

ECHA's work to implement REACH regulation for nanomaterials

04 May 2017 National Cancer Informatics Program (NCIP) Nanotechnology Working Group (Nano WG)

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 - Nanomaterials Expert Group (NMEG)
 - European Union Observatory on nanomaterials

1. A few words on REACH regulation





REACH: 'No data, no market'

- REACH = Registration, Evaluation, Authorisation (& restriction) of CHemicals
- Aim: 'ensure a high level of protection of human health and the environment while enhancing competitiveness and innovation'.
- Manufacturers, importers and downstream users have to demonstrate that their substance does not adversely affect the human health (HH) and the environment (ENV)
- Registration is required for substances manufactured/imported at more than 1 tonne/year
- Information requirement increases with increasing tonnage
- Each registrants to submit a dossier containing all required data on its substance (SID, phys-chem, environment and human health hazard characterisation, exposure, risk assessment).



REACH: data sharing and 'OSOR'

- Data sharing: if several manufacturers/importers register the same substance, they have to share data via a joint submission
 - → OSOR (one substance, one registration) principle
- Lead registrant submits a lead dossier containing data on:
 - *his* substance (substance identity, tonnage, uses ...)
 - the hazard of the substance (ENV, HH)
 - Chemical safety Report (CSR)
- Each member registrant submits a **member dossier** with data on
 - his substance (substance identity, manufacturing process, tonnage, uses, exposure ...)
 - Chemical safety Report [the hazard data is usually in the lead dossier]
- Data sharing along the supply chain:
 - From downstream users up to manufacturer (e.g. uses)
 - From manufacturer down to downstream users (hazard, risk management measures)

2. REACH and nanomaterials





ECHA is using the **EU recommendation for definition of nanomaterials:**

• Size of particle: 1-100 nm

<u>and</u>

• **Number** of nano-particles: >50%

- The definition also considers that a (agglomerated or aggregated) substance with constituent particles that are in nanosize should be considered as a nanomaterial
- NB: the nano definition is being reviewed by EU services (outcome expected in 2017; no drastic change foreseen)



REACH and nanomaterials

- Currently: no explicit reference to nanomaterials (NMs) in REACH, <u>but</u>:
 - NMs considered as covered by the substance definition under REACH
 - > REACH annexes are currently under revision (outcome foreseen in 2017)
- NMs can be either:
 - \rightarrow Substances on their own \rightarrow registered as such substances (e.g. CNT)
 - ➤ Nanoforms of a substance → included in the dossier of the corresponding bulk form of the substance* (e.g. CaCo3)

 [*this also applies to any other form, e.g crystalline form]
- Registrant needs to demonstrate the safe use of its substance, whatever the form



Dossier and substance evaluation

- Continuation of compliance checks for dossiers containing nanomaterials (mainly SID issues)
- Member states have sent 2 substance evaluation decisions and 5 more are scheduled between 2017-2019

Substance	SiO2	Ag	ZnO	MWCNT	TiO2	CeO2	carbon black
Year	sent	Sent	2017	2018	2018	2019	2019
MS	NL	NL	DE	DE	FR	DE	DE

- Decisions for nanomaterials have a higher appeal rate (pointing towards difference in opinions of the implicit requirements under REACH)
- Some cases are pending with the Board of appeal



REACH Annex changes: critical for success

- Lack of clarity of the existing implicit legal requirements for nanomaterials continues to hamper an effective implementation of REACH
- The European Commission's work on revising the REACH Annexes has been seriously delayed
- Even after a potential adoption of the revisions, uncertainties remains;
 - About timelines for the revisions
 - Implementation aspects such as date of application
 - Need for additional guidance

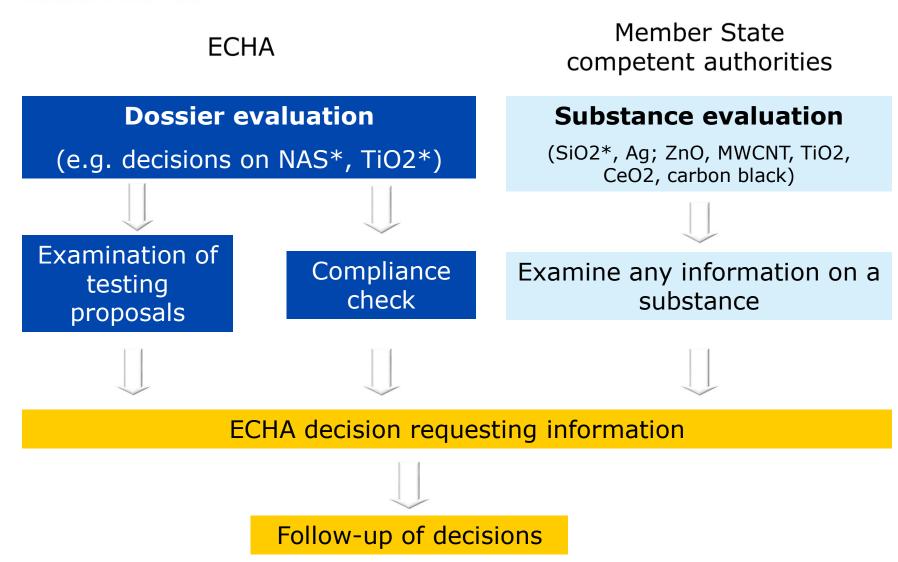


ECHA updating existing guidance for Nanomaterials

- ECHA is in the process of updating existing guidance ahead of 2018 deadline based on:
 - Development in regulatory science
 - Increased knowledge at OECD level
 - Experience gained in doing evaluations
- The guidance updates concerns:
 - Identification of nanoform
 - Read across between nanoforms of the same substance
 - Specific aspects of hazard assessment for human health
 - Specific aspects of hazard assessment for the environment
- All 4 guidances should be released by end Q2/2017



ECHA Evaluation of NMs under REACH



^{*} Registrants have submitted appeals against these ECHA decisions

3. Challenges for hazard characterisation of NMs under REACH





SID and Phys-chem characterisation of NMs

- Like for any registered substance, the SID and phys-chem characterisation of nanoforms is a <u>prerequisite</u> (to proper assess hazard and risks)
- SID and Phys-chem characterisation of nanoforms can be complex:
 - specialised analytical measurement tools are required
 - currently, none of the characterisation tools/analytical methods is validated for all NMs.
 - key influence of sample preparation



Substance identity/scope of REACH dossiers

Very few NMs are clearly identified in the REACH dossier

(i.e. indicated by ticking "nano" box by the registrants in the IUCLID dossier (section 2.1 & 4.1))



Nanomaterials in REACH registrations* (January 2017)

	2010 (>1000 t)	2013 (100-1000 t)	Others/Non phase-in
# substances	5	4	12
# dossiers in the joint submission	10, 100, 134, 1 individual submission, 54	1, 3, 81, 1 individual submission	NA

^{*}indicated by ticking "nano" box by the registrants in the IUCLID dossier (section 2.1 & 4.1)

NB: On 19 March 2017, ECHA's Database contained **39392 full registration** corresponding to **6672 unique substances**



Nanomaterials in REACH registrations (January 2017)

	2010	2013	Other/2017
Substance name (additionally to names claimed confidential under NONs)	 Carbon black Cerium dioxide Calcium carbonate Zinc oxide Silver 	 MWNT as a form of graphite Titanium dioxide Silicate(2-), hexafluoro-, disodium, reaction products with lithium magnesium sodium silicate 	 Diiron trioxide SWCNT iron manganese trioxide iron hydroxide oxide yellow

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Substance identity/scope of REACH dossiers (2)

- No/minimal information on coating/surface treatment
- Typically
 - no nano-specific substance identity information
 - no clear indication that nanoforms are within the scope of the substance registered
 - no nano-specific information on tonnages or uses

• In a **joint submission**:

- the lead registration may not cover nanoforms while member dossiers do.
- An indication that nanoforms are covered by registration may not be obvious (only apparent from the CSR or in the substance sameness documentation attached)



Hazard characterisation of NMs

Consider a case where the substance identity/scope of registration would be clearly described in the dossier

- Probably, **significant differences** in physico-chemical properties (and possibly differences in toxicological properties):
 - between bulk and nanoform(s) or
 - > between different nanoforms of a given substance.
- Uncertainty (data sharing, read-across approach is a challenge)

What ECHA observes:

- General lack of hazard data for NMs
- Tested substance often not clearly identified
- Often lack of characterisation of the tested material;

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Challenges: <u>Hazard</u> characterisation of NMs (2)

Which test protocol(s) to follow for NMs?

OECD recommendation (Sept. 2013):

RECOMMENDATION ENVIRONMENT



Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials

II. RECOMMENDS that Members, in the testing of manufactured nanomaterials, apply the OECD Test Guidelines, adapted as appropriate to take into account the specific properties of manufactured nanomaterials and using the tools listed in Section I of the Annex to this Recommendation, and the OECD Principles of Good Laboratory Practice, set forth respectively in Annexes I and II to the Decision of the Council concerning the Mutual Acceptance of Data in the Assessment of Chemicals [C(81)30(Final), as amended].

→ Use the current testing guidelines, 'adapted as appropriate'

HOW to adapt and **WHAT is appropriate**?



Example: genotoxicity data requirement under REACH

Test		Annex			
	VII	VIII	IX	X	
GM test in bacteria (Ames)	Yes	Yes	Yes	Yes	
CA test in mammalian cells in vitro		Yes	Yes	Yes	
GM test in mammalian cells in vitro		Yes ¹	Yes ¹	Yes ¹	
CA test in mammalian cells in vivo			Yes ²	Yes ²	
GM test in mammalian cells in vivo			Yes ³	Yes ³	
Germ cell mutagenicity test			Yes ⁴	Yes ⁴	

GM, gene mutation; CA, chromosomal aberration

¹ Performed only if Ames and CA vitro are negative

 $^{^{2}}$ required only to follow-up a positive result in CA vitro, if no results already available from an in vivo study

³ required only to follow-up a positive result in GM vitro, if no results already available from an in vivo study

⁴ to be considered only if positive result obtained in vivo somatic cell study



REACH Annex VII (1-10 tpa)

- A mutation study in bacteria (usually the Ames test) is required
- Further mutation studies may be considered if the bacterial mutation study is positive



Consensus statement (OECD workshop, Ottawa, Nov 2013):

The use of the Ames test is not a recommended test method for the investigation of the genotoxicity of nanomaterials. The test guidelines programme should consider modifying the applicability domain within this test guideline accordingly.

[main rationale: some/most NMs cannot penetrate the bacterial wall]

- Ames data may not be reliable for NMs:
 - how to interpret negative results from Ames test?
 - Should registrant demonstrate that the NMs has penetrated the bacteria?
- In REACH requirement, should Ames test (TG471, A. VII) be replaced by the gene mutation test in mammalian cells in vitro (OECD TG476 A.VIII), for <u>all</u> nanomaterials?
- NB: such modification is under consideration in the ongoing REACH annex review.



Hazard characterisation of NMs (3)

- REACH registration dossier can contain different forms of a substance,
 e.g. bulk and/or nanoform(s).
- Wide variety of NMs (e.g. chemical constituent, size, shape, absence/presence of coating, coating type)
- Current scientific knowledge is not sufficient:
 - To identify test protocols applicable to all NMs
 - to know the specific adaptation of protocols that should be applied to a given nanoform

4. Read-across: ECHA RAAF (and proposals for nanomaterials)





Read-across

- Data sharing or read-across (using data of form A to cover information requirement for form B) can be difficult to justify.
- Obvious challenge: which form(s) is(are) representative and should undergo testing?
- Example: dossier with 42 forms
 - 2 bulk forms (2 different crystalline forms)
 - 40 nanoforms: 2 crystalline forms, 4 particle sizes, 5 coatings (e.g. 3 acids, 2 silanes)
 - Can data generated with the bulk form be used for (all) nanoforms?
 - If not, which nanoform(s) can be used to generate data applicable to other nanoforms.
 - Is there data available to justify the grouping of nanoforms? To justify the read-across?



Read-across (2)

- Read-across issue is particularly crucial for studies with vertebrate animal testing (animal welfare and costs)
- Further complication:
 - different forms can be put on the market by different companies,
 - some substance identity data can be claimed confidential.



ECHA read-across Assessment Framework (RAAF)

RAAF document:

https://echa.europa.eu/documents/10162/13628/raaf_en.pdf/614e5d61-891d-4154-8a47-87efebd1851a

• Scenario 1:

https://echa.europa.eu/documents/10162/13628/raaf appendix a scenario1 en. pdf/a161792d-211f-4d75-a09c-c4499443ac43

Scenario 2:

https://echa.europa.eu/documents/10162/13628/raaf appendix b scenario2 en. pdf/a7671677-aff7-4a67-84d1-5f080f5e1c27

Scenario 3:

https://echa.europa.eu/documents/10162/13628/raaf appendix c scenario3 en. pdf/08d5f68e-af27-4839-8036-30322513a656

Scenario 4:

https://echa.europa.eu/documents/10162/13628/raaf_appendix_d_scenario4_en.pdf/8d1cf516-cdb4-4bb3-8a49-a2a5543513f9

Scenario 5:

https://echa.europa.eu/documents/10162/13628/raaf_appendix_e_scenario5_en.pdf/9d27cace-4d60-4cd7-90fc-cf7cb2f819e2

Scenario 6:

https://echa.europa.eu/documents/10162/13628/raaf appendix f scenario6 en. pdf/50e87d51-6c1d-4f24-b1cb-3feceb1cbfec



Short scientific introduction:

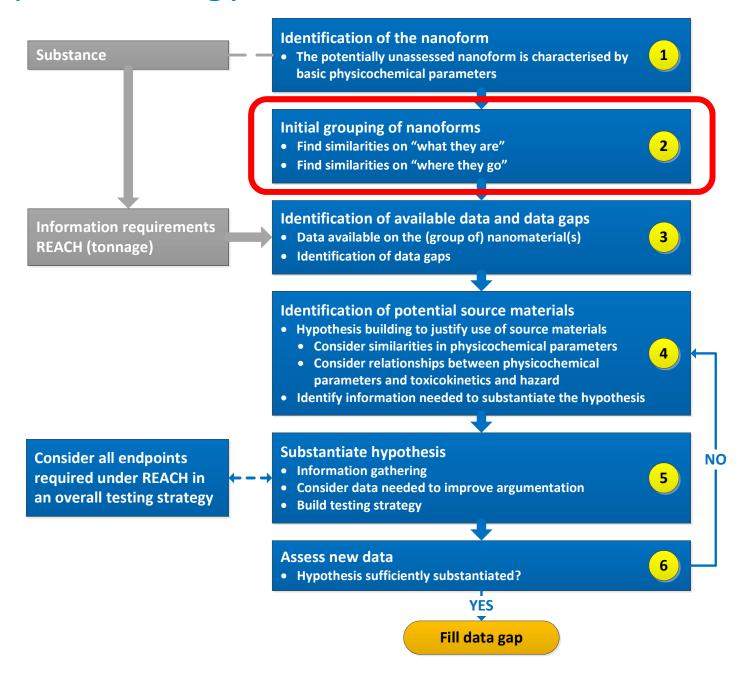
https://echa.europa.eu/documents/10162/13628/introduction to raaf en.pdf/00afcd9b-bd8e-4d71-9a7d-4e7b41355e01

ECHA Grouping of nanoforms of the same substance

• In March 2016, ECHA has realeased a publication on 'Usage of (eco)toxicological data for bridging data gaps between and grouping of nanoforms of the same substance':

https://echa.europa.eu/documents/10162/13630/eco toxicological for bridging grouping nanoforms en.pdf/245bf47d-4955-4202-b0d0-1d3c531346d4

Adapted strategy for read-across of nanomaterials

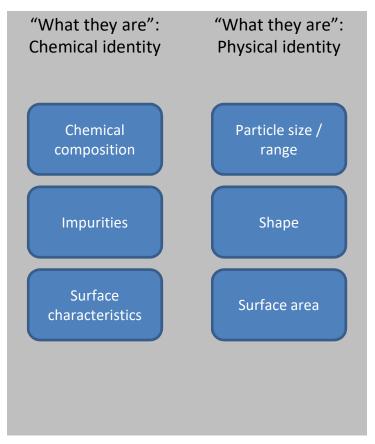


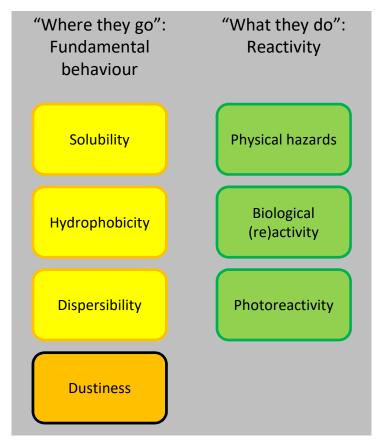
basic physicochemical parameters



Step 1 – Identification of the nanoform

Based on the basic physicochemical parameters of the nanoform





5. Additional actions taken to improve REACH implementation for nanomaterials



5a. ECHA Nanomaterials Expert Group (NMEG)





Nanomaterials Expert Group (NMEG): why?

NMEG webpage

https://echa.europa.eu/regulations/nanomaterials/nanomaterialsexpert-group

- Nano page on ECHA website <u>https://echa.europa.eu/regulations/nanomaterials</u>
- A need to seek consensus at EU level on scientific and technical challenges relating to the implementation of REACH, CLP and BPR for nanomaterials
- ECHA, member states, and stakeholders need a forum for addressing key scientific questions
- Aim to distil existing knowledge and provide the best scientific and technical advice possible

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Key issues addressed in the NMEG

- Provides an unique opportunity to build common views among Member States, NGOs and industry on;
 - Characterisation of nanomaterials
 - Assessing human health and environmental toxicity of nanomaterials
 - Technical reporting of nanomaterials in IUCLID
 - Approaches to dossier and substance evaluation of nanomaterials



NMEG future work 2017-2018

NMEG meets twice a year and will facilitate discussions on issues such as:

- EU coordination of common priorities as well as sharing of workload at OECD
- Support for development of EU-ON (i.e. nano-observatory)
- Additional guidance needs to implement the new REACH annexes (when they become available) including output from regulatory research projects
- Evaluate the need to potentially review the guidance for classification and labelling for nanomaterials
- How the guidance to implement the definition of nanomaterial will be incorporated under e.g. ECHA guidance

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5b. ECHA observatory on nanomaterials





Observatory – to increase transparency

- Originate from a request by the EU Parliament resolution in 2009, and COM 2nd regulatory review on nanomaterials 2012
- Based on an impact assessment COM concluded observatory is the best option
- Observatory is one part of wider policy discussion on nanos all equally important to generate substance specific information on nanomaterials





Build up in three phases

1st Phase -2017- make use of synergies

- New web-content for professionals and consumers
- Start with easily available basic information
- New micro-site for consumers
- New search functionality on ECHA dissemination site

2nd Phase - 2018 - expansion of content

- More edited content for different audiences
- Linking with national inventories?
- Linking with (or hosting) databases on research and innovation?
- More structured information from other legislations?

3rd Phase - 2019 - full operation

- More edited content for different audiences
- New IT solutions?
- And more to come...



Food for thought...

- Transparency is a core value for ECHA and the EUON is a tool to achieve this strategic objective
- Our aspiration: EUON will be trustworthy source of information which will contribute to the public debate by raising awareness on these materials
- Success of the observatory is also dependant on the buy in from our partners and stakeholders



Conclusion

- Hazard characterisation of a NMs can be challenging
- Hazard characterisation of NMs under REACH can be even more challenging (SID, adaptation of test methods, read-across)
- Comparison of hazard of nanoforms vs. bulkform is crucial
- Hazard characterisation should ideally cover impact of transformation (e.g. agglomeration, surface modification, dissolution ...)
- For NMs, need for progress (and agreement) in scientific knowledge on phys-chem characterisation and hazard characterisation (also use, exposure)
- This would allow to better understand the current uncertainty (better description of the scope of dossiers, an informed choice of the form to be tested, an improved hazard characterisation and finally a more accurate risk assessment for NMs)



Conclusion (2)

- The three ongoing policy discussions are linked: REACH annexes, review of the definition and EUON
- Lack of progress on revising REACH annexes hampers efficient implementation
- ECHA has continued to implement REACH for nanomaterials (conducting compliance checks and by clarifying existing guidance)
- ECHA has taken a leadership in trying to speed up revision of existing OECD Test Guidelines and alternative methods (Chairing the relevant Steering Group at OECD)
- Establishing EUON offers a vehicle to increase transparency around nanomaterials on the EU market



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