

Regulatory Research Roadmap NanoSafety Cluster

Vicki Stone and Adrienne Sipps

v.stone@hw.ac.uk

adrienne.sips@rivm.nl

Regulator Research Roadmap Team

Input from:

Vicki Stone

Jacques-Aurelien Sergent

Enrico Bergamaschi

Susan Dekkers

Wilson Engelman

Katrin Halling

Sonja Hartl

Andrej Kobe

Niklas Luhmann?

Serli Önlü

Agnes Oomen

Adriele Prina-Mello

Juan Riego-Sintes

Phil Sayre (US EPA)

Monita Sharma

Adrienne Sips

Ulla Vogel

Tom van Teunenbroek

Martie van Tongeren

Wilson Wengemann

NanoSafety
Cluster



Regulatory Research Roadmap Purpose

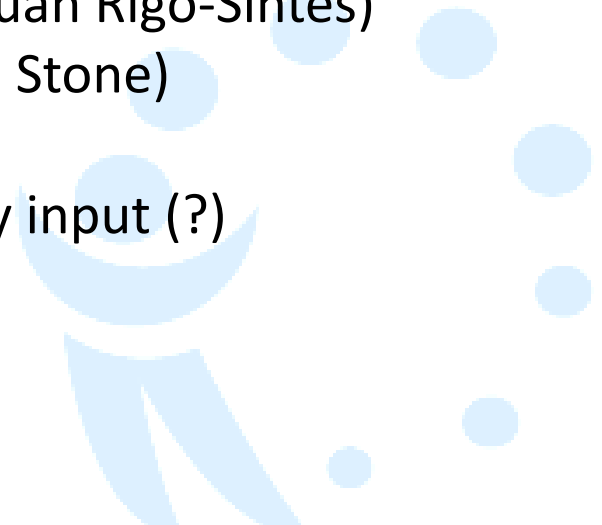
- To identify and structure the research required to deliver effective regulation of nanomaterial safety
- Including
 - Consumer
 - Occupational
 - Sector specific issues
- Excluding
 - Nanomedicine

*NanoSafety
Cluster*



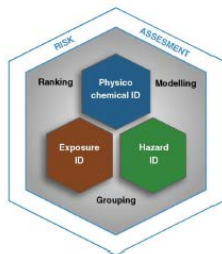
Stage 1 – Identifying activities relevant to the RRR

- ITS-NANO hexagon diagrams to illustrate research prioritisation (Vicki Stone)
- NANoREG gap analysis (Susan Dekkers)
- US research and regulatory development (Phil Sayes EPA)
- MARINA tiered approach for RA (Agnes Oomen)
- Nanonext.nl (Adrienne Sips)
 - Dutch nanotechnology development programme
 - Risk Analysis and Technology Assessment (RATA)
- NANoREG questions relevant for regulators (Juan Rigo-Sintes)
- Safety-by-Design – SUN and NanoGuide (Vicki Stone)
- REACH (Juan Rigo-Sintes, Wim De Coen)
- EU occupational and safety at work regulatory input (?)
- Educational framework (?)



Research Prioritisation to deliver an Intelligent Testing Strategy for Engineered Nanomaterials

RESEARCH PRIORITISATION TO DELIVER AN INTELLIGENT TESTING STRATEGY FOR THE HUMAN AND ENVIRONMENTAL SAFETY OF NANOMATERIALS

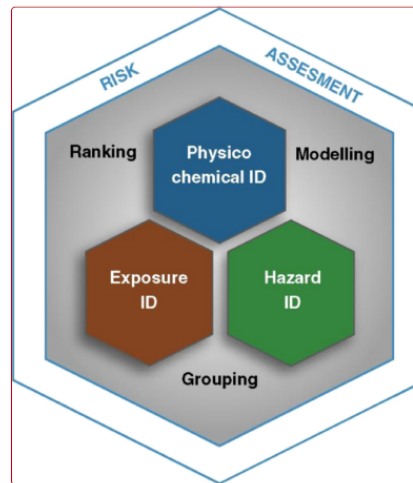


ITS NANO

<http://www.nano.hw.ac.uk/research-projects/itsnano.html>



PARTICLE AND
FIBRE TOXICOLOGY

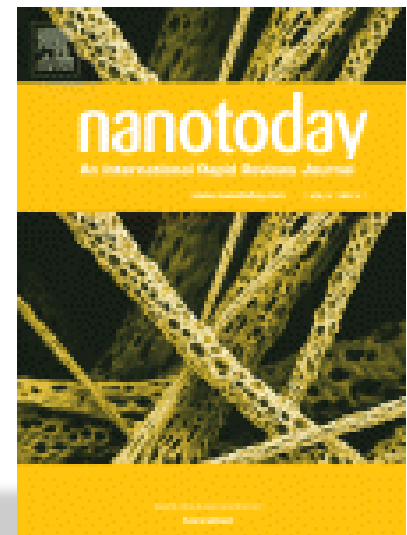


ITS-NANO - Prioritising nanosafety research to develop a stakeholder driven intelligent testing strategy

Stone et al.



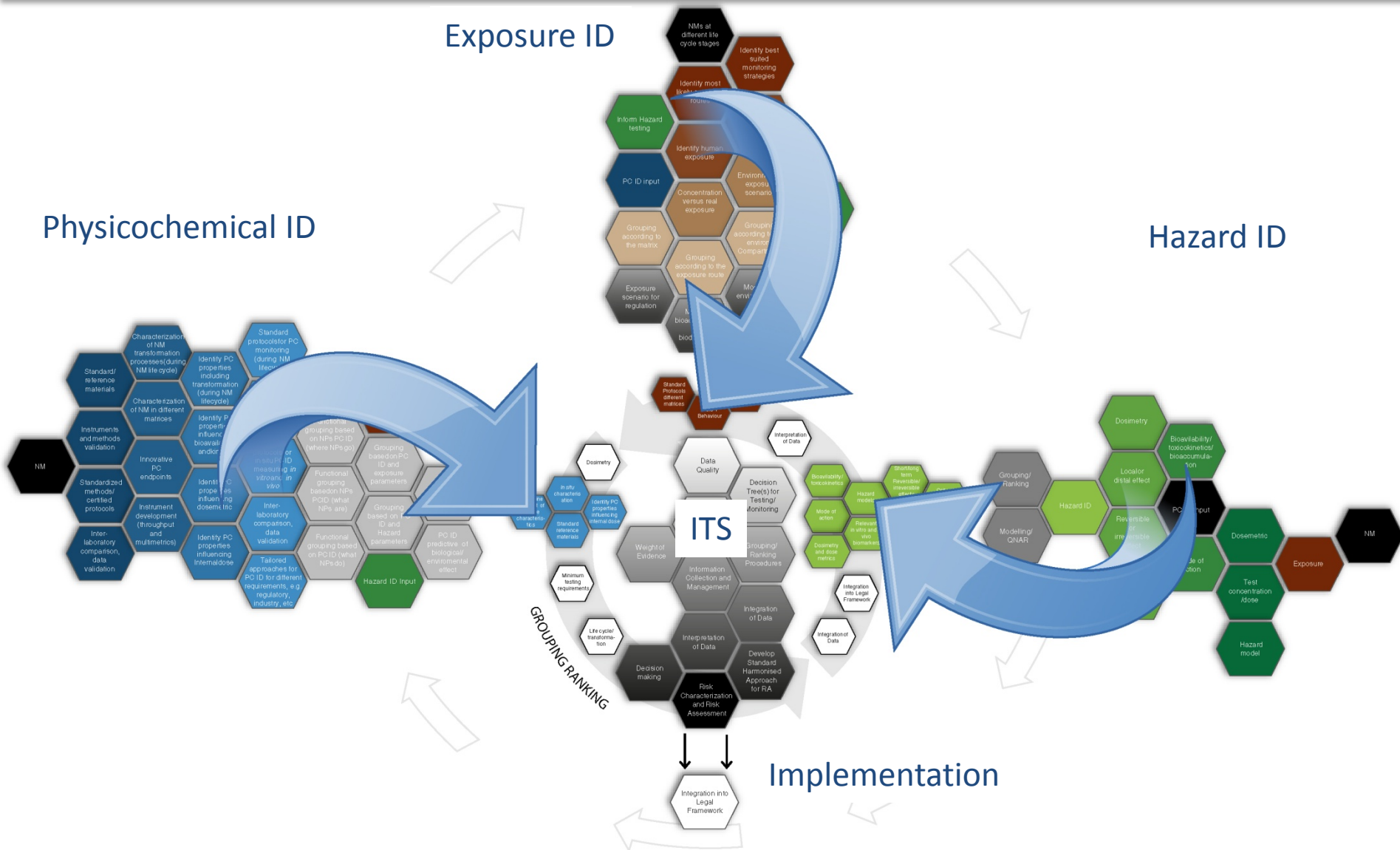
Stone et al. *Particle and Fibre Toxicology* 2014, **11**:9
<http://www.particleandfibretoxicology.com/content/11/1/9>



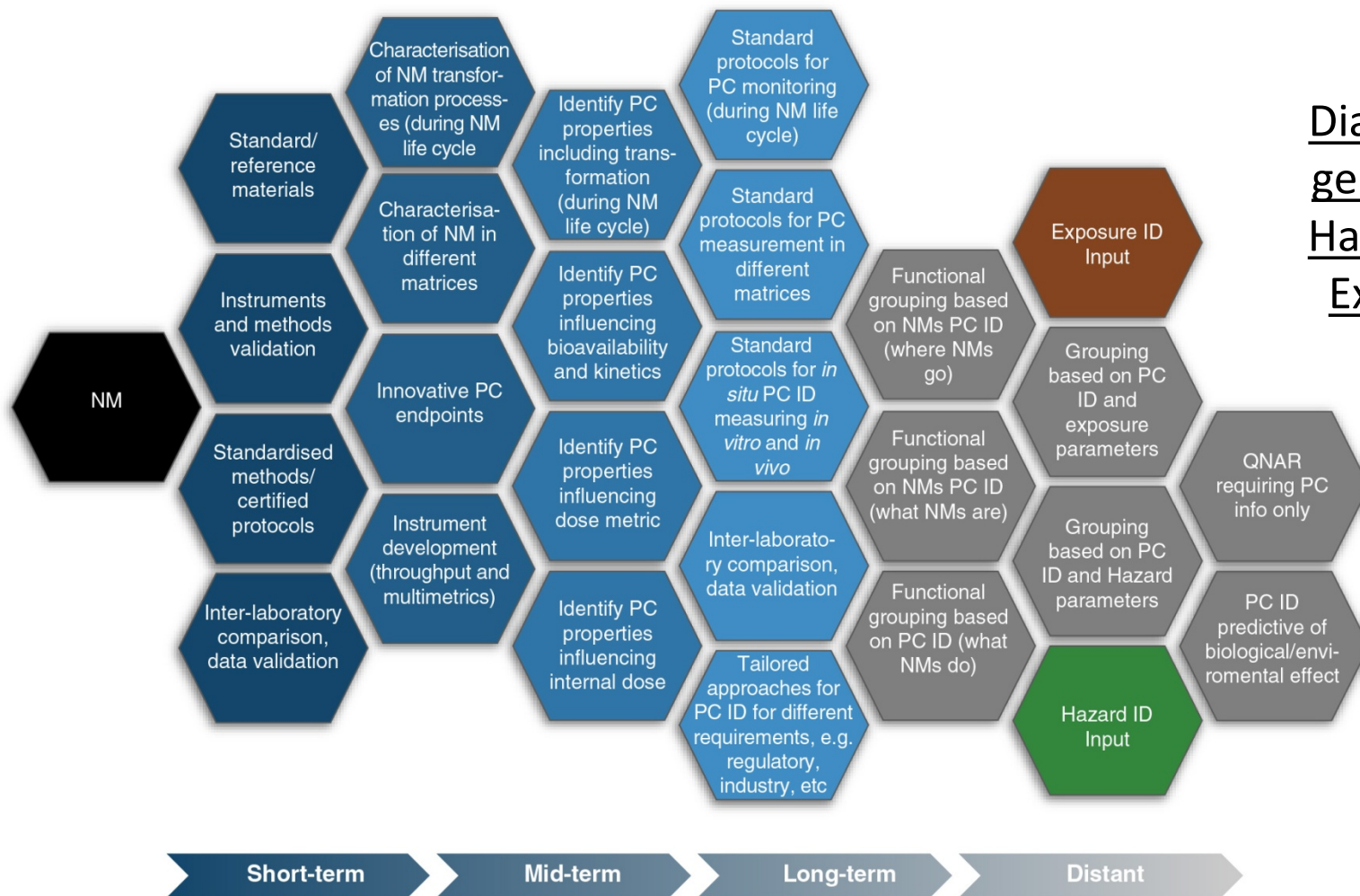
Stone et al., *Particle and Fibre Toxicology* 2014, **11**:9

ITS NANO

ITS-NANO Research Prioritisation



Physicochemical Priorities



Diagrams also generated for Hazard ID and Exposure ID

ITS-NANO hexagon approach

Regulatory research priorities

Core priorities

Product to market research priorities

Current position

Future

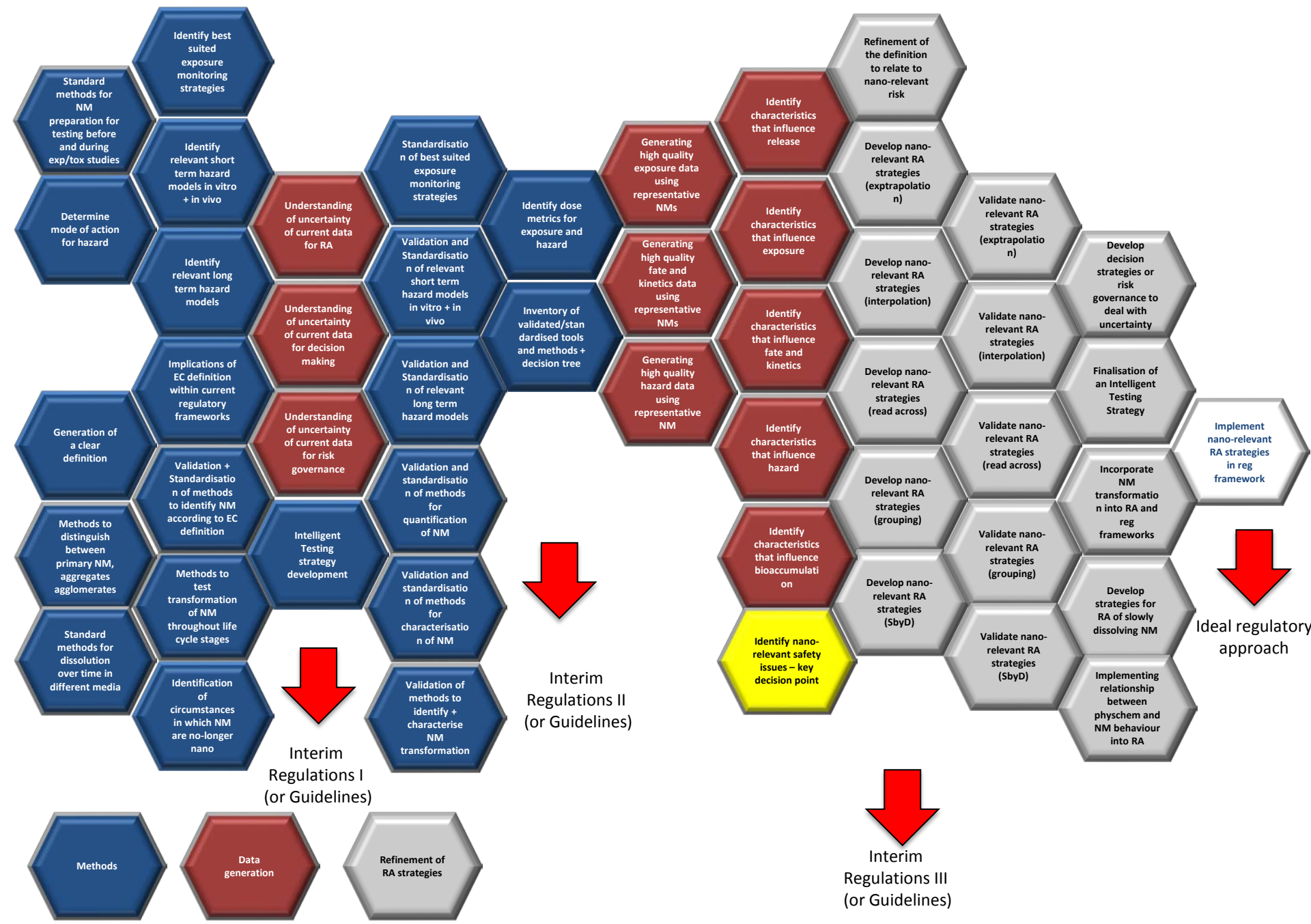


The Plan

- Convert NANoREG Regulation Research Gap analysis into a hexagon diagram.
- Colour code the hexagons by identifying which research priorities are relevant or common to both road maps.
- Interrogate the diagram using the Regulatory Questions from NANoREG and edit as appropriate.
- Interrogate the diagram in relation to current EU regulations (in particular REACH) and edit as appropriate.
- Compare and contrast the hexagon diagram generated with US activities and edit as appropriate.
- Generate one paragraph of text to outline each hexagon/priority and link to the relevant references, reports and projects.
- Put together the final text that introduces the roadmap, provides the roadmap diagram, the short description for each hexagon/priority with references, and the final conclusions.

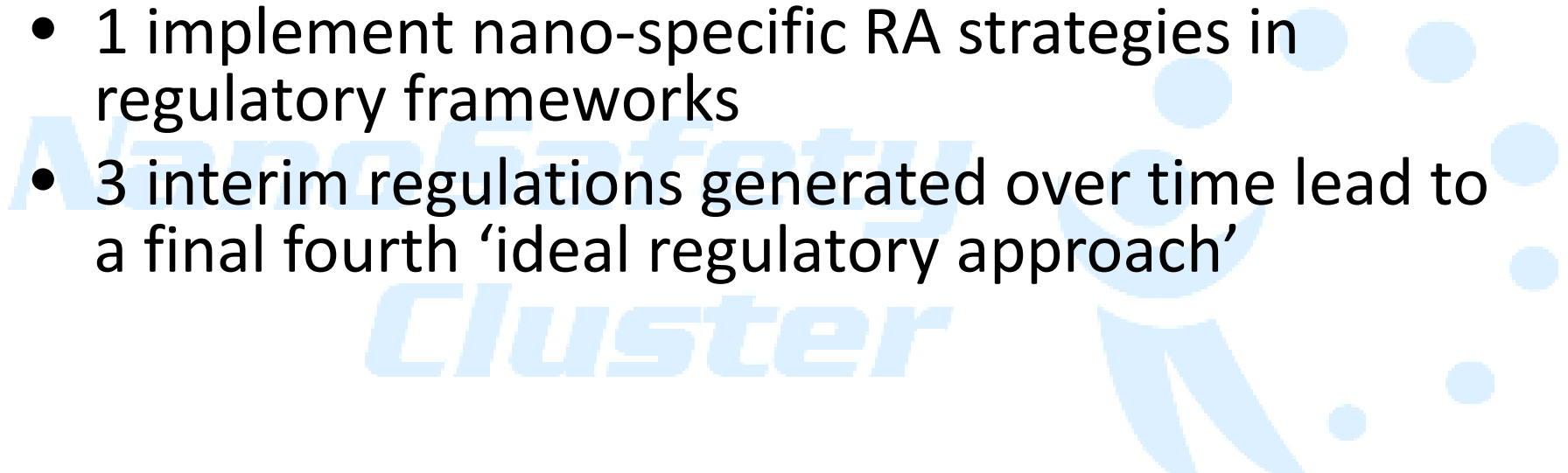
Short term

Long term

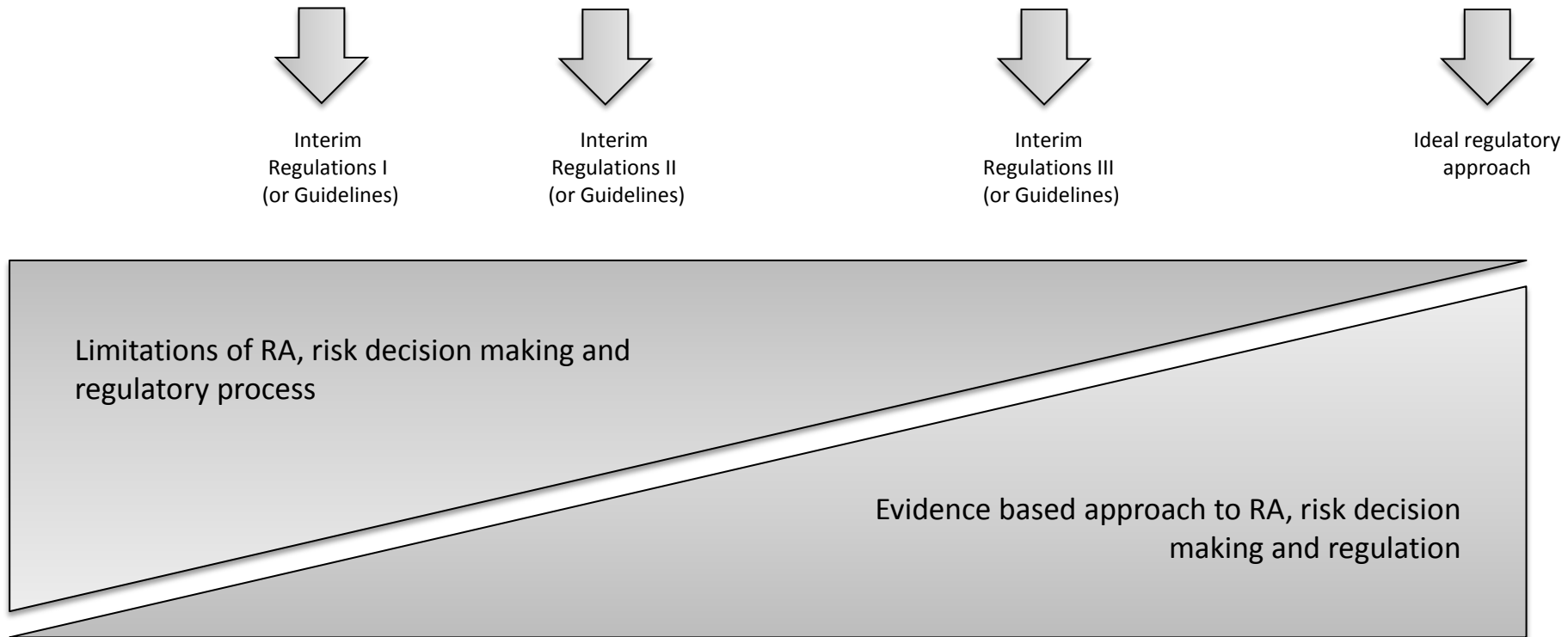


RRR diagram so far

- 50 Research priority hexagons identified
- 21 methods
- 11 data generation
- 16 Refinement of RA strategies
- 1 Identify nano-relevant safety issues – key decision point
- 1 implement nano-specific RA strategies in regulatory frameworks
- 3 interim regulations generated over time lead to a final fourth 'ideal regulatory approach'



We can't wait 15 years before identifying and acting upon nano-relevant regulation needs.....



Regulatory approaches could increase in sophistication with time as the knowledge base increases - 'something is better than nothing'

RRR text so far (25 pages)

021014

Methods

Data generation

Refinement of RA strategies

Identify best suited exposure monitoring strategies

The colour coding groups hexagons (research priorities) in order to simplify understanding

+	1.1	Generation of a clear definition
		<p>A clear definition of nanomaterial should be scientifically exhibit a well-defined scope and it should be possible to link the definition should be as uniform as possible across different global locations, in order to prevent that a material is not one framework and not in another.</p> <p>The European Commission (EC) published a recommendation of nanomaterials (2011/050 EU). http://ec.europa.eu/research/industrial_technologies/pdf/policy_recommendation-on-the-definition-of-nanomaterial-18102011_en.pdf</p> <p>The European Parliament and the Council, European Parliament 2013 on a new agenda for European Consumer Policy (EP). http://www.europa.eu/ides/getDoc.do?pubRef=-//EP//2013-0239-0-DO-0-HTML-0//EN/eng/page-EN</p> <p>Most probably the most distinguishing aspect of the EC recommendation is the use of particle size distributions based on the numbers of particles or mass or volume of the particles, as the main classification criteria.</p> <p>More recently (March 2014) Joint Research Centre Institute for Protection published a review of the EC definition recommendation of the EC Recommendation for a definition of the term 'nanomaterial'. Completion of information concerning the experience with the definition. http://publications.jrc.ec.europa.eu/epa/ibstare/11111/Term.pdf</p> <p>Lately (August 2014) Joint Research Centre Institute for Risk Assessment published the second review report, namely, EC Recommendation for a definition of the term 'nanomaterial' collected information concerning the experience with the definition. http://publications.jrc.ec.europa.eu/epa/ibstare/11111/def_report2_en/2014.pdf</p> <p>Based on the feedback received regarding the current definition report of the series, and its assessment, presented in this report, now working on a set of indicators on how the definition could be clearly, effectiveness and implementability. These recommendations</p>

021014

1.6	Standard methods for testing, assessment and testing	<p>• susceptibility/sensitivity according to species, age, status or genetic variation)</p> <p>ITS-NANO Phil Sayne Ulrich Vogel Viola Stone</p> <p>Standard methods for NM preparation for testing exposure/toxicology studies</p> <p>There is a need for more clarity regarding the best methods for human and environmental hazard testing. This is true for tests and monitoring, making it difficult to interpret the results. The need to improve understanding of dispersion characteristics and environmentally relevant media. This will enable better but at the same time there is a need to link to the knowledge of dispersion in the environment, in relation to the fate of the material.</p> <p>The above text suggests that development of a single method, however, is unlikely due to the variations in NM physical matrices and exposure scenarios/routes. In the future, a mix of dispersion options will be required to guide researchers/hazard most appropriate protocols. Protocols may not necessarily mono-dispersed suspensions. In many situations, they may be realistic situations with aggregated or agglomerated particles.</p> <p>Which projects have or are currently developing protocols for the distinction between primary NMs, agglomerates and aggregates?</p> <p>ITS-NANO Phil Sayne Ulrich Vogel</p>
1.8	Identify best suited exposure monitoring strategies	<p>Exposure monitoring can be done for a variety of needs: assessment, epidemiology, compliance testing, and testing measures (e.g., local exhaust ventilation systems, enclosures). The nature of the monitoring strategy will heavily depend on the assessment. For example, testing the effectiveness of compliance with standards (e.g., OELs) or quantitative assessment on the use of personal monitoring approaches. Exposure monitoring for NMs is complicated as:</p> <ol style="list-style-type: none"> 1) There is a lack of standard approaches and metrics (area, or other) that can be used for risk assessment/information. 2) The majority of direct reading instruments for NMs are not specific to engineered nanomaterials.

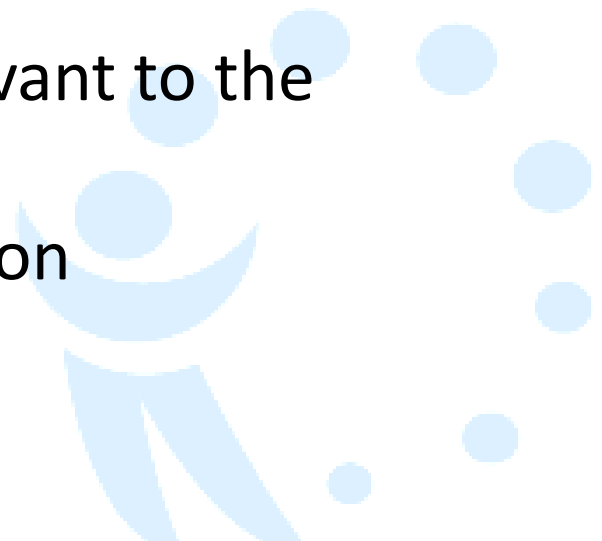
021014

4.6	Validate nano-specific RA strategies (Boyd)	<p>Arbeitsplatz-Beurteilung von Schuttmitteln (ASB) - Rahmenindex 2.0</p> <p>Von Broekhuizen, et al. (2012) Exposure Limits for Nanoparticles: Report of an International Workshop on Nano-Reference Values. Ann. Occup. Hyg., Vol. 50, No. 5, pp. 515-524. Available at: http://onlinelibrary.wiley.com/doi/10.1111/soo.12011</p> <p>Combine with 3.16</p> <p>Author</p>
4.7 <td>Develop decision strategies or risk governance to deal with uncertainty</td> <td> <p>What is required to validate?</p> <p>Combine with 3.19?</p> </td>	Develop decision strategies or risk governance to deal with uncertainty	<p>What is required to validate?</p> <p>Combine with 3.19?</p>
4.8 <td>Finalisation of an Intelligent Testing Strategy</td> <td> <p>Viola Stone</p> </td>	Finalisation of an Intelligent Testing Strategy	<p>Viola Stone</p>
4.9 <td>Incorporate NM transformation into RA and regulatory frameworks</td> <td></td>	Incorporate NM transformation into RA and regulatory frameworks	
4.10 <td>Develop strategies for RA of slowly dissolving NM</td> <td></td>	Develop strategies for RA of slowly dissolving NM	
4.11 <td>Implement relationships between physicochemical and NM behaviour into RA</td> <td></td>	Implement relationships between physicochemical and NM behaviour into RA	
4.12 <td>Implement nano-specific RA strategies into regulatory frameworks</td> <td></td>	Implement nano-specific RA strategies into regulatory frameworks	

Markup Area

Text requirements

- Potential authors have been identified for all missing research priorities
- Each section needs to
 - Clarify why it is a research priority
 - Clarify what research is already encompassed within the priority
 - Generate recommendations relevant to the priority
 - Provide links to further information



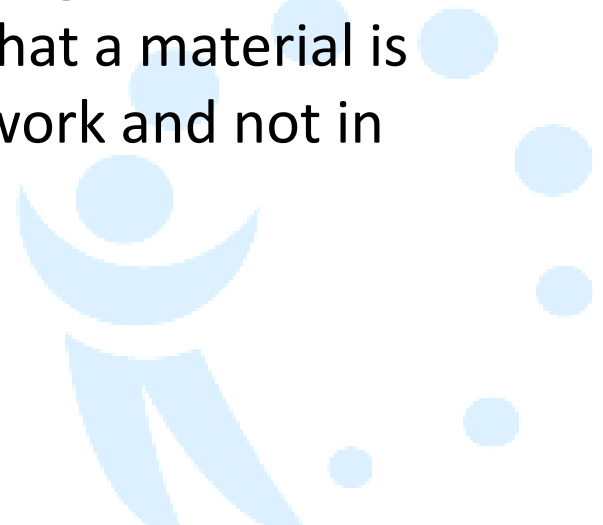
Example

Generation of a clear definition – Why?

A clear definition of nanomaterial should

- be scientifically driven (i.e. evidence based),
- exhibit a well-defined scope
- be possible to implement
- be as uniform as possible across different legal frameworks and global locations, in order to prevent that a material is regarded as a nanomaterial in one framework and not in another.

*Nanosafety
Cluster*



Example

Generation of a clear definition – What?

The European Commission (EC) published a recommendation in 2011 on the definition of nanomaterial (2011/696/EU):

http://ec.europa.eu/research/industrial_technologies/pdf/policy/commission-recommendation-on-the-definition-of-nanomater-18102011_en.pdf

Most probably the most distinguishing aspect of the EC nanomaterial definition is the use of particle size distributions based on the numbers of particles, and not on the mass or volume of the particles, as the main classification feature.

Lately (August 2014) Joint Research Centre Institute for Reference Materials and Measurements published the second review report namely, Towards a review of the EC Recommendation for a definition of the term "nanomaterial" Part 2: Assessment of collected information concerning the experience with the definition:

http://publications.jrc.ec.europa.eu/repository/bitstream/111111111/32544/1/jrc_nm-def_report2_eur26744.pdf

*NanoSafe EU
Cluster*

Example

Generation of a clear definition – Recommendation

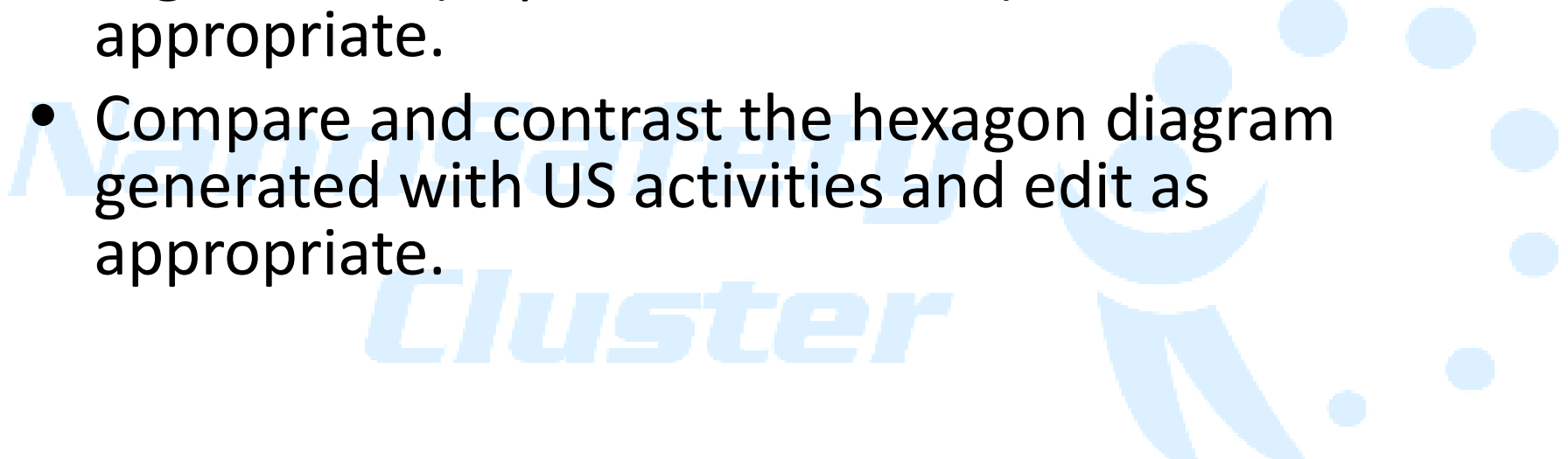
An attempt by different regulators to align their definitions (e.g. via an OECD workshop) would be helpful.

*NanoSafety
Cluster*



Next steps

- Finish first draft of report for circulation to cluster members
- Interrogate the diagram using the Regulatory Questions from NANoREG and edit as appropriate.
- Interrogate the diagram in relation to current EU regulations (in particular REACH) and edit as appropriate.
- Compare and contrast the hexagon diagram generated with US activities and edit as appropriate.



Nanocluster input

- Next draft will be circulated for comment in April

*NanoSafety
Cluster*



Regulator Research Roadmap Team Acknowledgements

Input from:

Vicki Stone

Jacques-Aurelien Sergent

Enrico Bergamaschi

Susan Dekkers

Wilson Engelman

Katrin Halling

Sonja Hartl

Andrej Kobe

Niklas Luhmann?

Serli Önlü

Agnes Oomen

Adriele Prina-Mello

Juan Riego-Sintes

Phil Sayre (US EPA)

Monita Sharma

Adrienne Sips

Ulla Vogel

Tom van Teunenbroek

Martie van Tongeren

Wilson Wengemann

NanoSafety
Cluster

