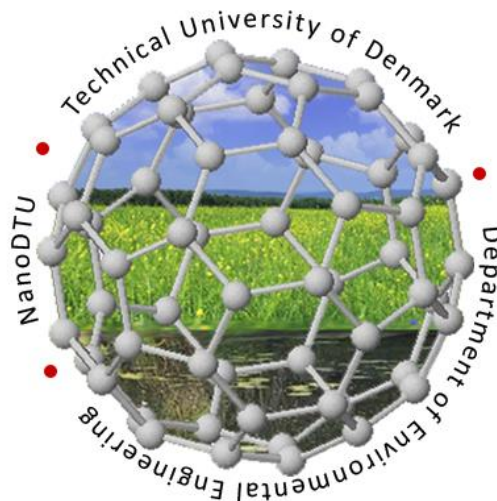


Regulering af nanomaterialer i EU



Regulation of NM

NM application are diverse and hence many pieces of EU legislation come into play

- Chemical legislation (REACH)
- Biocides
- Classification Legislation
- Water framework Directive
- Pharmaceutical legislation
- Novel foods
- Worker Directives
- IPPC
- Waste legislation

REACH

June 2007

- Registration, Evaluation, and Authorization of CHemicals
- Producers are required to submit eco-/toxicological information depending on tonnage
- Applicable > 1 ton/yr/producer or importer

L 396/850  Official Journal of the European Union 30.12.2006

DIRECTIVE 2006/121/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 18 December 2006

amending Council Directive 67/548/EEC
on the approximation of laws, regulations and administrative
provisions relating to the classification, packaging and labelling of
dangerous substances in order to adapt it to Regulation (EC) No 1907/2006
concerning the Registration, Evaluation, Authorisation and Restriction
of Chemicals (REACH) and establishing a European Chemicals Agency

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission,

Having regard to the Opinion of the European Economic and Social Committee¹,

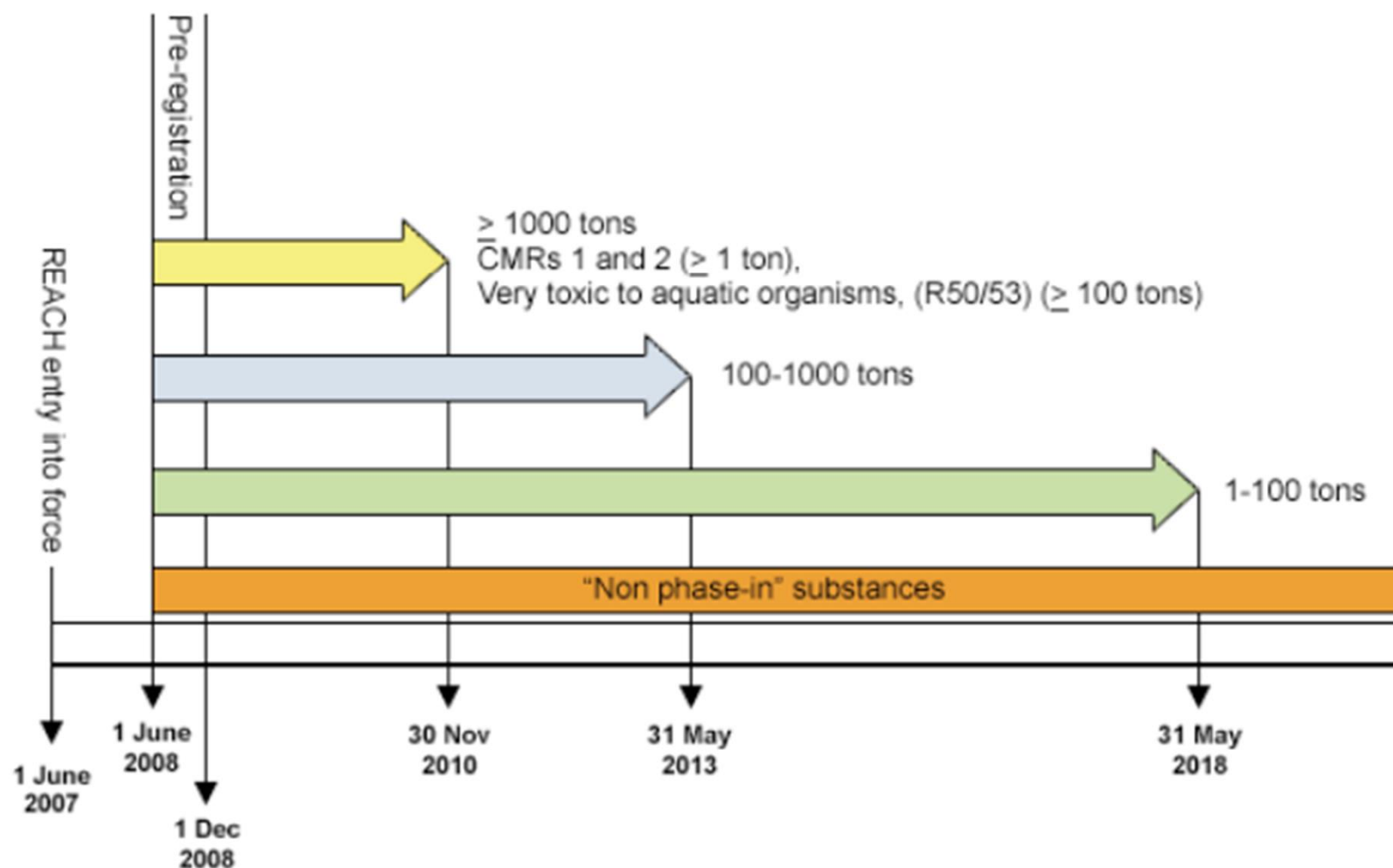
After consulting the Committee of the Regions,

Acting in accordance with the procedure laid down in Article 251 of the Treaty²,

¹ OJ C 294, 25.11.2005, p. 38.

² Opinion of the European Parliament of 17 November 2005 (OJ C 280 E, 18.11.2006, p. 440), Council Common Position of 27 June 2006 (OJ C 276 E, 14.11.2006, p. 252) and Position of the European Parliament of 13 December 2006 (not yet published in the Official Journal).

REACH Timeline



REACH Registration

- Substances manufactured or imported in volumes above 1 ton need registration
- A technical dossier has to be submitted to ECHA on
 - Physicochemical, ecological and toxicological data
 - How products are used
 - Potential for exposure is that might impact human health or the environment
 - Classification and labelling
 - Safe uses for each application
 - ECHA has indicated that it will assess each dossier for completeness within three weeks



Chemical Safety Reports

- For substances produced > 10 tonnes per producer per year a chemical safety report has to been produced
- It should include
 - human health hazard assessment;
 - physicochemical hazard assessment;
 - environmental hazard assessment;
 - persistent, bioaccumulative and toxic (PBT) and very persistent and very bioaccumulative (vPvB) assessment
 - Proposals for further testing to limit animal testing

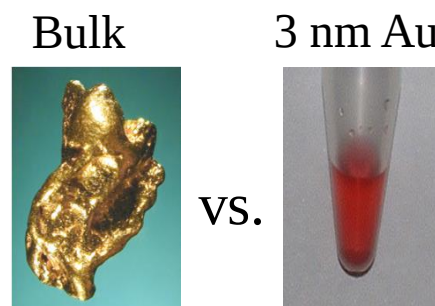
REACH Definition of Substance

Definition of a substance is key

- *"a chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used..."*
(EP & CEU 2006)
- Nanomaterials fall under the scope of REACH, but...

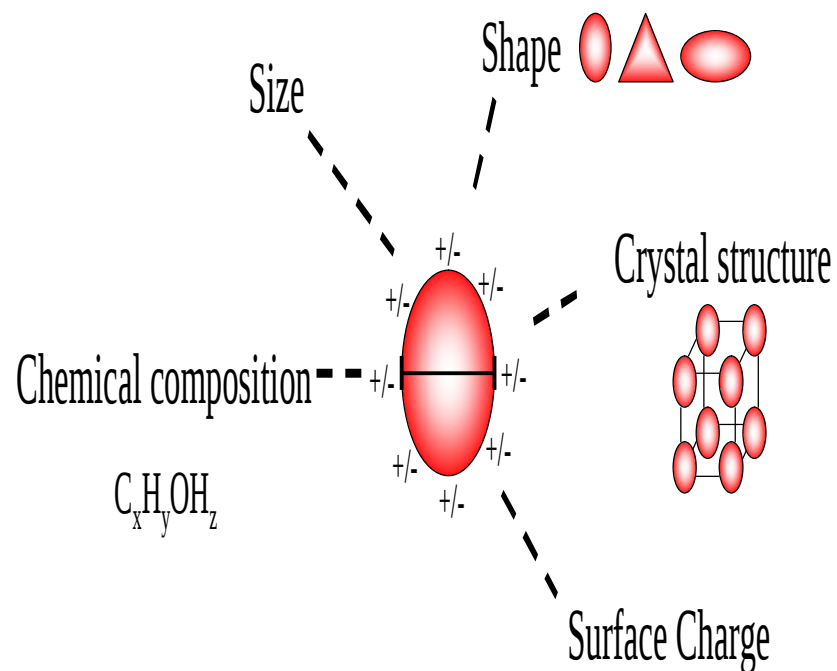
Nano vs. Bulk form

- Should a nano-equivalent of a substance be considered as the same substances under REACH?
- If yes, how to ensure the appropriateness of the hazard information data
- If no, hazard information would have to be generated*, but how should this be done?



NP variation

- Manufactured NPs can vary very much
 - chemical composition
 - degree and type of purity
 - $\approx$ Trillion combinations!!!
- Should all be registered?



Only 3 nanomaterials registered under REACH

May 2011

EN

E-0002756/2011

Answer given by Mr Potočník
on behalf of the Commission
(12.5.2011)

1. Regulation (EC) No 1907/2006¹ (REACH) deals with substances, in whatever size, shape or physical state. Substances at the nanoscale are therefore covered by REACH and its provisions apply, although REACH does not have special provisions for nanomaterials. Registrants could select "nanomaterial" as the state/form of the substance in section 2.1 (classification and labelling according to GHS) and section 4.1 (appearance/physical state/colour) or provide relevant information on nanoforms in other parts of registration dossiers submitted in the IUCLID 5.2 format. All dossiers submitted after 22 March 2010 were required to be in this format.

Of the dossiers received in IUCLID 5.2 format, 3 substances had "nanomaterial" selected as the state/form of the substance. However, as the assessment of the dossiers is still ongoing, it is premature to draw any conclusions about the number of dossiers covering nanomaterials.

<http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//TEXT+WQ+E-2011-002756+0+DOC+XML+V0//EN&language=ET>

DTU Environment

Department of Environmental Engineering

The NANO SUPPORT project



Ref. Ares(2012)314828 - 16/03/2012

NANO SUPPORT Project
Scientific technical support on
assessment of nanomaterials in
REACH registration dossiers and adequacy of
available information

AA N°07.0307/2010/581080/AA/D3
 between DG Environment (DG ENV) and the Joint Research Centre (JRC)

Final Report
on analysis and assessment
(Task I, step 3&4&5) and
options for adapting REACH (Task II, step 1)

Frans M. Christensen (JRC Technical Responsible)
 Nanosafety & Regulatory Methods Competence Group
 I.04 Nanobiosciences Unit
 JRC-IHCP

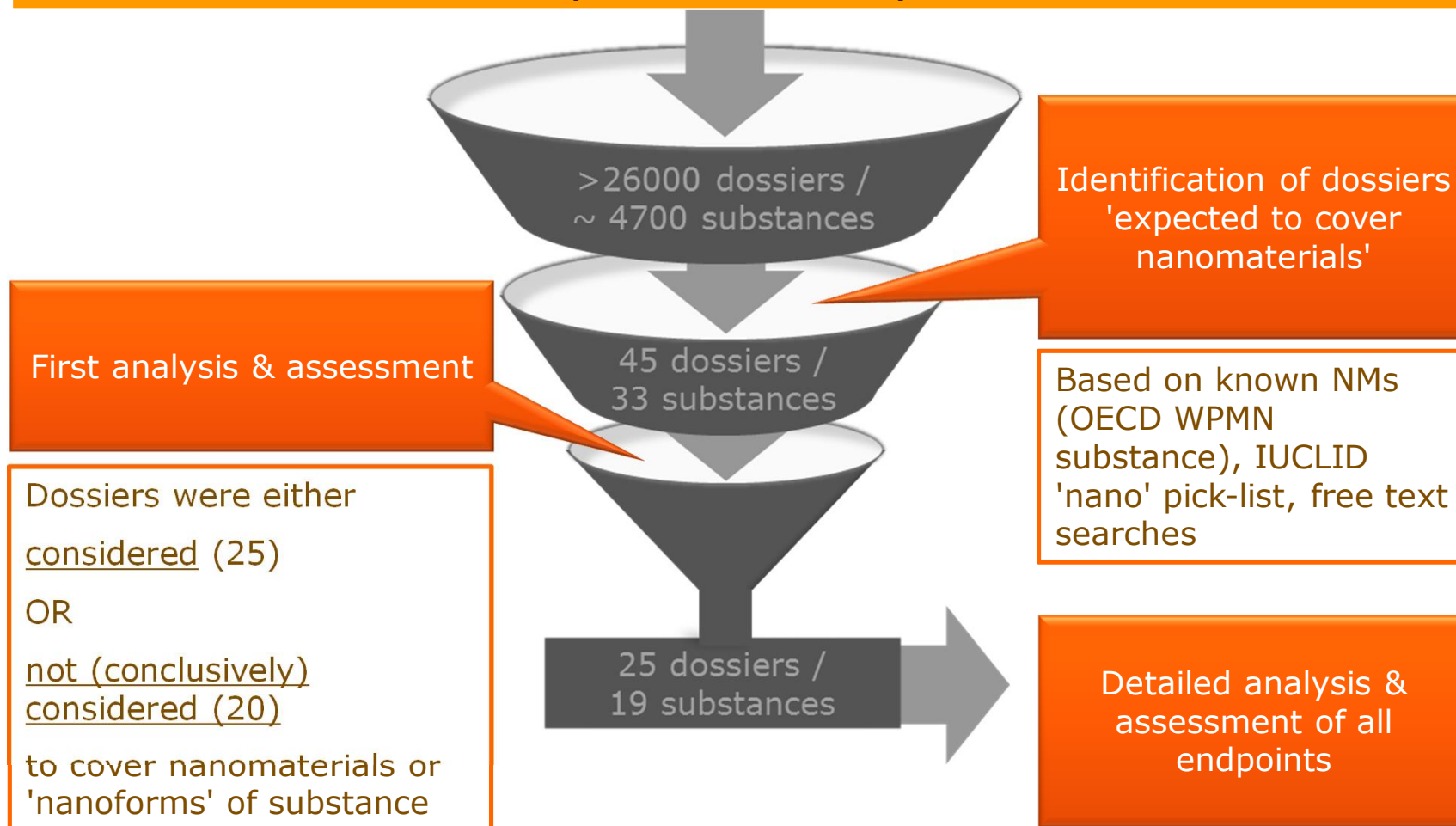
Addressed to DG ENV D.3
Attn.: Mr. H. Laursen (ENV D.3 Technical Responsible)

12 March 2012

Report available from:

<http://ec.europa.eu/environment/chemicals/nanotech/index.htm>

Dossiers in the REACH registration database (March 7th 2011)



Main observations: general issues

- Registrants did make some attempts to explicitly address nanoform(s)

- *However some gaps were identified, including....*

- **Scope of the registration not clearly described**

- Unclear whether nanoforms were included within a specific dossier.

Can be specified from:

- **2.1** "Classification and labelling according to GHS"
- **4.1** "Appearance/physical state/colour/"
- **Endpoint study records:** Nanoform as test material

- **Information for substance identification not detailed**

- Insufficient info on particle size, surface area, surface treatment etc.
- Identification mainly based on chemical composition.

Main observations: Endpoint studies

- Distinction between various forms within endpoints unclear
- Limited description of test material: form (bulk or nano)/size/coating/aggregation
- General lack of sufficient and detailed information on test sample preparation and dosimetry
- Suitability of test methods specifically for nanomaterials was generally not addressed...

Since then...

- **Commission Recommendation of 18 October 2011 on the definition of nanomaterial**

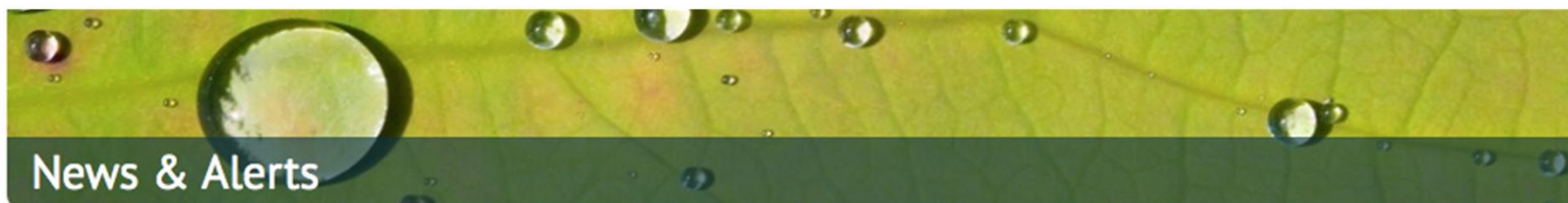
- **ECHA NM working group (Oct 2012/Jan 2013 →)**: ECHA, EC, Member States CAs, and stakeholders organisations. → Discussion of scientific and technical questions relevant to REACH and CLP processes and to provide recommendations on strategic issues.



- **Group Assessing Already Registered Nanomaterials (GAARN) (Jan 2012 →)**: EC, ECHA, Member States CAs and 3 representative lead registrants → Discussion on best practices for assessing and managing the safety of nanomaterials under REACH

Since then...

- **Three new appendices on registration of nanomaterials, updating Chapters R.7a, R.7b and R.7c of the REACH Guidance** on Information Requirements and Chemical Safety Assessment (IR & CSA) (*based on the RIP-oN projects*) (ECHA, April 2012)
- **IUCLID 5 Guidance and Support “Nanomaterials in IUCLID 5”** (ECHA, Updated in Feb. 2013)
- **New version 5.5 of IUCLID (April 2013). 13 new nano-relevant PC endpoint templates** implemented:
 - 1) Agglomeration/aggregation, 2) Crystalline phase, 3) Crystallite and grain size, 4) Aspect ratio, shape, 5) Specific surface area, 6) Zeta potential, 7) Surface chemistry, 8) Dustiness, 9) Porosity, 10) Pour density, 11) Photocatalytic activity, 12) Radical formation potential, 13) Catalytic activity



Early Results indicate total of 4 Nanomaterials registered by 2013 REACH Deadline

Posted on 03 Jun 2013

The [European Chemicals Agency \(ECHA\)](#)'s Director of Registration has stated [that](#) the agency has received REACH registrations for "4 substances registered as nanomaterials, and the number of dossiers corresponding to these...is 80". Speaking at a press conference, the representative did indicate that this is "a very preliminary number" and that full details would be revealed in early September 2013.

This latest REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals regulation) registration deadline, which was 31 May 2013, was for the 100 to 1000 tonnes per year range. The Director noted that the number "is not a bigger number than in 2010, despite a lot of advice [being offered] to the companies to indicate whether they use nanoform for their substance".

In total 9084 registration dossiers were submitted by 3215 companies [and](#), and ECHA's Executive Director "congratulate[d] all successful registrants on their hard work". Nevertheless there was a reminder that "complying with REACH does not end at registration. It's only the start". The final deadline, for 'substances manufactured or imported in the EU at or above one tonne a year', is 31 May 2018.

Follow this link to [view the press conference given by ECHA](#) [\(nanomaterials are mentioned from 38:01 until 38:37\)](#), and this to [read a press release about the registrations in general](#).

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Voice of Nanotech 22 May
@nanotechia
Swedish Chemicals Agency (KEMI) has been mandated to draft a #nanomaterials #register bit.ly/1HyWR1W #nanotech #regulation #Sweden
Expand

Voice of Nanotech
More

Limitations of Current Legislation

- Nanomaterials seem to be covered
- Unclear when it comes to the specific NMs and applications
- Main issues
 - Metrology tools are unavailable
 - Thresholds are not tailored to the nanoscale
 - Profound lack of (eco)toxicological data
 - No risk thresholds and occupational exposure limits cannot be established with existing methodologies.

The European Union's chemical legislation needs revision

To the Editor — In the *Second Regulatory Review on Nanomaterials*¹, the European Commission acknowledges that nanomaterials are revolutionary materials and that important challenges exist in regard to hazard and exposure assessments. Yet, they conclude that current risk-assessment methods are applicable to nanomaterials, and that the European chemical legislative (known as REACH: Registration, Evaluation, Authorisation and Restriction of Chemicals) "...sets the best possible framework for the risk management of nanomaterials"¹. Here, I argue that significant changes to REACH and the accompanying annexes are required to answer the call made by the public, downstream users and progressive businesses for clearer and more definite regulatory rules specific to nanomaterials².

Under REACH, unambiguous substance identification is essential³. Briefly, a chemical substance is defined by its chemical composition including any additive used to preserve stability and any impurity derived from the processes used for its manufacture⁴. Substance identity is therefore independent of, for instance, primary particle size distribution and various surface treatments, which are necessary to stabilize the substance. This means nanomaterials with markedly different properties — for example, the bulk and nanoform of a material, or various forms of surface-treated nanomaterials^{5,6} — are considered to be the same under REACH. In the European Commission's *Staff Working Paper*⁷, which accompanies the *Second Regulatory Review on Nanomaterials*¹, over 60 nanomaterials are cited to be on the market. Yet, a survey by the European Commission and the European Chemicals Agency (ECHA) found only seven nanomaterials were registered under REACH in the first round of registrations in 2010 as — among others — substances that were produced and imported at >1,000 tons per year¹³.

For correct and unambiguous substance identification, a distinction between the bulk and the nanoforms of a given material needs to be specified in the legal text of REACH³. Furthermore, the European Commission should acknowledge that nanomaterials cannot be identified solely by chemical composition, and that additional main

identifiers (such as primary particle size distribution, shape (including aspect ratio), specific surface area and surface treatment) should be included in the *Technical Guidance for Identification and Naming of Substances* provided by ECHA³. Only this will make clear that the properties and behaviour of nanomaterials differ fundamentally from each other and from the bulk².

Specific substance identification of nanomaterials could mean that some would not meet REACH's tonnage bands, which lay down the environmental, health and safety information requirements that need to be met by industry. Although lowering the tonnage band to, for example, 1 kg (ref. 10) has been suggested, I contend that if nanomaterials are commercialized in Europe, their registration should be independent of production volumes, and submission of (eco)toxicological data to regulators should be mandatory. Moreover, given the urgency of generating data on nanomaterials, registration fees must be reduced to encourage registration. As recommended by the consortium contracted by the European Commission to advise on fulfilling information requirements for nanomaterials under REACH, manufacturers should be required to perform accurate physicochemical characterization using multiple techniques because this is essential for assessing the potential (eco)toxicity of nanomaterials¹¹. Furthermore, ECHA should offer confidential technical assistance to small- and medium-sized enterprises to meet these requirements and to ensure the innovation of safe nanomaterials¹².

In contrast to the *Second Regulatory Review on Nanomaterials*¹, the *Staff Working Paper*⁷ highlights many of the challenges mentioned here and acknowledges that much more research and legislative grinding-out is needed. For instance, it recognizes that the information in REACH registrations pertaining to nanoform(s) is ambiguous, further underlining the importance of having REACH and the *Guidance for Identification and Naming of Substances* consider nanospecific properties and implement specific requirements for (eco)toxicological information. Furthermore, the *Staff Working Paper* acknowledges that nanomaterials may have a wide range of potential toxic

effects, that there are few measured exposure data and that few environmental fate and behaviour studies are available. It concludes that "...risk characterisation and combining hazard and exposure data necessarily remains at a very preliminary and qualitative level"⁷. Unfortunately, the limitations of current regulation and risk-assessment approaches outlined in it were not transferred to the *Second Regulatory Review on Nanomaterials*¹.

Referring to the 2009 report¹³ of the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), the European Commission repeatedly calls for a case-by-case risk assessment of nanomaterials. However, the issues crippling hazard identification are not easily overcome and merit more than a few caveats as stated by the European Commission¹. For instance, hazard-relevant physicochemical properties still need to be identified for nanomaterials. Furthermore, there are currently no standardized (eco)toxicity test guidelines in use¹¹. Moreover, monitoring and detection equipment for exposure assessment need to be developed and there are no standards on how to measure nanoparticle dose in humans, the workplace and the environment¹⁴. Even if required only for commercialized nanomaterials, case-by-case risk assessment of nanomaterials is time- and resource-intensive¹⁵ as outlined in the 2012 report by SCENIHR and two other scientific committees¹⁶. Under the heading '5.2. Towards a new conceptual framework in risk assessment', the report states "It is also evident that the risks posed by a number of products from new technologies (for example, biological products, manufactured nanomaterials) are unlikely to be adequately assessed using current methodologies alone"¹⁶.

Another disturbing aspect of the *Second Regulatory Review on Nanomaterials*¹ is that it focuses only on first-generation nanomaterials (that is, passive nanostructures such as nanoparticles). The *Staff Working Paper*⁷ acknowledges that second- and third-generation nanomaterials (for example, targeted drug-delivery systems and novel robotic devices) are entering early stages of market development, yet they offer no vision or strategic planning in ensuring the generation and development of

- Substance id needs revisions
- Tonnage triggers needs to be lowered
- Eco-/tox testing should be NM specific
- ECHA should provide technical support to SMEs

"Nano REACH annex changes on the horizon" – means far far away?



Nano REACH annex changes on the horizon

ECHA wants decision as soon as possible

29 January 2014 / Europe, Nanomaterials

The European Commission is finalising its impact assessment of six options for amending the annexes of REACH to better account for nanomaterials. According to the EU Executive, a proposal should be made to the REACH Committee either before or just after the summer break. It notes that the proposal can be adopted by committee procedure, which is faster than the ordinary regulatory procedure, which requires a co-decision to be reached between the EU Council and Parliament.

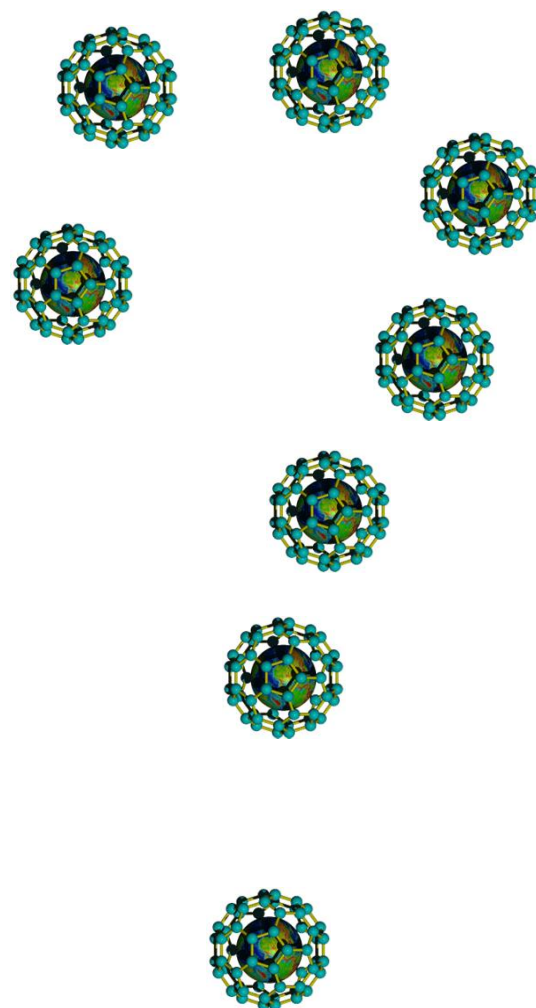
At present Commission services is working on the impact assessment of the changes to the REACH annexes. The Commission says it is keen to have the best possible evidence base in support of the

Policy options considered in Impact Assessment

1. Current situation under REACH is maintained
2. Changes to certain REACH Annex
 - ☞ Clarification of requirements for nanoform specific information in a number of specific end-point sections
 - ☞ clarification of how data is to be reported
- 3 Relying on non-legally binding measures only in order to provide more clarity
4. Full implementation of policy option 2 + demonstration of safe use
 - where the existing information requirements in REACH are not tailored for nanomaterials or
 - where specific considerations are required for nanomaterials.

Policy options considered in Impact Assessment

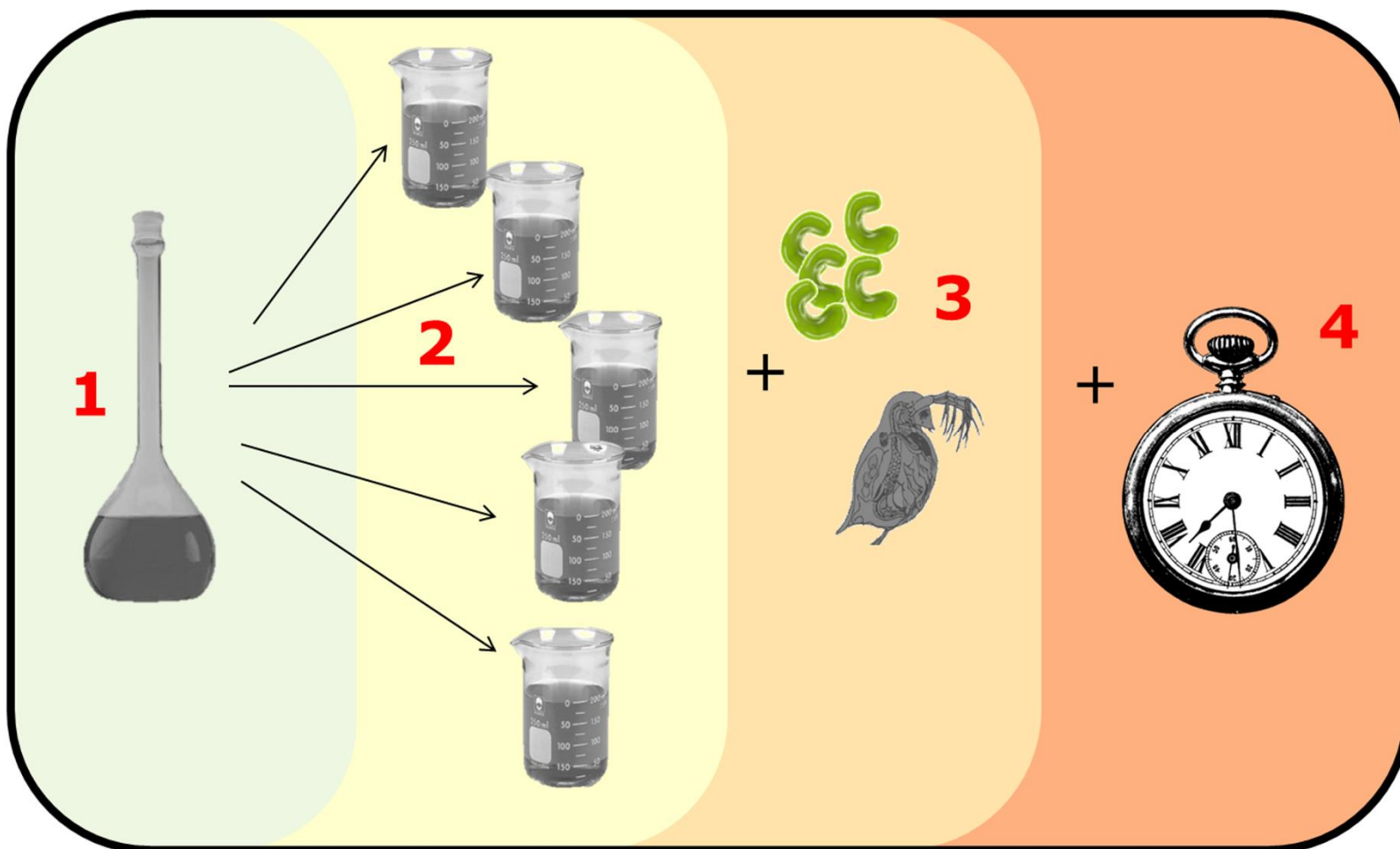
- 5: Tailored information requirements for nanomaterials placed on the market
 - clarification of regulatory provisions and
 - even reduction of certain information requirements.
- 6: Full implementation of option 2 & 4 + emphasis on the generation of targeted information regarding the influence of particle and nanomaterial specific properties on risk.
- **Industry prefers option 2 and 5 + NGOs prefer option 6 =
Seem to be heading towards option 4**



Risk assessment of NM - Challenges Ahead

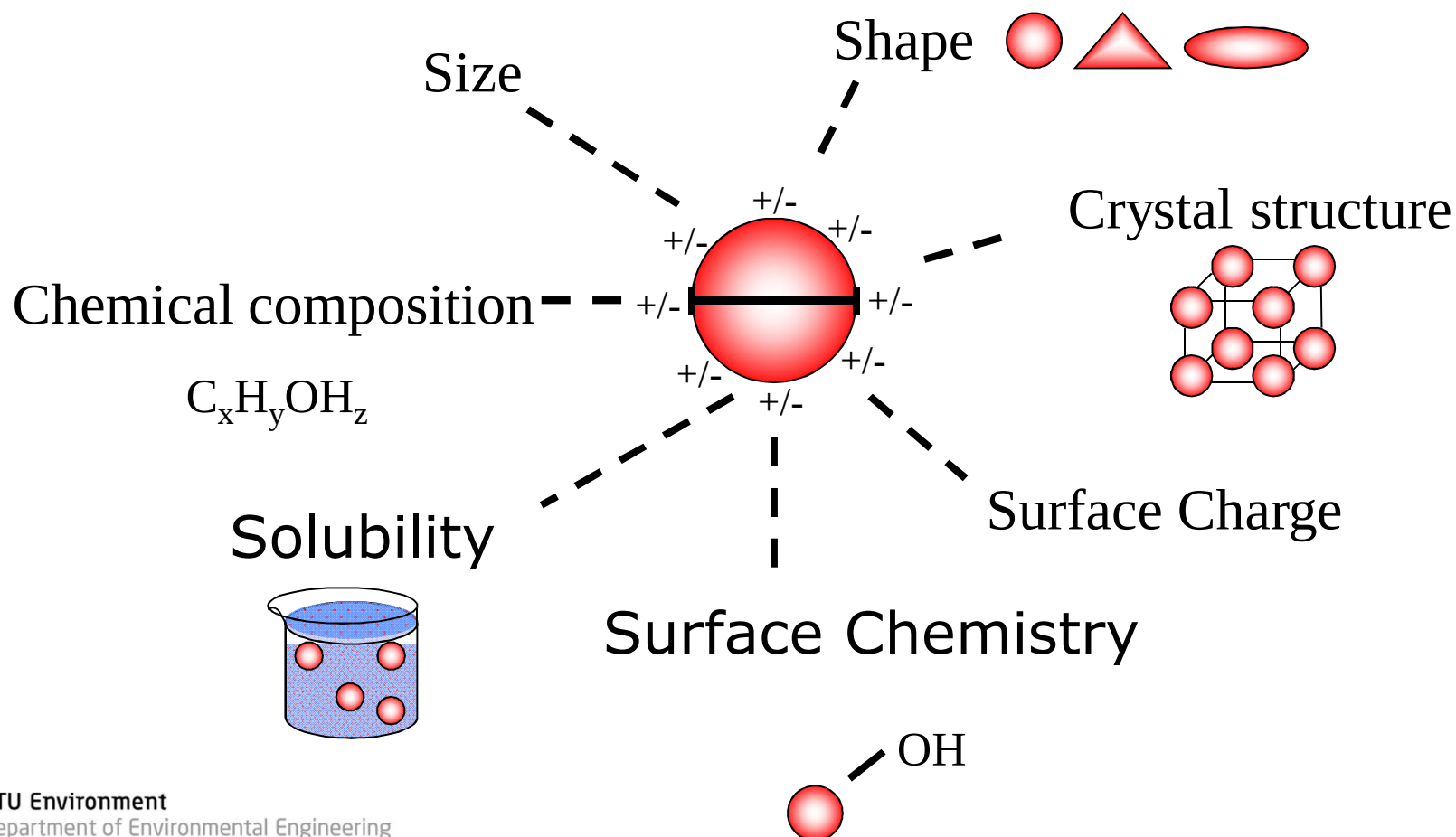


Meet the 4 horsemen of nanoeotoxic testing

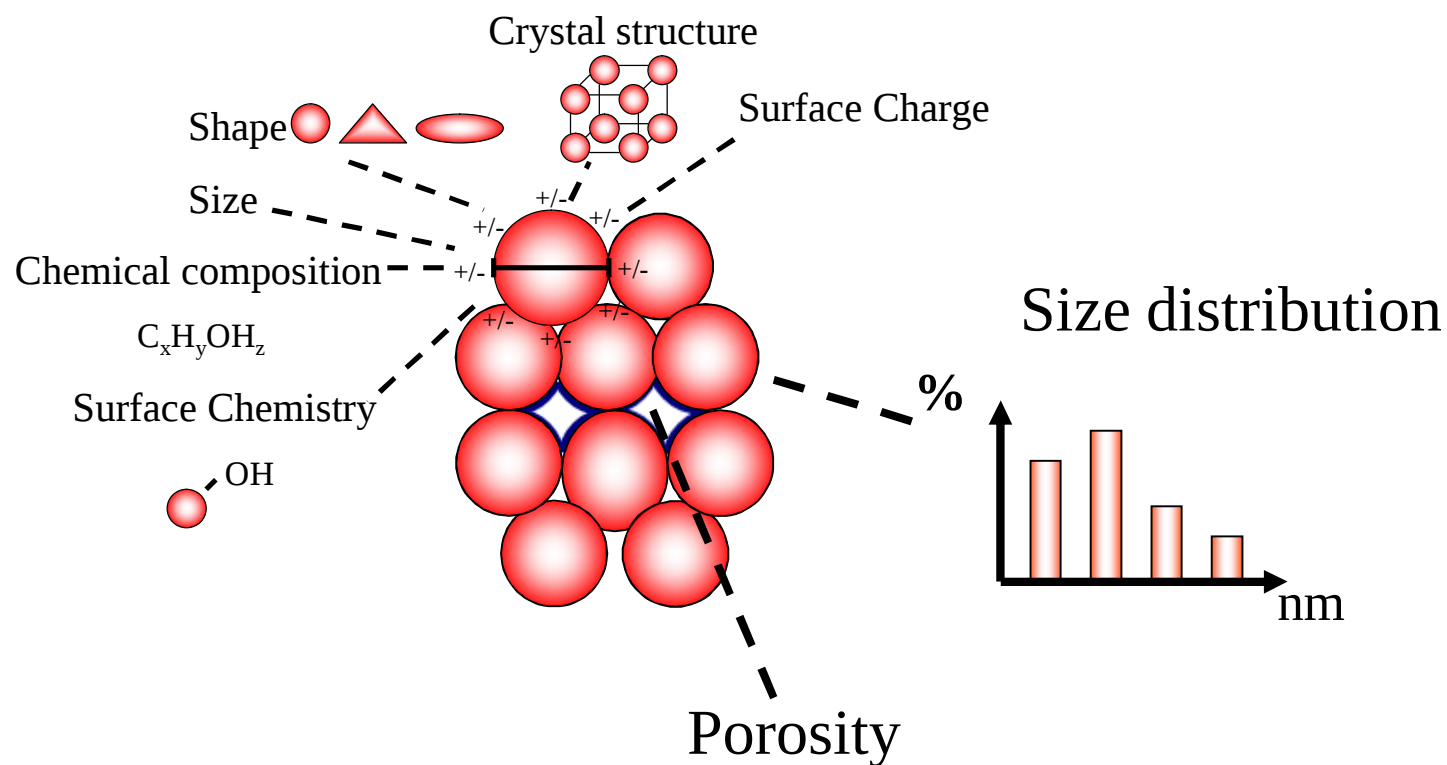


Horseman # I: Material characterization

Ideally we would know...



As well as...



Particle size

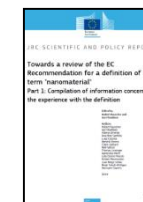


Table 4.1: Main characteristics of particle size methods relevant to the nanomaterial definition

Method name (abbreviation)	Measurement range and medium (limiting factors)	Type of size distribution of raw data	Can deal with challenges of particular types of nanomaterials? (scale: ++, +, 0, -, --)*				Standards for use of method for size analysis available?
			poly-dispersity	non-spherical particles	low-density materials	aggregates	
Electron microscopy (EM)	1 nm and higher; dry (dynamic range)	number-based	+	long: + flat: -	-	-	yes
Dynamic light scattering (DLS)	5 nm to 500 nm; suspension (sedimentation, scattering intensity)	(no distribution, or scattering-intensity-based)	--	--	+	--	yes
Centrifugal liquid sedimentation (CLS)	20 nm and higher; suspension (particle density)	extinction-intensity-based	+	--	-	--	yes
Small-angle X-ray scattering (SAXS)	5 nm and higher; suspension (dynamic range)	scattering-intensity-based	0	-	0	--	yes
Field flow fractionation (FFF)	1 nm to 200 nm; suspension (dynamic range)	(depends on detector)	+	-	+	--	no
Particle tracking analysis (PTA)	25 nm and higher; suspension (scattering intensity)	number-based	+	--	0	--	no
Atomic force microscopy (AFM)	1 nm and higher; dry (dynamic range)	number-based	+	long: + flat: +	0	-	yes
X-ray diffraction (XRD)	1 nm and higher; dry (only for crystalline materials)	(no distribution measured)	--	--	-	+	yes

* scale: ++ = very well, + = well, 0 = moderately, - = not well, -- = not at all.

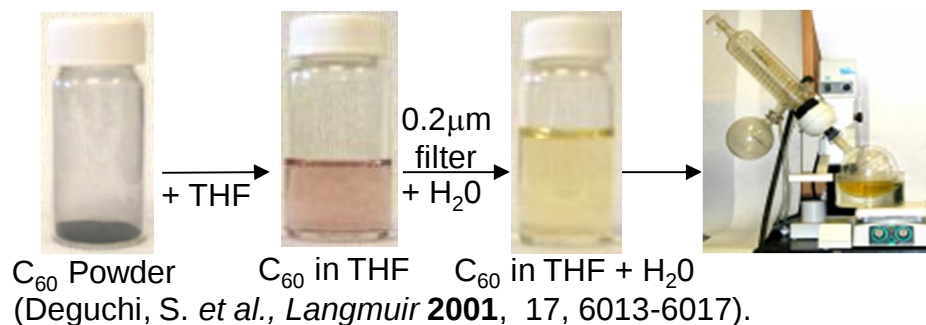
<http://bookshop.europa.eu/en/>

Horseman # II: Exposure preparation

4 published methods to preparing C₆₀



1. Solvents (THF/nC₆₀)



2. Stirring with water (aq/nC₆₀)



Stir for long period of time over low heat (40° C) (Cheng, X.; Kan, A. T.; Tomson, M. B. *J. Chem. Eng. Data* **2004**, 49, 675-683)

4. Encapsulation in PVP (PVP/C₆₀)



Mix C₆₀ dissolved in toluene with polyvinyl pyrrolidone dissolved in chloroform. Allow solvents to evaporate and resuspend dried PVP/C₆₀ in water. (Yamakoshi, Y. *J Org Chem* **1996**, 61, 7236-7237.)

DTU Environment
Department of Environmental Engineering

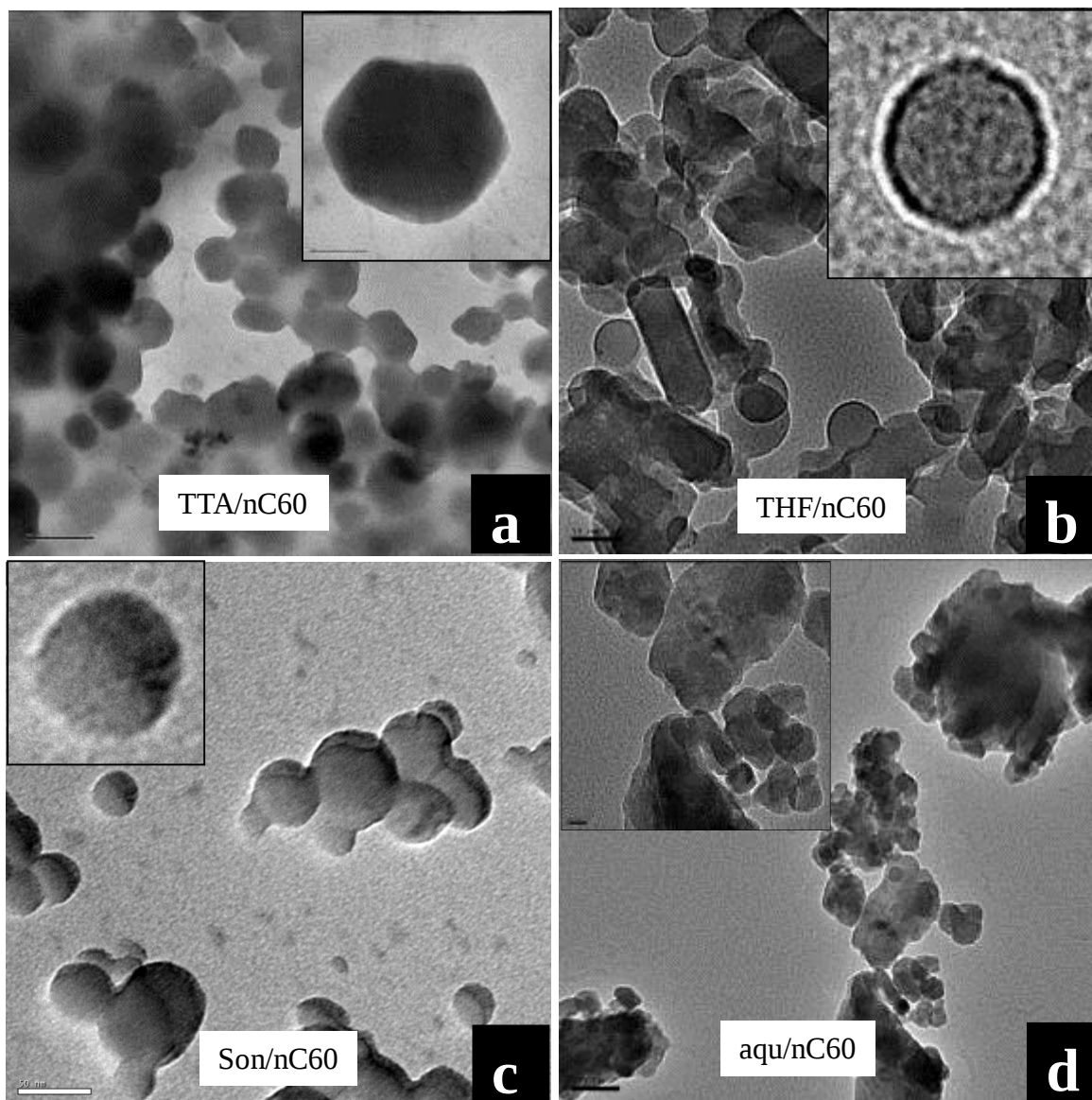
3. Sonication (son/nC₆₀)

Sonicate C₆₀ dissolved in toluene layered over water (Andrievsky, G. V. *et al. Chem Commun* **1995**, 1281-1282)



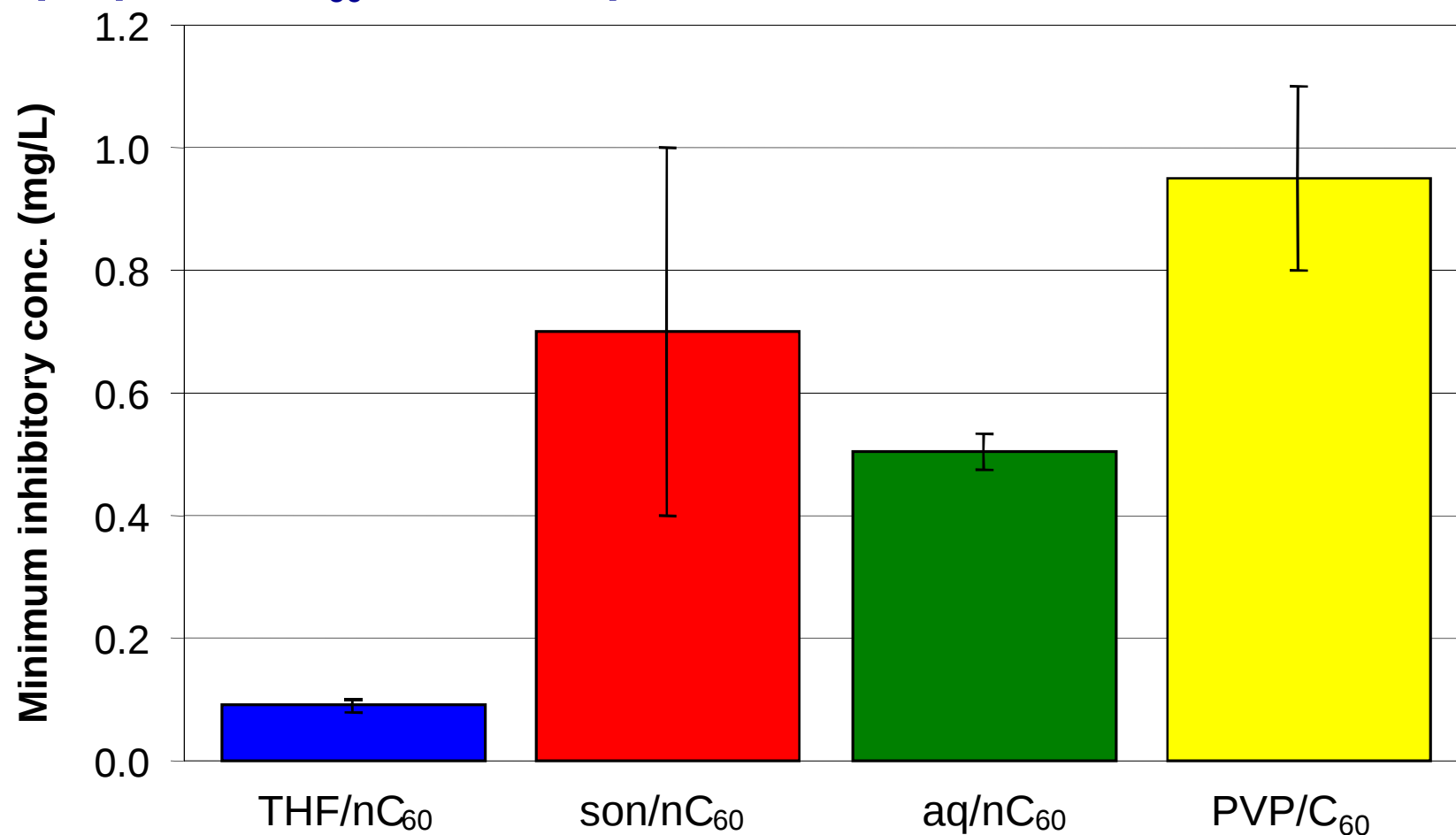
Courtesy of Pedro Alvarez,
Rice University

C60 preparation produce different aggregates



Brant, J.A., Labuille, J., Bottero, J.Y., Wiesner, M.R., *Langmuir*, 2006.

Comparing the toxicity to *B. subtilis* of four differently prepared nC₆₀ water suspensions



Controls with solvents & other ingredients showed *no toxicity*

Challenge III: Monitoring of stability during the tests

Media affect stability of nanoTiO₂

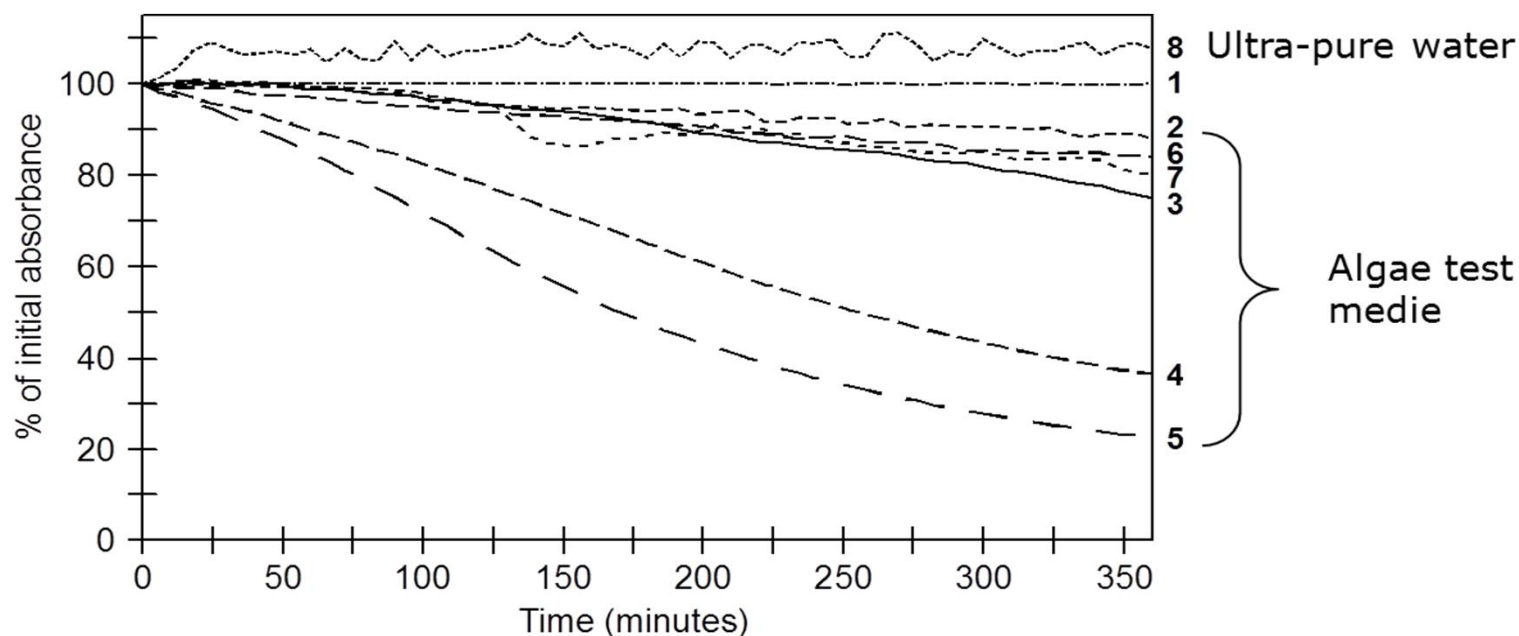


Figure 11. Reduction of absorbance ($\lambda=338$ nm (TiO₂) and $\lambda=523$ nm (Au)) as a result of sedimentation of Au and TiO₂ nanoparticles suspended in different media and concentrations. Sample 1 is absorbance of a colloidal dispersion of Au nanoparticles diluted to 10 mg/L in algal medium. Samples 7 and 8 correspond to 10 and 100 mg/L TiO₂, respectively, suspended in MilliQ water. Samples 2, 3 and 6 all correspond to 10 mg/L TiO₂ suspended in OECD algal test medium. Samples 4 and 5 are 40 and 100 mg/L TiO₂, respectively, in OECD test media. (Hartmann et al., 2011b – Paper IV).

Concentration affects stability of nanoTiO₂

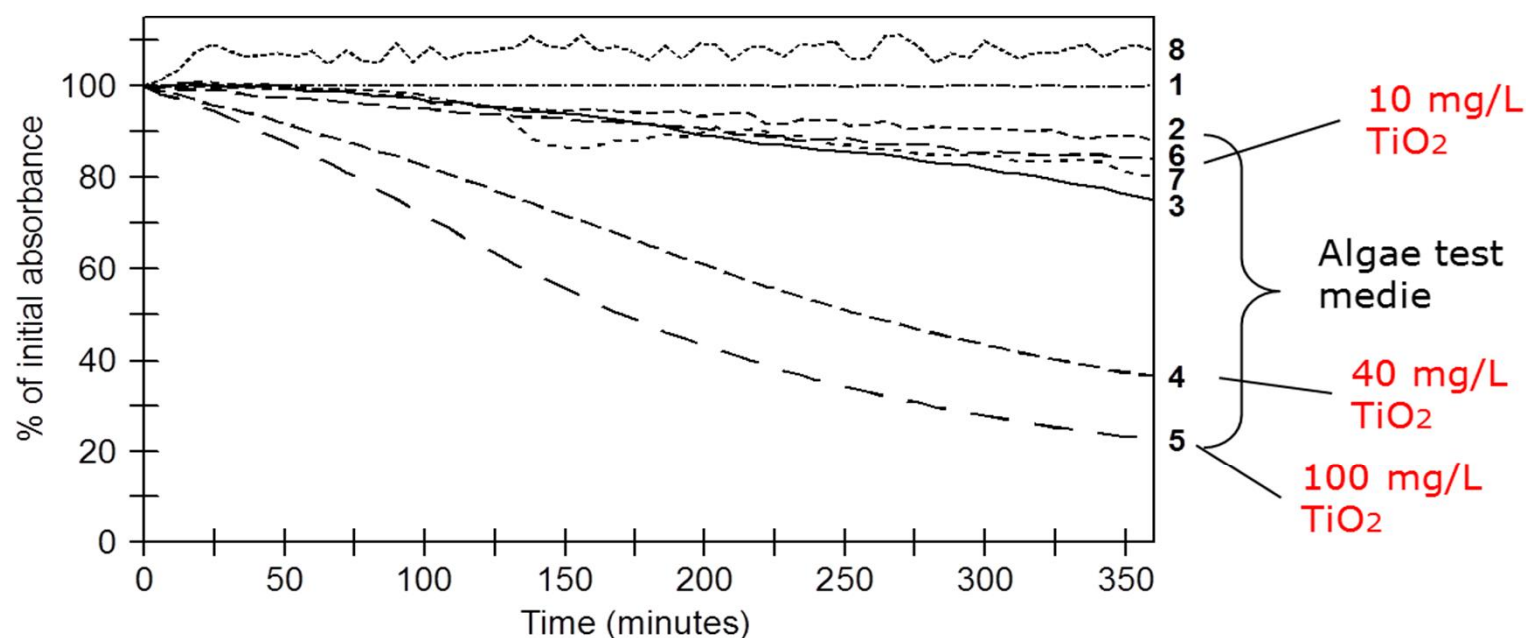


Figure 11. Reduction of absorbance ($\lambda=338$ nm (TiO₂) and $\lambda=523$ nm (Au)) as a result of sedimentation of Au and TiO₂ nanoparticles suspended in different media and concentrations. Sample 1 is absorbance of a colloidal dispersion of Au nanoparticles diluted to 10 mg/L in algal medium. Samples 7 and 8 correspond to 10 and 100 mg/L TiO₂, respectively, suspended in MilliQ water. Samples 2, 3 and 6 all correspond to 10 mg/L TiO₂ suspended in OECD algal test medium. Samples 4 and 5 are 40 and 100 mg/L TiO₂, respectively, in OECD test media. (Hartmann et al., 2011b – Paper IV).

Horseman # IV: Time

Dynamic test system

