

OECD WPMN Initiatives on "Grouping and read-across for the safety assessment of manufactured nanomaterials"

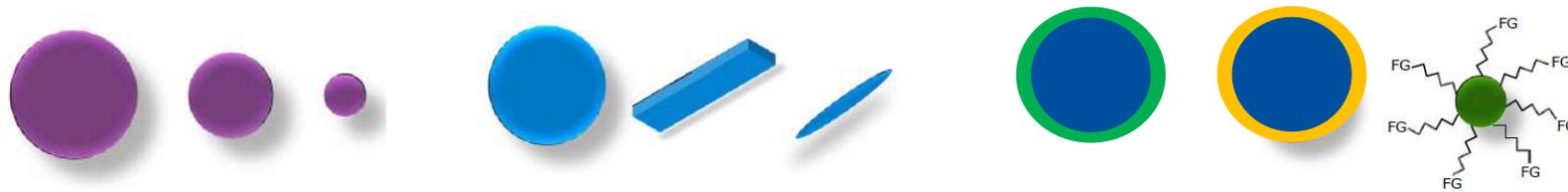
Juan Riego Sintes

Scientific Workshop – Grouping of Nanomaterials. NanoReg2 and Gracious H2020 Projects.
Paris, 12-13 September 2018,

**The European Commission's
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Grouping and Read-Across for Manufactured Nanomaterials

- A **Nanomaterial may exist in different nanoforms**, defined by specific physical-chemical characteristics such as particle size (distribution), shape, coatings, crystallographic structure, etc.



- It would be an **overwhelming** and **inefficient task to test all** MNs and each and every nanoform
- There is a need for **understanding how far data on one nanoform, e.g. also the bulk substance, is relevant for filling data gaps in hazard assessment of other nanoforms of the same substance/chemistry.**

The OECD Working Party on Manufactured Nanomaterials (WPMN) (1)

- Established in **2006**
- to **promote international co-operation** in **human health and environmental safety** related aspects of manufactured nanomaterials (MN)
- to **assist** in the development of **rigorous evaluation** of MN.

The OECD WPMN (2)

- The WPMN is organised in steering groups (SG).
- The **SG on Testing and Assessment (SG TA)** aims to:
 - Review, amend, propose and develop new or updated **OECD Test Guidelines (TG)** and **Guidance Documents (GD)** for all relevant endpoints and properties for hazard assessment and characterisation of MNs;
 - Exploring and developing **alternative approaches** for the safety assessment of MNs, e.g.
 - *in vitro* testing
 - **grouping and read-across** approaches

Some OECD Initiatives

Under the WPMN SG TA

7. OECD Expert meeting on **Categorisation of MNs**

8. OECD Expert Meeting: **Grouping and Read-Across for MNs**

Under the Working Party on Hazard Assessment:

Case Studies on Grouping and Read-Across: – Genotoxicity of Nano-TiO₂

OECD Expert meeting on Categorisation of MNs (1)

hosted by US EPA 17-19 September 2014, Washington D.C.,

GOALS

- Develop a grouping or **categorisation** of **MNs to improve regulatory decision-making**:
 - Streamlined regulatory decision-making process for both regulators and those subject to regulations
 - More accurate assessment of nanomaterials
 - Increased transparency
- Initiate the basis for development of a **consistent** approach to the **categorisation** of nanomaterials while **avoiding overlaps** among categories.

OECD Expert meeting on Categorisation of MNs (2)

AGENDA

Nine Sessions:

- 1: Context** for the Need for the Use of Categories and **Perspectives** on their Application to Nanomaterials
- 2: Risk Assessment** and Risk **Management**
- 3: Physical-Chemical Characterisation**
- 4: Environmental** Fate
- 5: Human Health** (Group 1)
- 7: Human Health** (Group 2)
- 8: Exposure** Assessment
- 9: Risk** Assessment



OECD Expert meeting on Categorisation of MNs (3)

RECOMMENDATIONS - 1

To develop fit-for-purpose decision frameworks for categorisation that can be utilised under different regulatory systems, the expert meeting **recommended**:

1. Identifying and developing **methods** for characterization of relevant **physical-chemical** properties for **toxicokinetics, fate, hazard,** and **exposure** assessments.
2. Using of methods that enable **comparability,** are **reliable,** and use the **OECD Guidance on Sample Preparation and Dosimetry** [ENV/JM/MONO(2012)40].
3. **Agreeing on or developing experimental models** (e.g., *in-vitro* and *in-vivo* assays) predictive of human health and environment effects and support categorisation.

OECD Expert meeting on Categorisation of MNs (4)

RECOMMENDATIONS - 2

4. **Adapting tools** and methodologies for categorisation **depending on the criteria** to be analysed for the assessment of MNs.
5. To clarify and apply consistently **definitions and terminologies**
6. **Adapting existing approaches** for conventional substances to fit specificities of categorisation frameworks for MNs
7. Performing **case studies** that inform categorisation schemes as they are developed and refined

OECD Expert Meeting on Grouping and Read-Across for MNs (1)

hosted by the European Commission in Brussels, on 13-14 April 2016.

OBJECTIVES

- Reach a **common understanding** of what aspects need to be considered in a regulatory context when applying grouping and read-across in completing hazard assessment of MNs
- Provide **initial input for a possible update of the 2014 OECD Guidance on "Grouping of chemicals", (ENV/JM/MONO(2014)4) Section 6.9: "Initial considerations applicable to manufactured nanomaterials"** (currently only one paragraph)
- Provide elements for designing a **roadmap/timetable** for the OECD to come forward with updated guidance proposals

The work complements the earlier OECD Categorisation Workshop in the US



OECD Expert Meeting: Grouping and Read-Across for MNs (2)

AGENDA

DAY 1:

A. Sharing experiences in developing/applying grouping and read-across for MN in different regulatory regimes from:

- research projects
- industry initiatives
- authorities' initiatives

B. Discussing experiences and extracting:

- lessons learnt
- best practices
- recommendations

OECD Expert Meeting: Grouping and Read-Across for MNs (3)

AGENDA

DAY 2:

Focused break-out group discussions

Break-out Group 1

Which **criteria** should be considered when conducting read-across in the context of MNs **HH hazard** assessment?

Break-out Group 2

Which **criteria** should be considered when conducting read-across in the context of MNs **ENV hazard** assessment?

Break-out Group 3

What **adaptations** of existing read-across approaches used for conventional substances are needed for MNs?

Break-out Group 4

Criteria to be considered for read across in the context of HA for MNs and **what data of what quality** are required?

OECD Expert Meeting: Grouping and Read-Across for MNs (4)

CONCLUSIONS - 1

- Grouping and read-across for MN hazard assessment **based on the general scheme used for conventional chemicals** is in principle **possible**
- However, **MN-specific guidance is needed** on:
 - how to assess **sameness and similarity** between MNs of the same substance or different substances
 - what **information to consider** for developing a robust justification for read-across between MNs
- There is **already material to initiate developing MN-specific guidance**. However, the guidance would need to be **updated as soon** as new information/better knowledge becomes available and will need to be tested **with case studies**

OECD Expert Meeting: Grouping and Read-Across for MNs (5)

CONCLUSIONS -2

- The **parameters/criteria proposed** by the ... presented approaches are ... **valid elements** for initiating grouping and read-across. Depending on the MN and endpoint or concern addressed, **these parameters/criteria need to be adapted** (may differ). **Grouping and read-across are endpoint based** (one by one).
- Starting points for building a hypothesis on grouping and read-across for MNs could be the "**generic categories**" presented at Categorisation Workshop and the US NIOSH categories based on **solubility, shape and mode of action**
- **Uncertainties** need to be transparently addressed in any justification for MN grouping and read-across

OECD Expert Meeting: Grouping and Read-Across for MNs (6)

CONCLUSIONS - 3

- Data of **physico-chemical parameters** for each nanoform are **crucial starting points**.
- Benchmark values to define "**sameness**" or "**similarity**" not yet possible because:
 - Systematic testing for PChem – effect correlation is missing
 - Limitations in (quality of) available test data
 - To date best we can do is to identify the PChem that matter (most)
- **Data quality is critical:**
 - Monitoring of phys-chem parameters during testing
 - Harmonisation and standardisation of test methods

OECD Expert Meeting: Grouping and Read-Across for MNs (7)

RECOMMENDED FURTHER WORK

- **Terminology** to be further clarified and consistently applied
- **Nanospecific guidance** to be developed and tested with **case studies**. It is suggested that the guidance should provide users with **tiered approaches** for addressing data needs and concerns in MN grouping and read-across
- OECD **Test Guidelines** to continue being adapted to MNs specificities
- Further (international) **coordination and collaboration in research** is advisable (e.g. confirmatory testing, in vitro methods)
- **Harmonised dispersion** protocols to be further developed
- **Harmonised reporting** templates to enhance **comparability** of test results to be developed



European
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Working Party on Hazard Assessment Case Study on Grouping and Read- Across for Nanomaterials – Genotoxicity of Nano-TiO₂

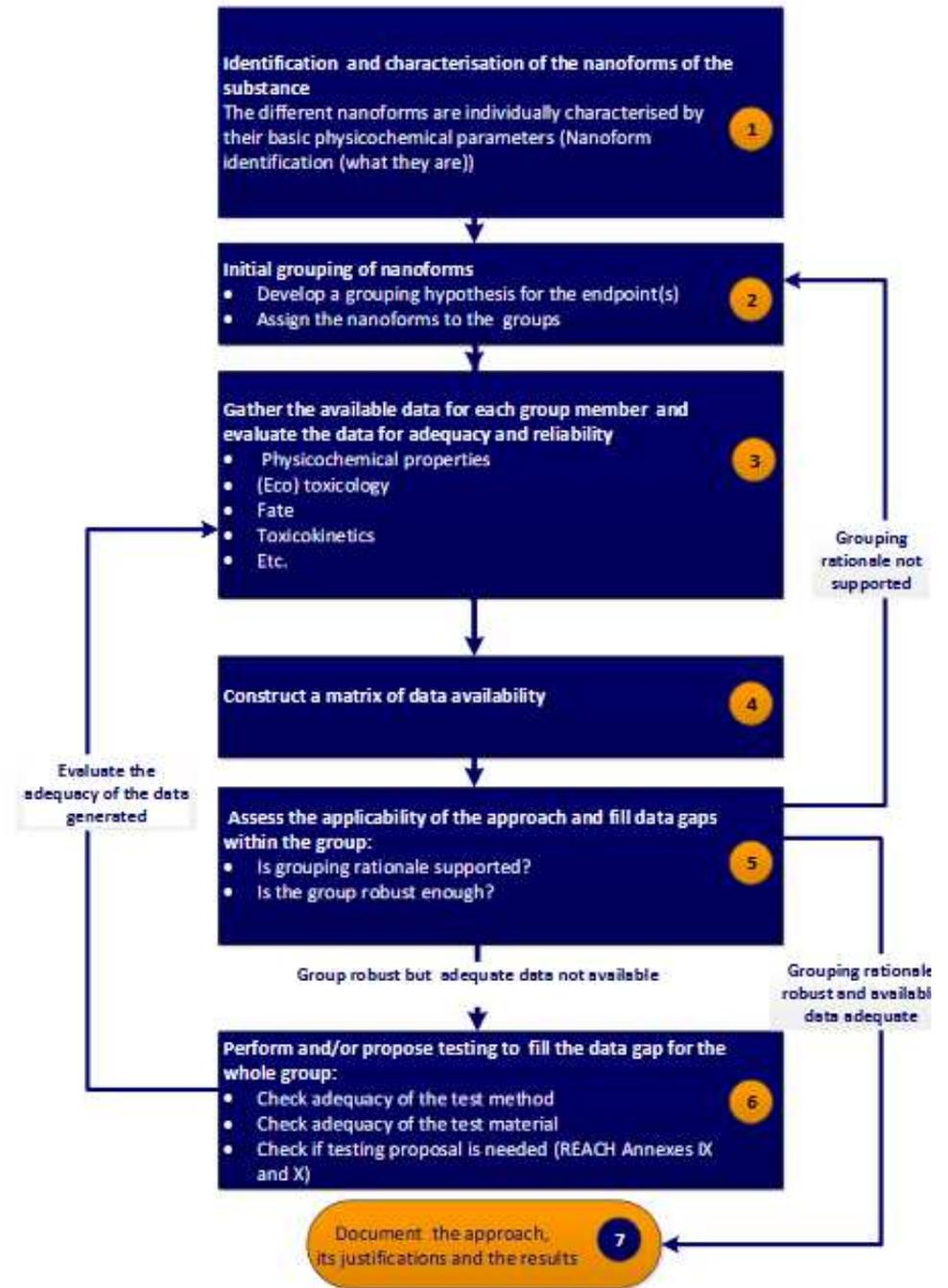
Evaluated the applicability of the workflow for grouping and read-across proposed in the REACH guidance update for nanomaterials

Identified sources of uncertainty associated with the read-across.

Purpose: determine the genotoxic hazard potential of 2 nano-TiO₂ target substances, by reading across *in vitro* comet assay results.

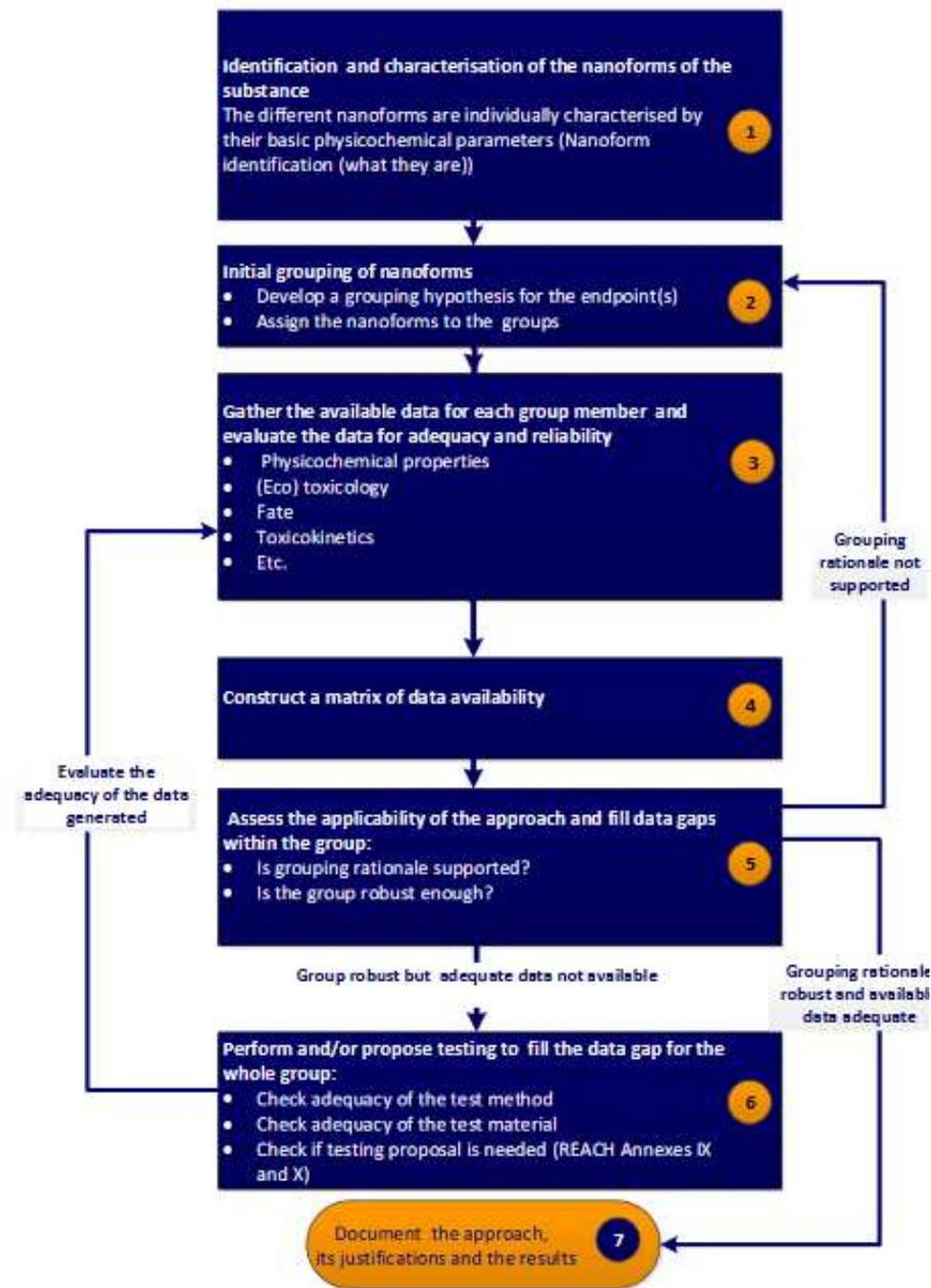
Dataset of the analogues: 6 NMs with different properties

Grouping hypothesis: nano-TiO₂ uncoated form may damage DNA, but this would be masked by the presence of non-reactive coating and large amounts of impurities on the surface

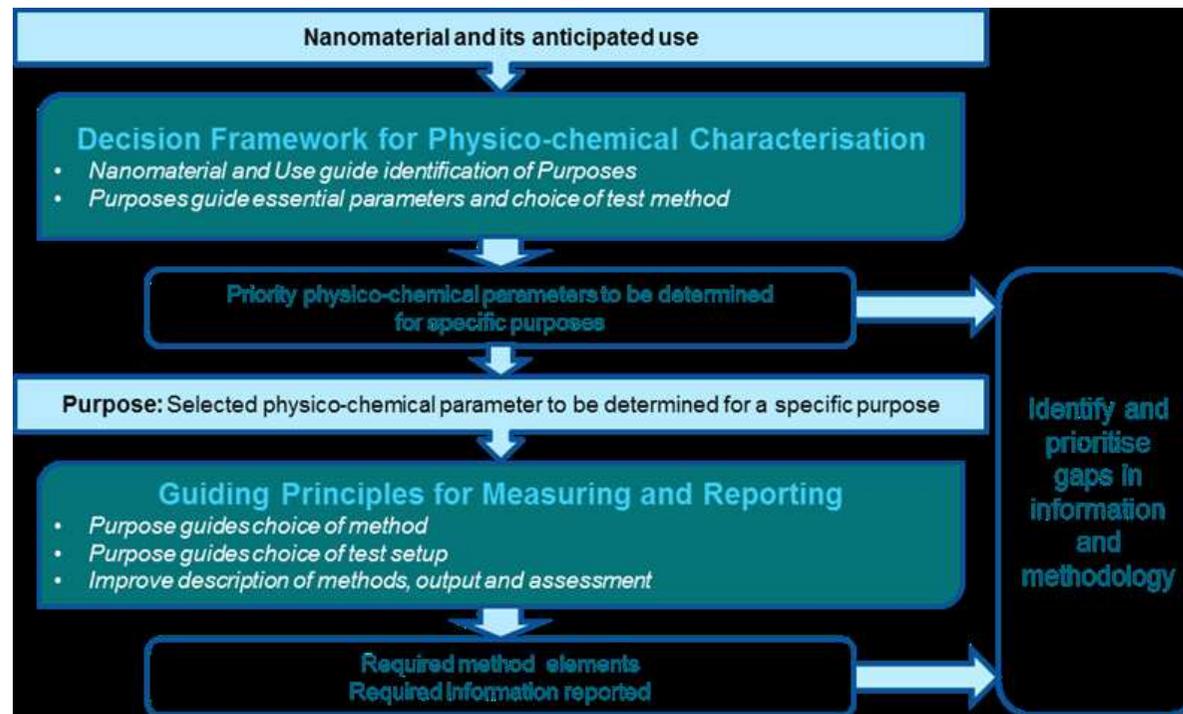


Case Study-2

- The workflow was **generally applicable** (some adaptations) to MNs.
- The **outcome** of the *in vitro* comet assay was **predicted** for the two target TiO₂ MNs, negative for the coated one, and positive for the uncoated one.
- **Results** were **verified** by experimental literature data.
- **Chemoinformatics** tools are **useful** to support the grouping hypothesis by identifying the differences between nanoforms and by supporting the weight of evidence
- The concept of **similarity** needs to be **extended**. For MNs other principles, added to structural similarity should be included.
- **Uncertainties** were identified; they relate to the **identification** of the (non-)nanoforms, **experimental variability** of the physicochemical and toxicological information and due to **the lack of measurement protocols** for MNs, and to the lack of **knowledge on their mechanisms** of genotoxic action



OECD WPMN Expert Meeting on a Physicochemical Parameters Framework for the Risk Assessment of MNs



and Guiding Principles for Measuring and Reporting

CONCLUDING

- Needs and Gaps identified
- Feasibility (in some cases) demonstrated
- Time to develop and demonstrate solid tools and approaches
- All stakeholders to collaborate to develop guidance

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**Thank you for your
attention!**

Juan Riego Sintes
Consumer Products Safety Unit

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YouTube: [EU Science Hub](https://www.youtube.com/EU_Science_Hub)**



FURTHER READING

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SOME PROJECTS TO FOLLOW

NANoREG

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