



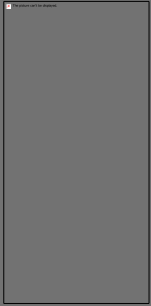
THE SAFETY ASSESSMENT OF NANOMATERIALS



About this talk

This talk will describe:

- The value of harmonised test guidelines for chemicals for use in hazard identification and risk assessment;
- The role of OECD's test guidelines programme and the benefits for both governments and industry in using OECD test guidelines;
- It will cover the process by which many test guidelines were found to be suitable for nanomaterials;
- Not all test guidelines are suitable for nanomaterials and it should with the example of inhalation toxicity how new nano specific approaches have been developed.



MUTUAL ACCEPTANCE OF DATA, TEST GUIDELINES AND GOOD LABORATORY PRACTICES



Mutual Acceptance of Data (MAD)

Recommendation
on the Safety
Testing and
Assessment of
MN

→ **Test
Guidelines**

A single quality standard
should be applied for
testing of all chemical
substances

**Good Laboratory
Practice**

A single quality
standard for
test facilities
throughout OECD

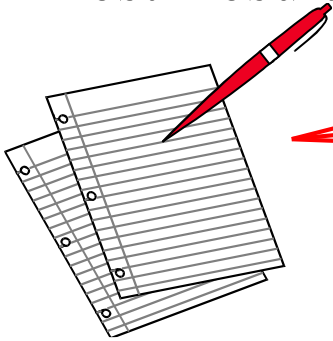
Mutual Acceptance of Data
Legally binding on OECD Member countries
and other MAD Adherents

- Avoids duplication of testing: around Euros 150 million saved each year
- Reduces use of animals
- Reduces trade barriers

C(81)30 Council Decision on MAD

Country A Lab *Chronic Tox*

Test Results



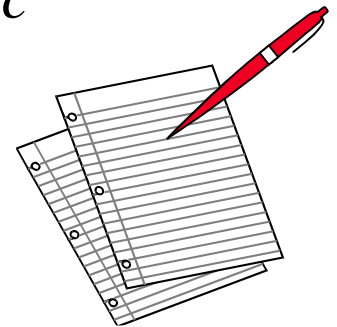
Country B regulator

Country C regulator

Country D regulator

Country B Lab *Aquatic Tox*
Test Results

Country A regulator



Note: key aspects are “no repeat testing” and interpretation of test results *is government prerogative*



SAVINGS FROM MAD



- BY AVOIDING DUPLICATIVE TESTING:
 - At least € 150 Million / Year
 - Reduction in animal testing
 - More chemicals can be evaluated quicker

www.oecd.org/ehs/publications



Test Guidelines

Approximately 150 Test Guidelines:

- Section 1: Physical Chemical Properties
- Section 2: Effects on Biotic Systems
- Section 3: Degradation and Accumulation
- Section 4: Health Effects
- Section 5: Other Test Guidelines (i.e. Pesticides residues)




Difference between OECD Test Guidelines and Guidance Documents

Test Guideline

- Regulatory need explained by the SPSF*
- **Covered by MAD**
- Fixed test protocol with **validity criteria**
- Thorough experimental validation needed with fixed protocol
- *Takes time and resources and more cumbersome to update*

Guidance Document

- Regulatory need
- **Not** covered by MAD
- Can be a test method, or it provides technical guidance for the use of test guidelines
- Scientific validation could be limited and based on published literature
- *Faster to develop and revise*

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Fullerenes(C60)	Japan, US		China
SWCNTs	Japan, US		Germany, Canada, EC, France, China
MWCNTs	Japan, US	Korea, BIAC	Germany, Canada, EC, France, China
Silver nanoparticles	US, Korea	Germany, Canada	Australia, EC, France, China
Iron nanoparticles	China		Canada, US
Carbon black			Germany, US
Titanium dioxide	Germany	Canada, Spain, BIAC, Korea, US	France, China
Aluminium oxide			Germany, US
Cerium oxide	UK/BIAC, US	Netherlands,	Australia, Germany, EC
Zinc oxide	UK/BIAC	BIAC	Australia, Canada,
Silicon dioxide		BIAC, Korea	EC, France
Polystyrene			Korea
Dendrimers		Spain	US
Nanoclays			US



<http://www.oecd.org/chemicalsafety/nanosafety/testing-programme-manufactured-nanomaterials.htm>

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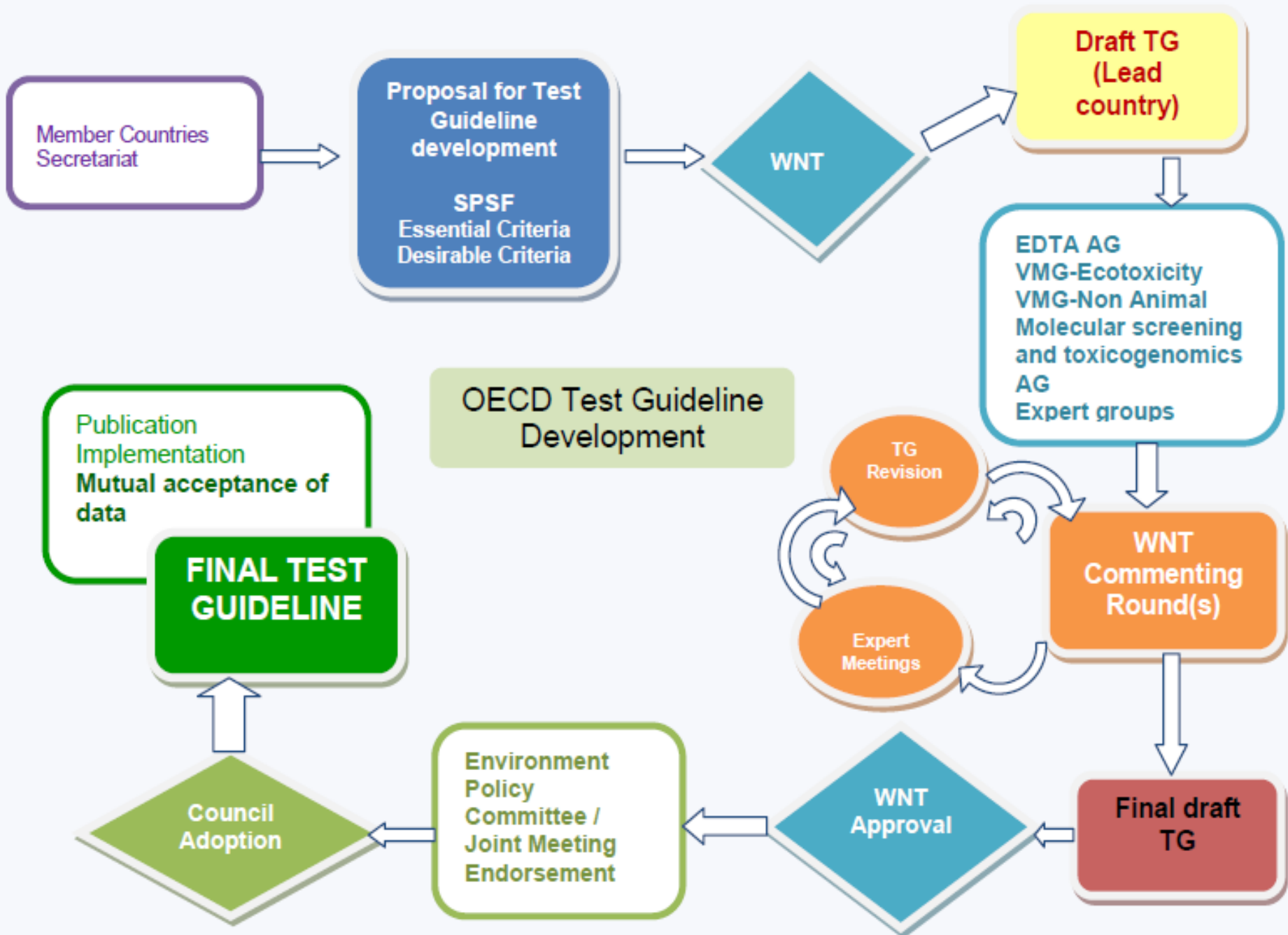


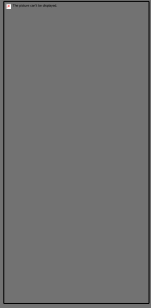
Process for Project proposals (SPSF) for the Test Guidelines Programme

- New and updated **Test Guidelines** are developed to:
 - Meet regulatory needs of member countries
 - Reflect scientific progress
 - Address animal welfare aspects
 - Improve cost-effectiveness of test methods

Standard Project Submission Form (SPSF)

Submission: November for discussion at the following WNT Meeting





NANOSAFETY



Test Guidelines/ Guidance Documents under preparation

- **Amendments to the Inhalation TGs and GD to Accommodate NM**
- **GD on Aquatic (and Sediment) Toxicology Testing of NM**
- **GD for Dispersion and Dissolution of NM in Aquatic Media – Decision Tree**
- **GD on Assessing the Apparent Accumulation Potential of NM**
- **TG for Dispersibility and Dispersion Behaviour of NM in Aquatic Media**
- **(new) TG for NMs Removal from Wastewater**
- **GD on the Adaptation of *In Vitro* Mammalian Cell Based Genotoxicity TGs for Testing of MNs**

New SPSF under development - review TG 110 - Particle Size Distribution/Fibre Length and Diameter Distributions



An example: Relationship to the test guidelines on dispersion stability and dissolution rate of nanomaterials in **aqueous** media

GD on dissolution rate and dispersion stability of nanomaterials for environmental risk assessment



TG 318 on dispersion stability in simulated environmental media (published)



TG on dissolution rate in aquatic media (1 draft April 2017)



Explanations and recommendations for a (jointly) consideration of testing, interpreting and usage of data on both dissolution rate and dispersion stability of NMs



What is Needed

Session 1: Physical Chemical Properties

- TG 105 - Water Solubility – Specific Modification Suggested
- TG 108 - Complex Formation Ability in Water (Polarographic Method)
- TG 109 - Density of Liquids and Solids
- TG 112 - Dissociation Constants in Water
- TG 115 - Surface Tension of Aqueous Solutions

Session 4: Health Effects

- TG 428 Skin Absorption: *In Vitro* Method
- TG 431 *In vitro* skin corrosion: reconstructed human epidermis (RHE) test method
- TG 437 Bovine Corneal Opacity and Permeability Test Method for Identifying Ocular Corrosives and Severe Irritants



What is Needed

Session 2: Effects On Biotic Systems

- TG 201 - Freshwater Alga and Cyanobacteria, Growth Inhibition Test
- TG 202 - Daphnia sp. Acute Immobilisation Test
- TG 210 - Fish, Early-life Stage Toxicity Test
- TG 216 - Soil Microorganisms: Nitrogen Transformation Test
- TG 217 - Soil Microorganisms: Carbon Transformation Test
- TG 220 - Enchytraeid Reproduction Test
- TG 222 - Earthworm Reproduction Test (*Eisenia fetida*/*Eisenia andrei*)
- TG 225 - Sediment-Water *Lumbriculus* Toxicity Test Using Spiked Sediment



Status of Revisions on Inhalation

- The amended TGs 412 and 413 **are finalised** published at the end of October 2017 – **First TGs amended for NM!**
- The amendments concern:
 - Bronchoalveolar lavage (BAL) measurements;
 - Particle-Size Distribution For Test Atmospheres;
 - Post-Administration Duration; and
 - Lung Burden Measurements.



TG 318- Dispersion behaviour of NMs in different environmental media

- This **new** TG is **finalised** and published
 - **First TGs for NM!**
- This TG aims to determine the dispersion stability of NM in aqueous media in dependence of environmental conditions.



NEW PROPOSALS (Agreed, February 2018)

- Determination of solubility and dissolution rate of nanomaterials in water and relevant synthetic biologically mediums
- Identification and quantification of the surface chemistry and coatings on nano- and microscale materials
- Determination of the Dustiness of Manufactured Nanomaterials
- Applicability of the TG 442D in vitro skin sensitisation for nanomaterials
- Aquatic (Environmental) Transformation of Nanomaterials
- Development of new Test Guideline on Toxicokinetics or Amendments to OECD TG 417 to accommodate NM
- Assessment of the durability of nanomaterials and their surface ligands in environmental surroundings



Thank you!

Safety of
Manufactured Nanomaterials
www.oecd.org/env/nanosafety