Nanotechnology Regulation and the OECD

- Under the Working Party on Manufactured Nanomaterials, the OECD aims to "promote international co-operation in human health and environment safety related aspects of manufactured nanomaterials in order to assist their safe development."
- The WPMN has four steering groups on:
  - Testing and Assessment of Manufactured Nanomaterials (SGTA),
  - Risk Assessment and regulatory programme (SGAP)
  - Exposure Measurement and Exposure Mitigation.
  - Environmentally Sustainable Use of Manufactured Use
- A set of 13 representative nanomaterials was tested for 50 endpoints. The second phase of the programme to assess and analyze the data produced by the testing programme will start in 2015.
- A number of guidance documents (including on sample preparation and dosimetry for testing) were already published.
- 34 projects focusing on the evaluation/revision/creation of test guidelines for Nanomaterials are at various stages of completion.
- Several projects looking at the developing regulatory tools for the risks assessment and management of Nanomaterials are underway, including projects on grouping of nanomaterials, assessing species variability, addressing dissolution in environmental risk assessment, and identifying alternative testing strategies.
- Several projects looking at various aspects of exposure and exposure measurement are underway.
- A guidance manual to support life cycle approaches in decision-making in relation to nanomaterials is being developed.
- There are opportunities to engage the process and provide input to the work of each of the steering groups.

The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organization playing a significant role in the regulation of chemicals through its Environment, Health and Safety programme (EHS). The OECD is the place where member states come together to, among other things, agree and validate test guidelines and Good Laboratory Practices (GLP) for chemicals (including nanomaterials) (See text box 6). Data produced according to these guidelines benefit from the Mutual Acceptance of Data (MAD) mechanism among all states that have signed the MAD agreement (See text box 5) . These validated methods are then integrated in regulatory risk assessment processes all across the OECD states.

Within the OECD, chemical related work is organized under the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology (The Joint Meeting). The joint meeting oversees 12 main subsidiary bodies called working groups or task forces. They include working groups on test guidelines; endocrine disrupters testing and assessments; task forces on Exposure assessment, on Hazard assessment, PRTR and more.[1]

Two OECD working parties address questions raised by nanotechnologies:

- **Working Party on Biotechnology, Nanotechnology and Converging Technologies** to "advise on emerging policy-relevant issues in science, technology and innovation, related to the responsible development and use of nanotechnology,"[2] and

- **Working Party on Manufactured Nanomaterials (WPMN)** to "promote international co-operation in human health and environment safety related aspects of manufactured nanomaterials in order to assist their safe development."[3]

Working Party on the Safety of Manufactured Nanomaterials (WPMN)

The WPMN, created in 2006, promotes international cooperation in human health and environmental safety in manufactured nanomaterials through the work of several steering groups (SGs). The WPMN brings together OECD member countries and several non-member partners, including Brazil, Thailand, China, South Africa, The Russian Federation, as well as intergovernmental organizations (such as UNITAR, WHO, FAO, and UNEP) and delegation from industry , Trade Unions , and Environmental NGOs. Observers can participate in all aspects of the work of the WPMN and its steering groups.

The work of WPMN is currently organized in four steering groups:

1. **Testing and Assessment of Manufactured Nanomaterials (SGTA),**
2. **Risk Assessment and regulatory programme (SGAP)**
3. **Exposure Measurement and Exposure Mitigation.**
4. **Environmentally Sustainable Use of Manufactured Use.**

Testing and Assessment of Manufactured Nanomaterials (SGTA, former SG 3/4/7)

This merged steering group combines SG3 on the Testing Programme (Sponsorship Programme), SG4 on Manufactured Nanomaterials and Test Guidelines and SG7 the Role of Alternative Methods in Nano Toxicology

The Sponsorship Testing Programme aims at testing a selection of 13 representative nanomaterials[5] for a large number of endpoints in order to (1) understand the kind of information on intrinsic properties that may be relevant for exposure and hazards assessment, (2) gain practical experience and evidence on whether current test guidelines and other methods are applicable, and (3) to help design standardized tests. Endpoints to be tested included endpoints on:

- *Physico-chemical properties and material characterizations* (17 endpoints including water solubility, particle size, crystallinity, surface characteristics etc..);
- *Environmental fate* (15 endpoints, including biodegradability, adsorbtion, accumulation etc..);
- *Environmental toxicology* (6 endpoints including effects on aquatic and terrestrial organisms);
- *Mammalian toxicology* (9 endpoints including inhalative toxicity, reproductive toxicity, genotoxicity etc…); and
- *Material safety* (3 endpoints, including flammability).[6]

Experimental data was produced for each of the 13 representative nanomaterials during the first phase of the programme, which ended in 2013. The program is now entering in its second phase, to assess and analyze the data. This phase is expected to begin in 2015.

Box 1: OECD & the WPMN

The OECD is an intergovernmental organization of 34 countries with market economies working together to boost employment, support sustainable economic growth, contribute to growth in world trade, and maintain financial stability. The OECD membership comprises the most economically advanced countries in the world and accounts for 63 per cent of the world's GDP.[4] The 34 member states are the main decision makers and usually take a very hands-on approach to the work. They decide the organization's program of work and budget on a biennial basis, who attends meetings, and set the rules governing internal procedures.

The work of the Working Party on Manufactured Nanomaterials is conducted principally in the context of the its steering groups, which operate independently, according to specific objectives, work plans and timelines adopted by the WPMN. Participation and specific roles in the various steering groups is voluntary. Each of the steering groups self organizes under a chair nominated by the WPMN (usually two co-chairs). The results of each project are evaluated and subsequently endorsed by the WPMN before being published more widely according to a complex internal procedure (see text box 5)

The WPMN meets every 8 months, and brings together delegates from ministries and agencies responsible for human health and the environment together. In the intercessional period, steering group activities, including experts meetings, workshops, conference call etc… take place.

When the WPMN was first established, 9 steering groups were established. They were reorganized into the 4 steering groups outlined in the factsheet at the 12th WPMN in 2013.

The experimental data from the first phase of the sponsorship program was compiled in IUCLID format dossiers. These are now in the process of being declassified with an executive summary and preamble (with caveats on use of the data). An analytical paper is also being prepared to identify the lessons learned from the first phase and establish the path forward for the second phase of the programme. In addition, the WPMN secretariat will prepare a publication (in the form of a brochure or leaflet) explaining the testing programme and its findings so far.

(Oct. 2015 update) A dedicated public website was launched in June 2015 to communicate the results from the Testing Programme. The website contains a compilation of over 160 documents in a EUCLID format and includes a very useful synthetic view of the content of the dossiers and available information as well as an endpoint finder in the form of a searchable excel spreadsheet: http://www.oecd.org/chemicalsafety/nanosafety/testing-programme-manufactured-nanomaterials.htm

Box 2: Who Does What?

The testing of each material in the sponsorship programme was done collectively by a team including:

- A Lead Sponsor (who coordinates the testing which is deemed appropriate for each specific nanomaterials);
- A Co-Sponsor (who conducts some of the testing deemed appropriate for each nanomaterials); and
- A Contributor (who provides the test data, reference or testing materials relevant to the lead and co-sponsors)[7]

In the context of the sponsorship testing program, OECD produced a series of guidance manuals. These included a guidance manual for the testing of manufactured nanomaterials to support the work of lead sponsors, co-sponsors and contributors[8] and a preliminary guidance note on sample preparation and dosimetry for the safety testing of manufactured nanomaterials.[9]

ECHA chairs the merged SG. It includes 34 projects at various stages of completion focusing on the evaluation/revision/creation of test guidelines relating to:

- Physical chemical properties
- Effects on biotic systems
- Environmental fate, degradation and bioaccumulation
- Effects on human health

One of the overall objectives of this SG is the assessment of the applicability of the test guidelines and guidance documents for nanomaterials to evaluate whether or not the existing Test Guidelines are adequate for addressing Manufactured Nanomaterials, and question whether or not new ones should be created. A number of expert workshops organized in the past 5 years have addressed inhalation toxicity testing, environmental fate and eco-toxicology, genotoxicity, toxokinetics and grouping. As a consequence, seven projects are being carried forward to undertake test guideline development.

Box 3: OECD Test Guidelines

The OECD Test Guidelines for the testing of chemicals are "a collection of the most relevant internationally agreed testing methods used by governments, industry and independent laboratories to assess the safety of chemical products."[10] The test guidelines are applied in situations of regulatory safety testing and chemical notification and registration. They are supposed to be regularly updated to reflect scientific discoveries and the changing regulatory scene. The update process can, however, be lengthy and costly.

The Test Guidelines are divided into five sections:

1. ***Physical Chemical Properties*** – examples of test guidelines include testing for the determination of pH, acidity and alkalinity, boiling point (among others);[11]
2. ***Effects on Biotic Systems*** – examples of test guidelines include Fish Embryo Acute Toxicity (FET) Test, Fish Sexual Development Test, Avian Reproduction Test;[12]
3. ***Degradation and Accumulation*** – examples of test guidelines include bioaccumulation in terrestrial oligochaetes, photo-transformation of chemicals in water (direct photolysis), Biodegradability in Seawater;[13]
4. ***Health Effects*** – examples of test guidelines include Acute Eye Irritation/Corrosion, In-Vitro Skin Irritation, Carcinogenicity Studies, Neurotoxicity Study in Rodents;[14]
5. ***Other Test Guidelines*** – examples of test guidelines include stability of pesticides residues in stored commodities, crop field trials, magnitude of pesticide residues in processed commodities.[15]

Box 4: WPMN procedures for publication of outcome docs

Proposed documents are identified in the programme of work as agreed by governments. Initial draft may be prepared by the secretariat or more often (in particular in the case of the WPMN) by one or more lead governments working together.

Drafts then go through several rounds of discussion in the WPMN before a consensus is reached. As part of this process, although the member states are the decision-makers, comments and participation in the elaboration of the document from other stakeholders are welcome and actively encouraged. Comments generally need to be transmitted to the lead drafter and/or secretariat through an official delegation (either national delegations, or delegations of specific groups, such as the environmental NGO, currently led by CIEL, the delegation of the Trade Unions Advisory Committee to OECD (TUAC) or the delegation of the Business and Advisory Committee to OECD (BIAC).
Once a consensus is achieved in the WPMN, the document then goes to the supervisory committee, the Chemicals Committee, where it is declassified and then published. Declassification and publication of a document can take up to 2 years after consensus is reached in the WPMN.

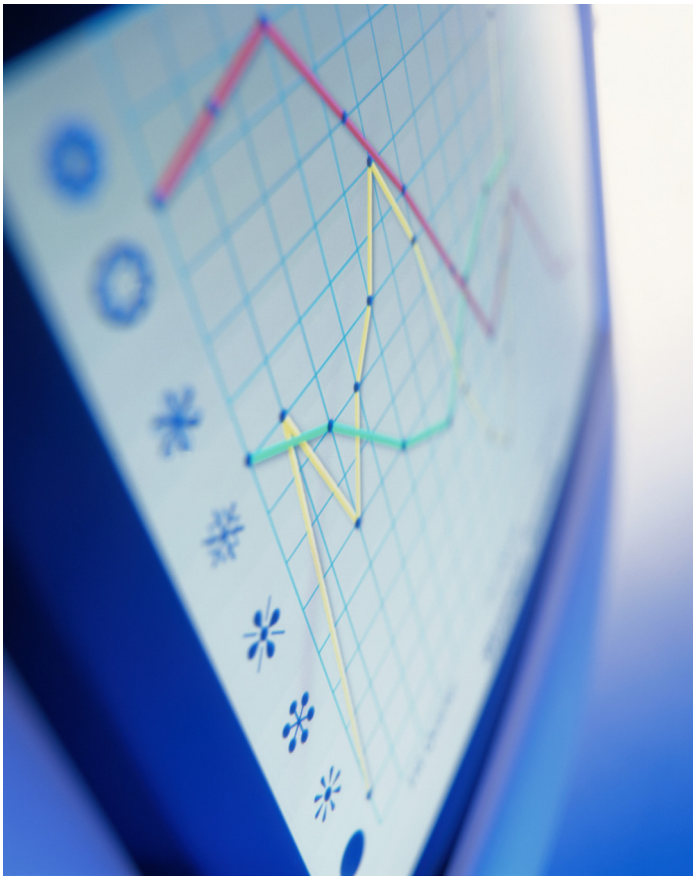
All declassified documents published by the WPMN are available at http://www.oecd.org/science/nanosafety/publicationsintheseriesonthesafetyofmanufactured-nanomaterials.htm

Risk Assessment and regulatory programme (SGAP, former SG 5/6)

This steering group combines SG5 on Cooperation on Voluntary Schemes and Regulatory Programmes and SG6 on Cooperation on Risk Assessment. It is co-chaired by Germany and Canada. SG5 was tasked with creating reports on regulatory regimes (from information gathered from national surveys) and promoting cooperation on voluntary schemes. SG6 sought to evaluate opportunities to strengthen risk assessment capacity through information exchange and opportunities to strengthen risk assessment capacity.

The overall objective of SGAP is to support the OECD Council Recommendation, which concluded that nanomaterials could be managed through existing chemical regulatory frameworks or other management systems, adapted to take into account the specific properties of manufactured nanomaterials. SGAP work led to the publication of "Important issues in risk assessment of manufactured nanomaterials" in 2012. The important issues identified were later prioritized in 2013.

The newly merged steering group now focuses on cooperation in risk assessment and other regulatory programmes. This involves working with member states to develop targeted projects on risk assessment priorities[16] and interacting with other SGs and OECD bodies to determine areas for cooperation. Projects include:



- Identifying and reviewing studies from the Sponsorship Programme and the published literature addressing the toxicity of a single nanomaterial (similar nanomaterials) in different mammalian species (led by Germany)
- Addressing dissolution in environmental risk assessments using silver as a case-study and then extrapolating to MNs of different types (led by Canada)
- Approaches to develop or use concepts of grouping, equivalence and read-across based on p-chem properties of MNs for human health and eco hazard assessments (led by Japan)
- Alternative Testing Strategies: State of the Science for Read Across and Risk Assessment Guidance (led by the US and Canada).

Exposure Measurement and Exposure Mitigation (SG 8)

This steering group, chaired by OSHA (the U.S. Occupational Safety and Health Administration) seeks to collect exposure data on nanomaterials necessary to do a thorough risk assessment and determine the appropriate methods for exposure mitigation. This steering group operates through exposure-specific end points: for example, examining human occupational, human non-occupational and biota endpoints. Examples of such projects include the project on Techniques and Sampling Protocols for Determining the Concentrations of Manufactured Nanomaterials in Air, which was led by Australia.[17]

A survey on available methods and models for assessment on exposure to MNs issued in March 2011 led to a Project Compilation of Available Methods and Models Used for Assessing Exposure to Manufactured Nanomaterials. Some notable case studies include the exposure assessment for nanosilver done in August 2011. The collection of exposure information, for example on an estimation of individual workers' exposures that would allow for the development of a job-exposure matrix, allows for progress on guidance documents on exposure assessments.

Another fundamental issue addressed by this steering group is determining a cohesive policy for the disposal and treatment technologies for manufactured nanomaterials.

Box 5: Mutual Acceptance of Data

In 1981, the Council adopted the decision on Mutual Acceptance of Data – stating that "the test data generated in any OECD country along the Test Guidelines and under the Principles of Good Laboratory Practice should be accepted in other countries for assessment and for the purpose of protecting human health and the environment."[18]

This system is intended to reduce duplicative testing, increase collaboration between governments and save important testing resources, thereby allowing more chemicals to be tested.[19]

There are two different types of participation in the MAD agreement: OECD member states who comply with Test Guidelines and GLP, and non-member states who can demonstrate that their test facilities produce data to an equal level of quality. This allows for OECD states to have tests done in MAD-compliant non-OECD states.

There are currently 40 countries parties to the MAD agreement, with the most recently joined country Malaysia as of April 2013.[20]

Box 6: Principles of Good Laboratory Practices

The "Principles of Good Laboratory Practice" (GLP) is a quality management system, adopted by the OECD in 1981 that allows the OECD to maintain high standards for how laboratory studies are "planned, performed, monitored, recorded and reported." This system, along with the MAD, seeks to create international harmonization of test methods, allowing high quality data to be obtained in the same way across all participating states.

Although GLP was originally developed to ensure uniformity, consistency, reliability, reproducibility, quality, and integrity of chemical safety data, and avoid outright scientific misconduct and fraud, it has been criticized for being too strict and leading to the exclusion of certain valid results from the regulatory processes of risk assessment and risk management. This has particularly been the case for results produced by academic laboratories published in peer-reviewed journals because of the expense and extent of the equipment, personnel and resources needed to adequately follow the regulations.

These extensive guidelines come at a great cost and require intense documentation, which can put great pressure on those that cannot satisfy the requirements – and in turn lead to an unnecessary duplication of data.

Recent developments in SG8 include:

- Harmonized tiered approach for the measurement and Assessment of Airborne Exposure to Engineered nano-objects in the workplace; with declassification of the report scheduled for February 2015;
- Completed Exposure Assessment Study on Nanogold (led by South Africa): declassification and publication of the report is now being discussed;
- A study on the Assessment of Biodurability of Nanomaterials and Their Surface Ligands (led by South Africa); will be presented as room document at WPMN-14 (Feb 2015);
- A new work proposal by the US: survey of exposure studies, focus on Silver, Titanium Dioxide, multiwall Carbon Nanotubes;
- A database planned for products containing nanomaterials.

Environmentally Sustainable Use of Manufactured Use (SG9)

This steering group seeks to explore the potential benefits of the applications of manufactured nanomaterials. The aim of this steering group is to gain information about the life cycle of nanomaterials and different applications of different stages of this cycle: either in addressing an environmental problem or indirectly contributing to environmental objectives,[21] or mitigating uncertainties surrounding the new technology.

This steering group's work began with the nano-benefits conference of July 2009. In this conference, the steering group sought to enhance knowledge about life cycle aspects of manufactured nanomaterials (with tests done at different stages of development).

Currently, SG9 is developing a Guidance Manual aiming at supporting decision making in various situations, including research, innovation, product development, scaling-up of production, marketing, and end-of-life, as well as regulatory decisions. This Guidance Manual aims particularly to better link risk assessment and life cycle analysis information. Its recommendations will be checked on the basis of a "data-rich" case study, i.e. CNTs in semiconductors.

This SG is also involved in reviewing a study on the Sustainable Development of tires involving Nanotechnology. This is a joint project with WPN, strongly led by the tire industry.

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