN**
TG on determination of surface hydrophobicity of manufactured nanomaterials **(EU) WNT 1.7**		GD on environmental abiotic transformation of nanomaterials **(AT) WNT 3.16**	
TG on determination of the dustiness of manufactured nanomaterials **(DK/FR) WNT 1.8**		Scoping review for a tiered approach for reliable bioaccu. assess. of MNs in environ. organisms minimising use of higher tier vertebrate tests **(UK) WPMN**	
GD on the determination of concentrations of nanoparticles in biological samples for (eco)toxicity studies **(UK) WNT 1.10**		Assessment of the durability of NMs and their surface ligands in env. surroundings (biodurable/ biodegradable) **(SA/Korea) WPMN**	

European Union's Horizon 2020 research and innovation programme grant

National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

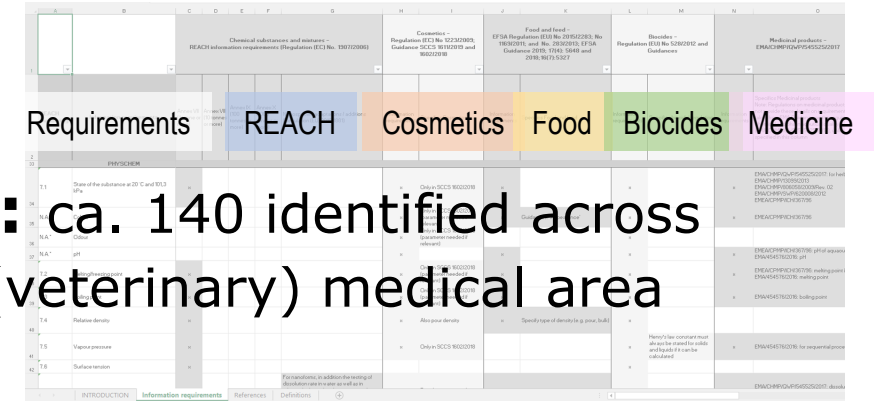
Testing of nanomaterials for different EU legislations and (potential) needs for updating OECD TGs

Eric A.J. Bleeker

E. Swart, H. Braakhuis, M.L. Fernández-Cruz, S. Friedrichs,
I. Gosens, F. Herzberg, K.A. Jensen, F. von der Kammer,
J.A.B. Kettelarij, J.M. Navas, K. Rasmussen, K. Schwirn, M. Visser

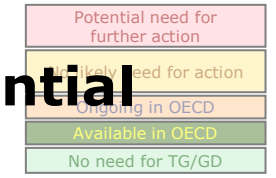
B. Halamoda-Kenzaoui, R. Geertsma, R. Smith, S. Hoy, J. Holmqvist, A. Rodríguez Ruiz,
M. Groenewold, B. Hakkert, J. van Engelen, A. Sips

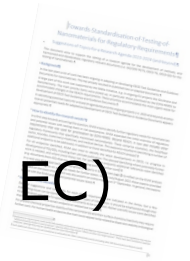
What did we do?



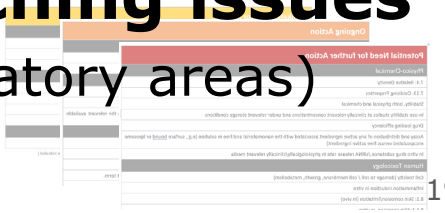
- **Overview of information requirements:** ca. 140 identified across industrial, cosmetics, biocides, food and feed, and (veterinary) medical area

- **For each requirement:**
  - **RIVM:** assessment of ongoing actions, published documents and **potential need for further action** to accommodate nanospecific issues
  - **EU experts: reflection on analysis.** Representation from research, EU regulatory bodies and each regulatory area. Experts involved in EU projects/OECD harmonisation programmes (NL, AT, DE, DK, ES, UK, and EC)





- Identification of potential **priority needs** and **overarching issues**
  - Expert comments & Relevance (multiple requirements / regulatory areas)



Overarching needs for action on test methods[1]:

1. Resolving issues around nanomaterial sample preparation, agglomeration, dispersion stability and dosing in toxicity testing for especially human health endpoints

2. Further development of tests or guidance on degradation and transformation of organic nanomaterials or nanomaterials with organic components to better assess environmental fate of this group of nanomaterials

3. Further development of tests and guidance to measure (a)cellular reactivity of nanomaterials, which will be critical
   - e.g. needed in high-throughput systems (for ever-increasing diversity of (newly) developed (advanced) nanomaterials)

› Exact actions to take to be determined and responsible stakeholders to be identified

[1] Based on expert assessment (RIVM and EU experts)

What about other advanced materials ?

- Biopolymers (based on DNA, RNA, proteins, sugars and lipids)
- Composites (macroscopic, hybrids, fibre-/particle reinforced)
- Porous materials (micro, meso, macro-porous)
- Metamaterials (electromagnetic, acoustic)
- Particle systems (Quantum Dots, Supraparticles, Nanoflowers, Graphene)
- Advanced Fibres(organic, carbon-based, inorganic)
- Advanced Polymers (electro-active, magneto-active, self-repairing, co-polymers)
- Advanced Alloys

Working description of AdMa within WPMN

- To describe the playing field of AdMa within WPMN
- To describe in which context WPMN is engaged with AdMa
- Starting with but not limited to nano-scaled materials and materials containing nanomaterials
- Acknowledges that what is considered as an AdMa of relevance for WPMN may change over time, due to increased knowledge, technical progress or established regulatory implementation

Advanced Materials: Working Description

I. The ***Working Party on Manufactured Nanomaterials' (WPMN) Working Description on Advanced Materials*** aims to illustrate the content of the Advanced Materials playing field and the purpose of WPMN's engagement regarding these materials[2].

II. In this context, AdMa are understood as materials that are rationally designed to have

- new or enhanced properties, and/or
- targeted or enhanced structural features

with the objective to achieve specific or improved functional performance3. This includes both new emerging manufactured materials, and materials that are manufactured from traditional materials. This also includes materials from innovative manufacturing processes that enable the creation of targeted structures from starting materials, such as bottom-up approaches. It is acknowledged that what are currently considered as AdMa will change with time.

III. The considerations within the WPMN will build on the knowledge gained on manufactured nanomaterials, and possibly include other AdMa with relevance to safety, sustainability and regulatory issues considering their whole life cycle. Advanced Materials under consideration of WPMN are aimed to be assessed in order to improve their safety, sustainability and regulatory coverage within the strategic approach to identify knowledge gaps and recommendations for action. The AdMa in focus will evolve as additional knowledge is gained and appropriate strategies are developed.

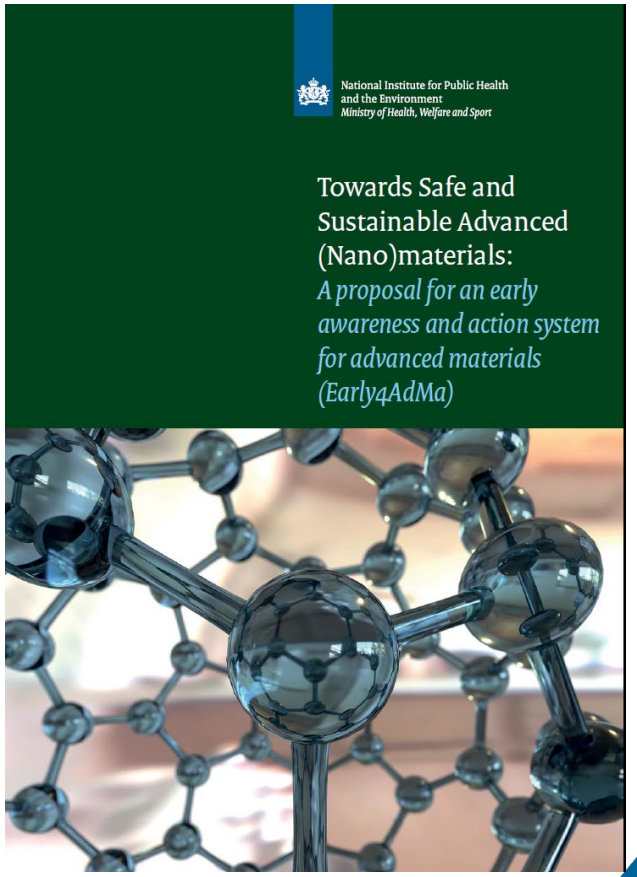
IV. Examples of possible cases of AdMa that could be considered are given in the Annex.

ENV/CBC/MONO(2022)29
https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-CBC-MONO(2022)29 &doclanguage=en

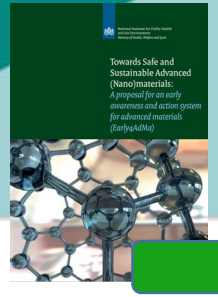
Strategic Approach for Advanced Materials

- On the basis of the proposed **EARLY4AdMa** system
  - Developed under the lead of NL (RIVM)
  - Contribution by GER (colleagues from BfR, BAuA, UBA)
- Tiered Approach with Questions on Safety and Sustainability including a Scoring-System
  - Discussion and Identification of Warnings
  - Prioritisation of Warnings
  - Derivation of Recommendations for Actions
- General Agreement but further refinement needed to meet the needs of WPMN
- Discussion and exercises during the SG AdMa Expert Meeting in February 2022 and upcoming EU H2020 Harmless Workshop in November 2022

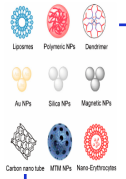
➢ EARLY4AdMa: ***Early Awarness and action for AdMa***



Early4AdMa brochure | RIVM

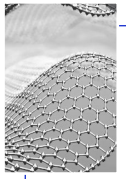


OECD
BETTER POLICIES FOR BETTER LIVES



NanoCarriers

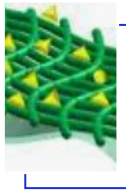
3D Printing



Graphene

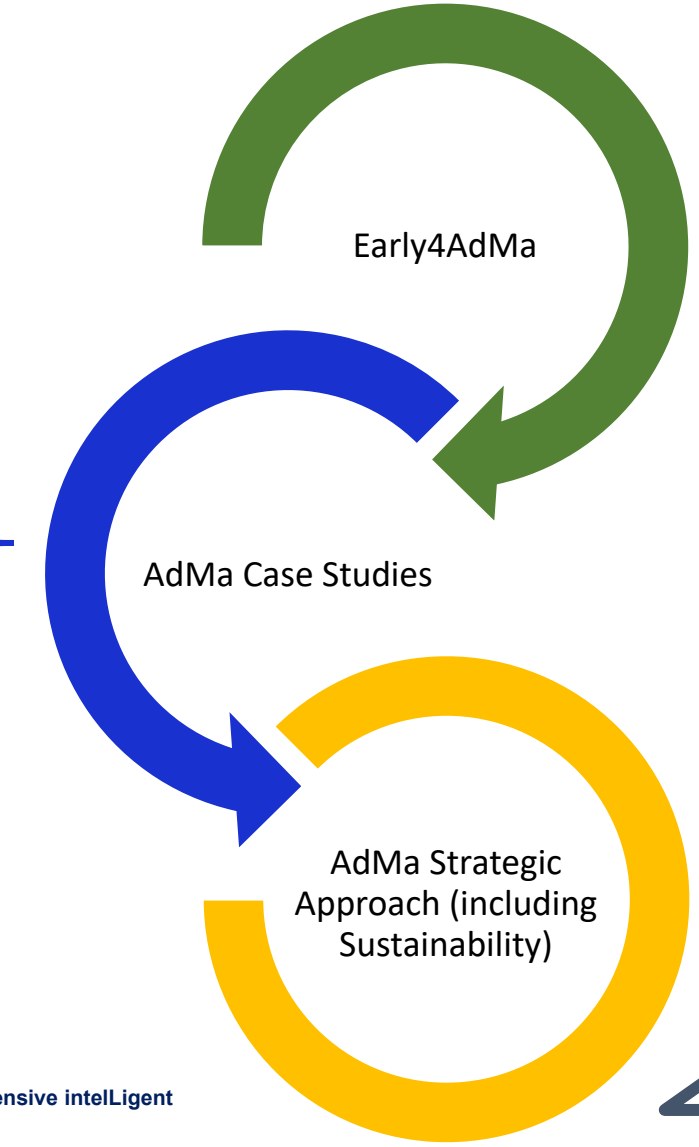
Fibre-aerogel-mats for façade insulation

Harmless



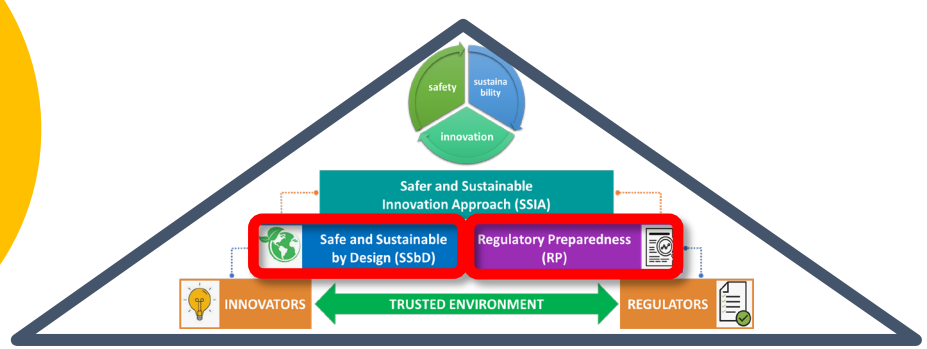
Silver cellulose articles/encapsulate cosmetic

ASINA



Other approaches

- Arvidsson et al.
- Kennedy et al.
- InnoMat.Life
- 2030 Materials Manifesto
- Others?



*HARMLESS: Advanced High Aspect Ratio and Multicomponent materials: towards comprehensive intelLigent tEsting and Safe by design Strategies

*ASINA: Anticipating Safety Issues at the Design Stage of NAno Product Development

Future-proof Approaches for Risk Governance

–

Lessons Learned from Nanotechnologies

The three NMBP-13 projects have received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement No. 814401, 814530, and 814425.

Organised in collaboration with the OECD's Working Party on Manufactured Nanomaterials (WPMN), supported by the EU project NANOMET. Financial support by the Research Council of Norway.

Aim(s) of this conference

The purpose of this conference is to help shape international approaches to addressing **future challenges in risk governance of nano- & advanced materials.** This includes safe- and sustainable by design (SSbD), harmonisation and standardization with more.

The main aim of this conference is to ensure maximized continuation the progress achieved, to

- support the implementation of the Sustainable development
- address future challenges in risk governance of new- and advanced materials
- be inclusive by addressing a fragmentated landscape and support early awareness

Sustainability needed in methods harmonisation

- To keep Test Guidelines / Standards up to date and fit for future needs:
  - to cover new/advanced materials
  - to cover method adaptations and development
  - to support e.g., CSS, SSbD and Green Deal
  - …
  - Malta Initiative Position Paper:
    - a European Test Methods Strategy that ensures continuous financial support for the systematic (further) development of OECD TGs. This strategy should also consider and promote international cooperation in the spirit and context of the OECD collaborative effort.

The three NMBP-13 projects have received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement Nos. 814401, 814530, and 814425.

Aim of the H&S Roundtable

- Discussion of open issues on the future of H&S in Europe

- Identification of key elements to pursue
  - Platform on Harmonisation and Standardisation
  - Roadmap towards such a platform
  - Funding of platform and method development

- The results from round table discussion will used to promote and set up a European Test Method Strategy as proposed by the Malta Initiative.

The three NMBP-13 projects have received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement Nos. 814401, 814530, and 814425.

1) Platform on Harmonisation and Standardisation

- A Framework / Platform is needed to ensure coordination and dialogue between relevant international stakeholders to ensure continuity and timely identification of test method development needs
  - For new (advanced) materials and/or new essential endpoints.
  - To provide the structure / strategy to promote science towards OECD TGs/GDs.
  - Discussing (reviewing) and setting TG priorities for development
  - We need an effective, long-term engagement of different stakeholders for successful TG developments
- Ensure good data / mandatory valid methods (also by editors of journals)
- Essential to connect and provide clarity on necessary steps for stakeholders (including citizens)

The three NMBP-13 projects have received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement Nos. 814401, 814530, and 814425.

2) Roadmap towards a platform on H & S

A formal organisation is required to ensure participation by regulators.

Steps to implement the platform:

- Establish an expert committee to identify key stakeholders and to define strategy and goal
- Promote clear messaging around the vision of the platform and its scope
- Who to involve: industry & industry associations, scientists, OECD, regulatory community
- Connect with RTD call on infrastructures (e.g. like NanoCommons)
- Connect with new programme on regulatory aspects

Need to initiate the platform by 1st quarter 2024 to avoid loss of current moment & collaborative networks

The three NMBP-13 projects have received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement Nos. 814401, 814530, and 814425.

3) Funding

- Constant funding is needed within a European Test Methods Strategy to support:
  - Researchers for the development, validation and harmonisation of test methods
  - International platform for collaboration and exchange between stakeholders
- Lessons learned in TG developments of NMs are a good starting point for AdMa test method strategy
- Stakeholder community needs to make voices heard in terms of the need to drive funding/financial input
  - Return on investment = industrial growth and societal protection/benefits
- Whilst PARC exists as an initiative for chemicals, nanomaterials/AdMa are not included, therefore there is the need for a synergistic initiative

The three NMBP-13 projects have received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement Nos. 814401, 814530, and 814425.

- Long-term and continuous effort into OECD TG amendments and developments for (advanced) materials
- Platform for stakeholder exchange and priority setting towards harmonisation of test methods

The three NMBP-13 projects have received funding from the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement Nos. 814401, 814530, and 814425.

Acknowlegdements to all NMBP-13 & 34 partners and OECD WPMN delegates