REACH Implementation Project on Nanomaterials – RIP-oN2: Information Requirements

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Outline

- Background & Project Scope
  - Objective
  - Overview of RIP-oN2
  - Key Tasks
- *Summary* of Outcomes
  - Recommendations for Guidance Update
    - Existing Guidance
    - Suggested New Guidance chapters
  - Recommendations for R&D

Acknowledgement & Disclaimer

We acknowledge gratefully the contributions / feedback from:

Cefic co-authors (principally BASF and Evonik)
Members of the Project's Expert Network

Members of the Project's Stakeholder Consultation Group
The Project's EC Steering Group (JRC, DG ENV, DG ENT, ECHA).

The RIP-oN2 project has not yet concluded.

This presentation highlights the authors' pre-finalised findings and advice in the RIP-oN2 project, for consideration.

The information provided does not represent the position of the European Commission or ECHA.

REACH & Nanomaterials

- EU REACH Regulation represents a fundamental shift in chemical regulation in the EU
- Under REACH, manufacturers/importers of nanomaterials as single substances or within articles at volumes ≥ 1 t/yr must register their substances and provide a technical dossier
- Uncertainty over the adequacy of the regulation and guidance for the nanotechnology industry
- A need exists to review the scope and guidance for REACH in terms of substance identity, information requirements, chemical safety assessment, test methods and metrics for risk assessment in relation to nanomaterials.
- These reviews have started and are known as the RIP-oN projects.

REACH Implementation Projects on Nanomaterials

RIP-oN 1 (Substance Identification)

RIP-oN 2 (Information Requirements)

RIP-oN 3 (Exposure & CSA)

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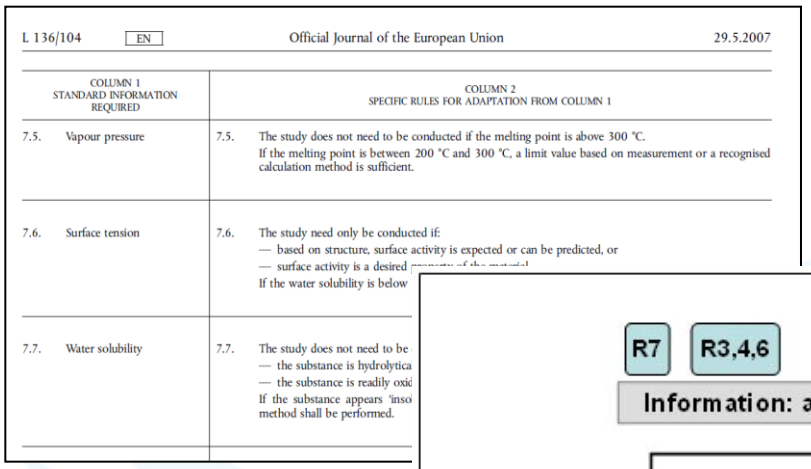
The Regulation, IRs and Guidance for the REACH Process



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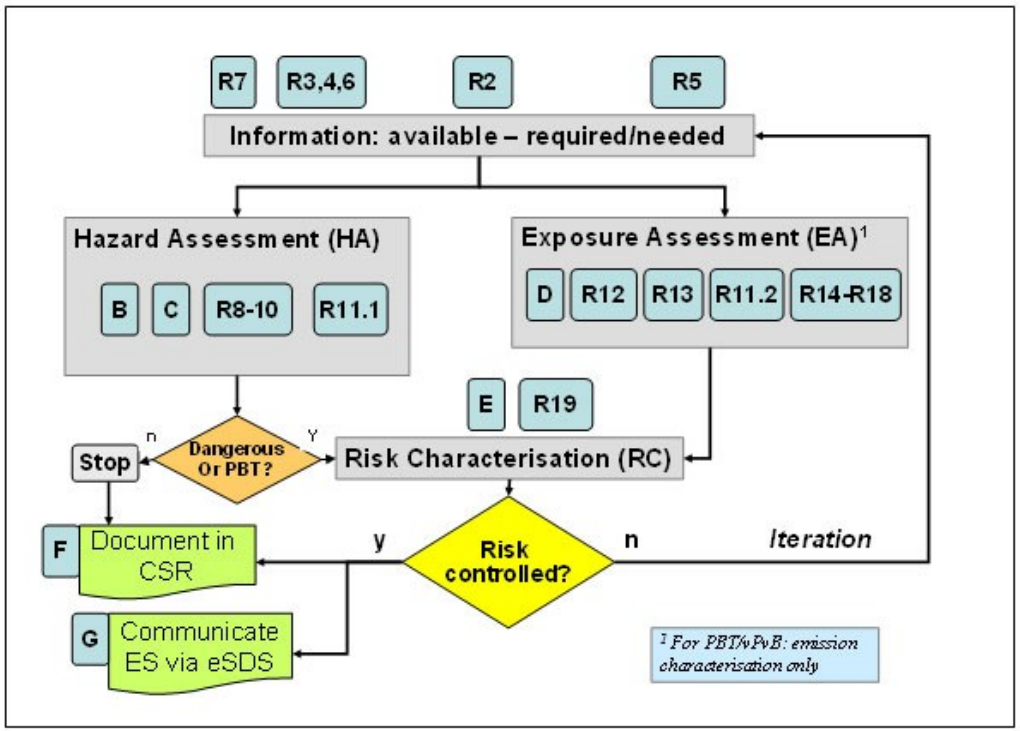
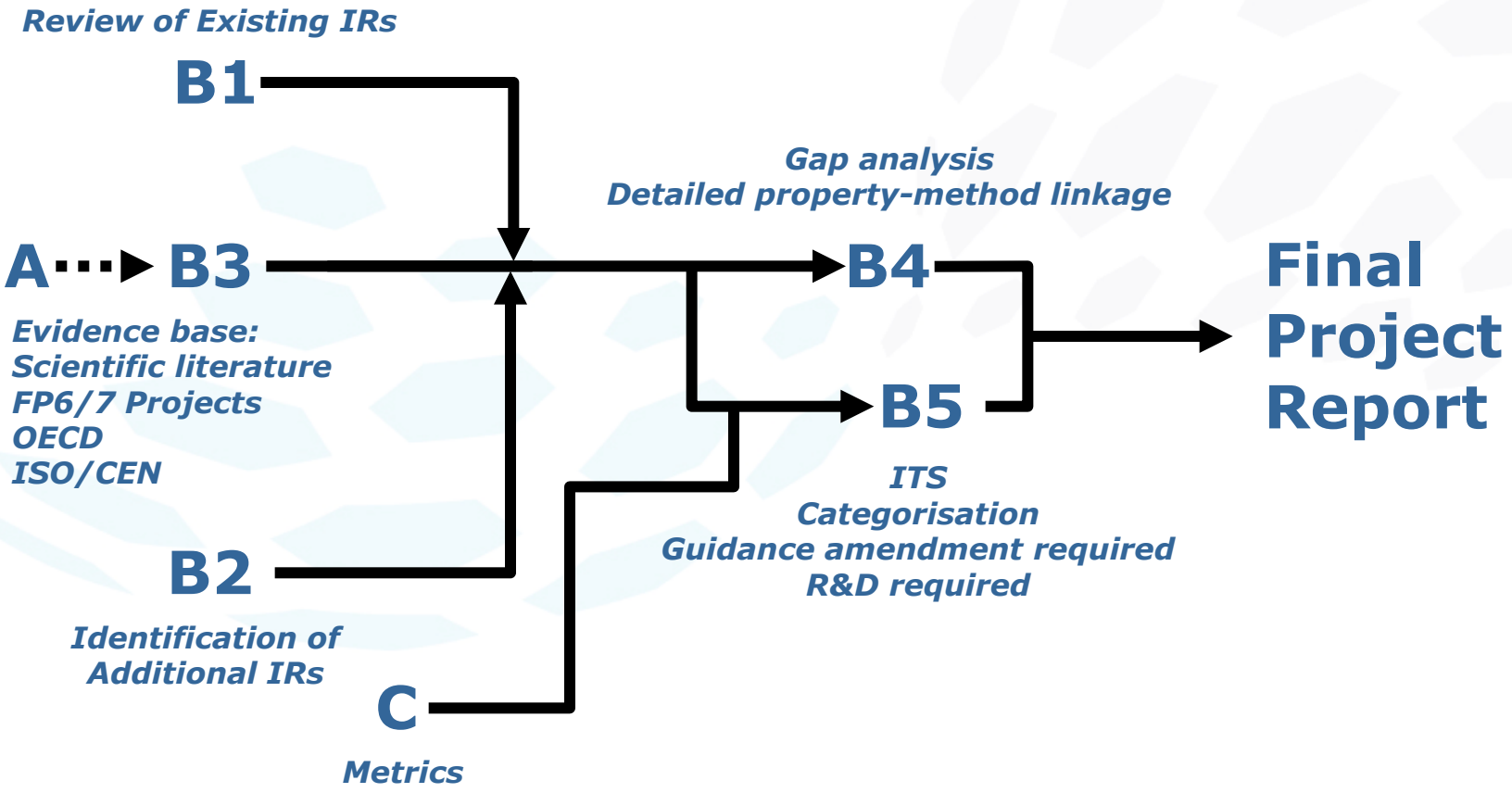
COLUMN 1 STANDARD INFORMATION REQUIRED	COLUMN 2 SPECIFIC RULES FOR ADAPTATION FROM COLUMN 1
7.5. Vapour pressure	7.5. The study does not need to be conducted if the melting point is above 300 °C. If the melting point is between 200 °C and 300 °C, a limit value based on measurement or a recognised calculation method is sufficient.
7.6. Surface tension	7.6. The study need only be conducted if: — based on structure, surface activity is expected or can be predicted, or — surface activity is a desired If the water solubility is below
7.7. Water solubility	7.7. The study does not need to be — the substance is hydrolytica — the substance is readily oxid If the substance appears 'inso method shall be performed.



Objectives of RIP-oN 2

- Develop specific advice on how REACH information requirements on **intrinsic properties** of nanomaterials can be fulfilled
  - Address and advise on appropriateness of relevant test methods and outline specific testing strategies
- Develop specific advice on the **information needed** for **safety evaluation and risk management** of nanomaterials
  - In particular, if information is needed beyond current REACH Information Requirements listed in Annexes VI-X.

Overview of RIP-oN 2



Task A – Sources of Information

- 89 published reports and standards from key organisations;
- 54 reports and standards under development from key organisations;
- 161 reports and publications from EU FP6/7 and other relevant international projects;
- 557 reports and publications reviewed in the ENRHES literature review (recent FP7 project);
- 931 additional publications from the peer-reviewed literature.

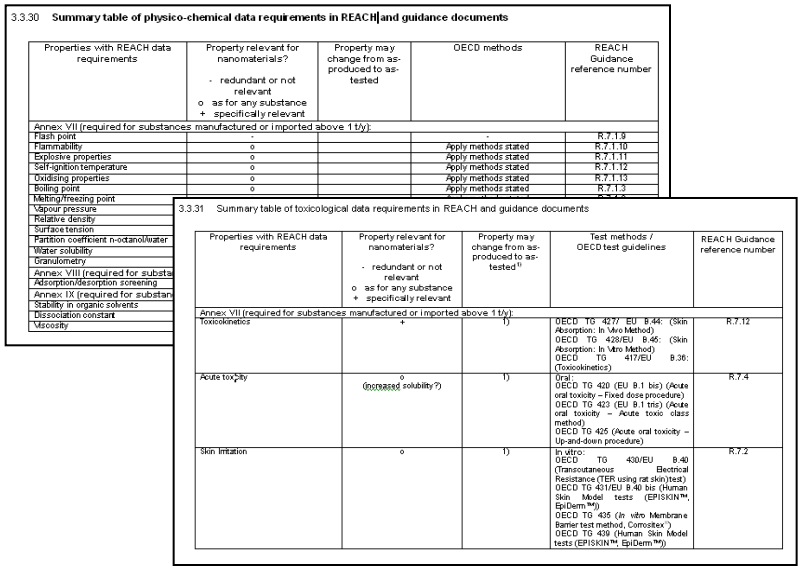
Task B1 – Existing IRs

Objective:

To evaluate how existing information requirements under REACH apply to nanomaterials.

Task report provides:

Analysis of the current guidance text, to establish if there are any differences in application between what could be called conventional substances and those at the nano scale.



3.3.30 Summary table of physico-chemical data requirements in REACH and guidance documents

Properties with REACH data requirements	Property relevant for nanomaterials? - redundant or not relevant o as for any substance + specifically relevant	Property may change from as-produced to as-tested	OECD methods	REACH Guidance reference number
Annex VII (required for substances manufactured or imported above 1 t/y):				
Flash point	-		-	R.7.1.9
Flammability	o		Apply methods stated	R.7.1.10
Explosive properties	o		Apply methods stated	R.7.1.11
Self-ignition temperature	o		Apply methods stated	R.7.1.12
Oxidising properties	o		Apply methods stated	R.7.1.13
Boiling point	o		Apply methods stated	R.7.1.3
Melting/freezing point				
Vapour pressure				
Relative density				
Surface tension				
Partition coefficient n-octanol/water				
Water solubility				
Granulometry				
Annex VIII (required for substa				
Adsorption/desorption screening				
Annex IX (required for substan				
Stability in organic solvents				
Dissociation constant				
Viscosity				

3.3.31 Summary table of toxicological data requirements in REACH and guidance documents

Properties with REACH data requirements	Property relevant for nanomaterials? - redundant or not relevant o as for any substance + specifically relevant	Property may change from as-produced to as-tested[1)]	Test methods / OECD test guidelines	REACH Guidance reference number
Annex VII (required for substances manufactured or imported above 1 t/y):				
Toxicokinetics	+	1)	OECD TG 427/ EU B.44: (Skin Absorption: In Vivo Method) OECD TG 428/EU B.45: (Skin Absorption: In Vitro Method) OECD TG 417/EU B.36: (Toxicokinetics)	R.7.12
Acute toxicity	o (increased solubility?)	1)	Oral: OECD TG 420 (EU B.1 bis) (Acute oral toxicity – Fixed dose procedure) OECD TG 423 (EU B.1 tris) (Acute oral toxicity – Acute toxic class method) OECD TG 425 (Acute oral toxicity – Up-and-down procedure)	R.7.4
Skin irritation	o	1)	In vitro: OECD TG 430/EU B.40 (Transcutaneous Electrical Resistance (TER using rat skin)test) OECD TG 431/EU B.40 bis (Human Skin Model tests (EPISKIN™, EpiDerm™)) OECD TG 435 (In vitro Membrane Barrier test method, Corrositex®) OECD TG 439 (Human Skin Model tests (EPISKIN™, EpiDerm™))	R.7.2

Task B2 – Additional IRs

Objective:

To provide a scientific report and table/grid identifying additional relevant specific intrinsic properties for nanomaterials.

Task report provides:

Underlying limitations and challenges for nanomaterials.

Candidate additional relevant specific intrinsic properties for nanomaterials.

'Conditions' influencing the relevance and quality of the determination of properties or endpoints.

Candidate property / endpoint	Suggested IR 'incorporation' status		
	New IR	Subordinate to an existing (R) or updated (U) IR	Guidance recommendation (with or without an update to the appropriate Column 2 rule)
Particle shape		U/E (7.14)	
Surface area		U/E (7.14)	
Surface energy		U/E (7.14)	
Surface chemistry		U/E (7.14)	
Surface charge		U/E (7.14)	
Redox potential	✓		
Cell-free ROS/RNS production capacity	✓		
State of dispersion*			✓ (7.14 & 9.3)
State of agglomeration*			✓ (7.14 & 9.3)
Cell uptake*			✓ (8.3, 8.4, 8.5)
Cell stability			✓ (8.1, 8.2)
Oxidative stress			✓ (8.4, 8.5, 8.6)
Inflammation			✓ (8.1, 8.2, 8.5, 8.6)
Fibrosis			✓ (8.6)
Immunotoxicity (sensitisation)			✓ (8.3)
Cardiovascular toxicity		E (8.6)	
Ventilation rate			✓ (9.1)
Gill pathologies			✓ (9.1)
Mucus secretion			✓ (9.1)

Task B3 – Evidence base

Objective:

To provide a summary analysis report containing sections on:

Practical advice on the relevance and applicability of the experience reported in the **scientific literature** and gained in several finalised and on-going **FP6/7 projects** on nanomaterials characterisation and hazard identification and assessment for workers, consumers and environment into the REACH context;

Practical advice on the use of information from **OECD-WPMN** and other sources on the appropriateness of existing testing methods and results from the sponsorship programme in fulfilling the REACH data requirements;

Practical advice on the basis of on-going work in **ISO and CEN** (and, as identified, other harmonisation bodies) in relation to whether relevant methods for substance characterisation could be used in fulfilling REACH data requirements.

Task C - Metrics

Objective:

- To identify the critical items on exposure / dose descriptors and related parameters, outlining the needs for adequate metrics / parameters for exposure assessment compatible with those for hazard assessment

In other words…

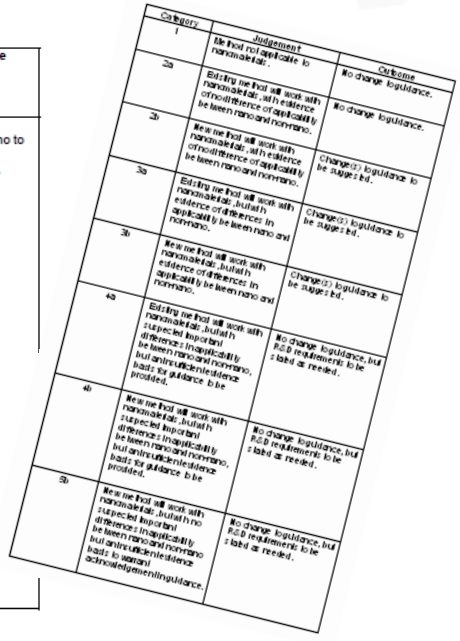
- Identify the metric(s) which:
  - drive toxicity
  - can link toxicology & exposure and are appropriate for risk assessment
- Specifically, can these metrics be related (e.g. particle size and surface area) and can they be converted?

B4: Gap Analysis

- Objective

  To provide a **summary report on a gap analysis** of relevant intrinsic properties for nanomaterials, which may not be addressed by standard test guideline methods and for which further development of *in vitro*, *in vivo*, or other methodologies is required.

Method name	Conclusion from B1/B2/B3	Judgement on property/ endpoint/ method	Decision regarding Guidance	Method type S = Standard NS = Non-standard N = Widely-accepted R&D	Commentary	Applicability S = Substance P = Particle N = Nanomaterial	Type of data	Suggested Guidance amendments
Cascade Impactor	Although this method is well established for fine particles with diameters in the micrometer range, it fails to describe the dimension of nanoparticle aerosols as they no longer follow aerodynamic rules. Can be used to determine the MMAD of agglomerates. Cascade impaction is currently included in Table R.7.1-31 of the Guidance. The limitations of this method for nanomaterials require to be highlighted in the amended Guidance.	Existing methods will work with nanomaterials, but with evidence of differences in effectiveness between nano and non-nano.	3a - Change(s) to Guidance to be suggested.	NS (ISO/TR 27628:2007 provides informative description)	*Applicability of method for nanomaterials* - Measures particles in air; - Can be used to determine the mass median aerodynamic diameter of agglomerates. Method is therefore still valuable and essential for inhalation studies with nanomaterials (Ma-Hock et al., 2007); - Has useful application in relation to exposure estimation. *Limitations of method for nanomaterials* - Fails to describe the dimension of nanoparticles as they no longer follow aerodynamic rules (Ma-Hock et al., 2007); - Only some cascade impactor will have size selective stages which are relevant from small-end nanomaterials. Requires aerosolisation. *Additional comments* - A definitive, standardised method description has not been identified. - Current Guidance states "Size range: 0.1-20 and 0.5-80 microns"; this is ambiguous and requires clarification; - This is a sampling method only and requires an offline measurement to be made to yield the size distribution.	P	Size distribution based on mass per size interval, from which MMAD (m) can be calculated.	R7.1.14 - Limitations of cascade impaction for nano to be highlighted in revised version of Table R.7.1-31, including reference to informative description in ISO/TR 27628:2007.



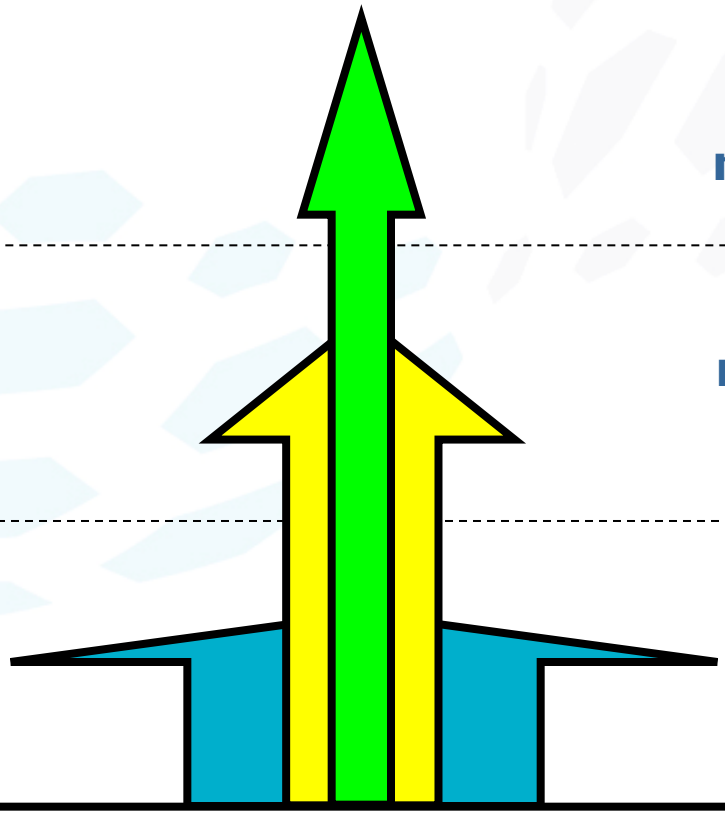
Task B5: Testing & Strategies

Objective

To provide:

- Advice on **integrated testing strategies** relevant to specific nanomaterials properties and how the specific intrinsic properties of nanomaterials might affect the need for adaptations to the testing regime;
- Advice on the scientific basis for the **categorisation** of nanomaterials and application of *in silico* methods, read-across and category approaches for deriving hazard information for nanomaterials from the information on bulk substances or from comparison between nanomaterials;
- Proposals for further **amendment of the REACH guidance documents** in regard to information requirements, test methods or testing strategies for nanomaterials, where appropriate, taking into account the provisions to minimise use of animals for testing;
- Proposal for **further research and development** of test methods and other data generation methods/strategies in regard to nanomaterials.

Concluding Remarks



Achievable in REACH

Guidance update recommendation

Of value in REACH

R&D recommendation

Relevant to nanomaterials in REACH

Identified

Evidence Base of

Properties & Endpoints, Methods & Techniques, Practice & Standards

Concluding Remarks: Recommendations for Guidance Updates and R&D

As the RIP-oN2 project has not yet concluded, an overview of the pre-finalised recommendations from the project will be highlighted in the remainder of the presentation.