Regulatory Research Roadmap NanoSafety Cluster

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Regulator Research Roadmap Team

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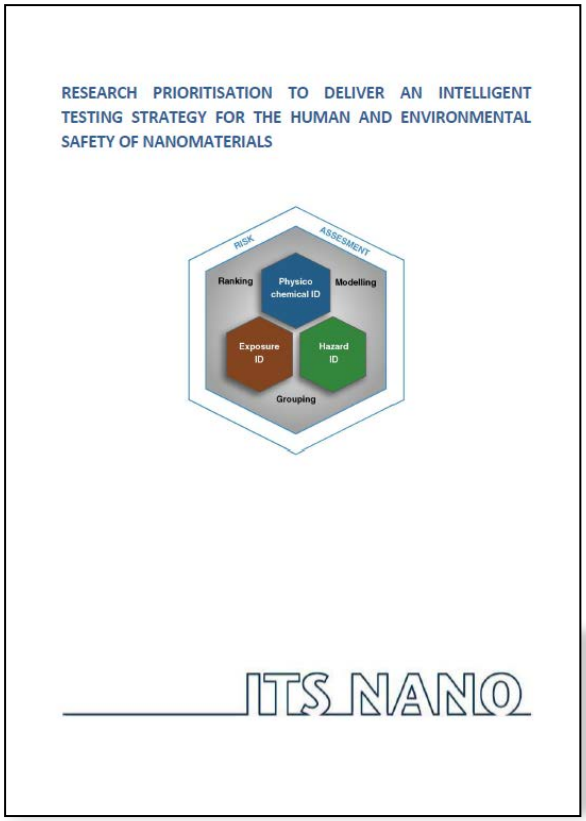
Regulatory Research Roadmap Purpose

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

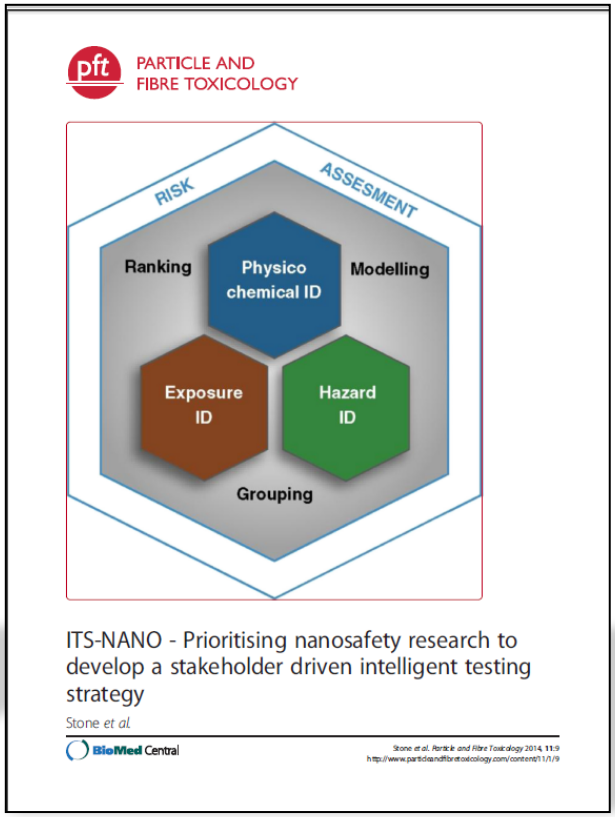
Stage 1 – Identifying activities relevant to the RRR

- 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 (?)

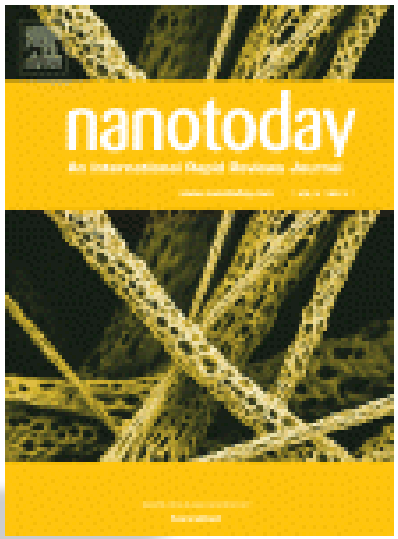
Research Prioritisation to deliver an Intelligent Testing Strategy for Engineered Nanomaterials



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

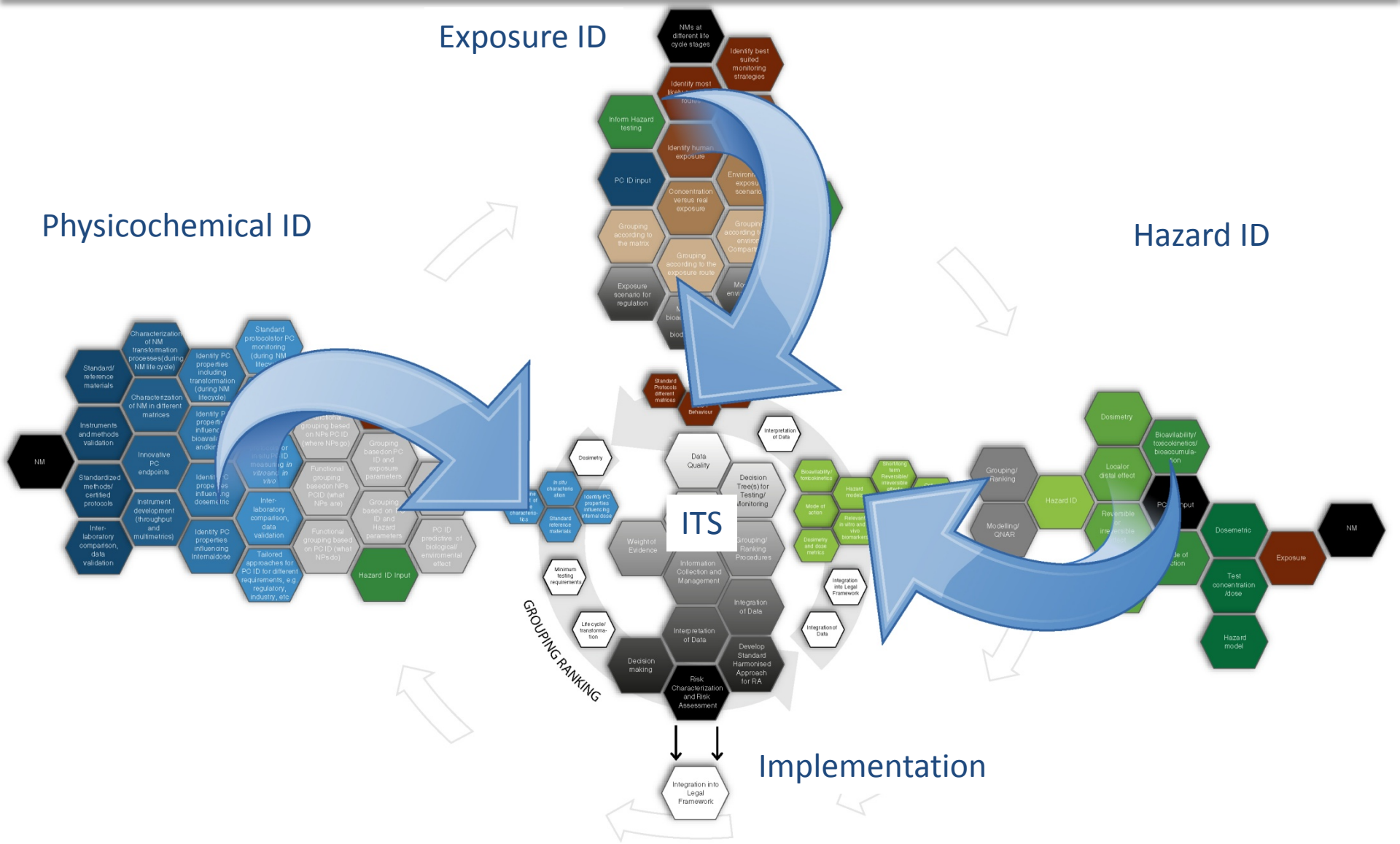


Stone et al., Particle and Fibre Toxicology 2014, **11**:9

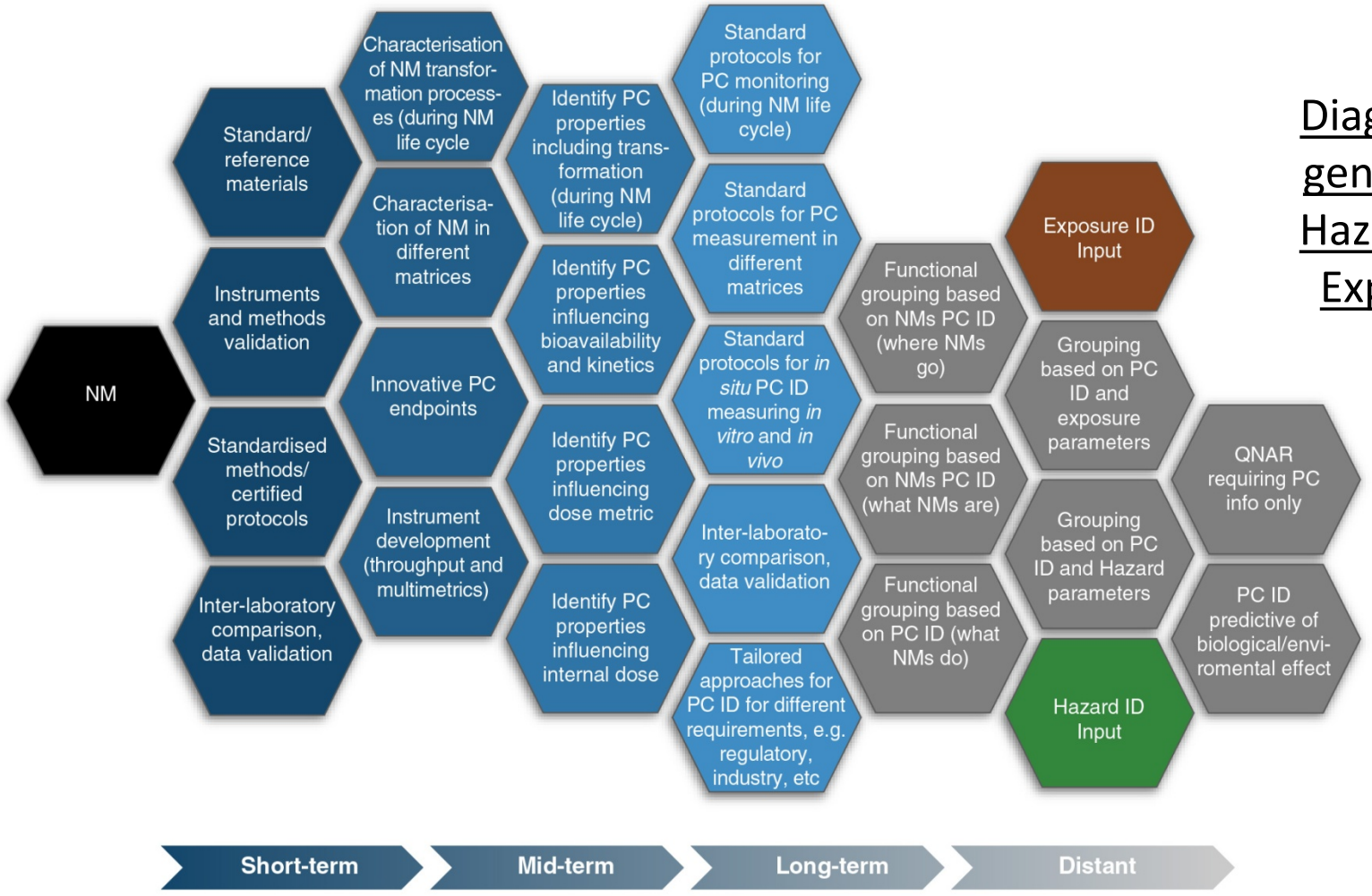


ITS NANO

ITS-NANO Research Prioritisation



Physicochemical Priorities



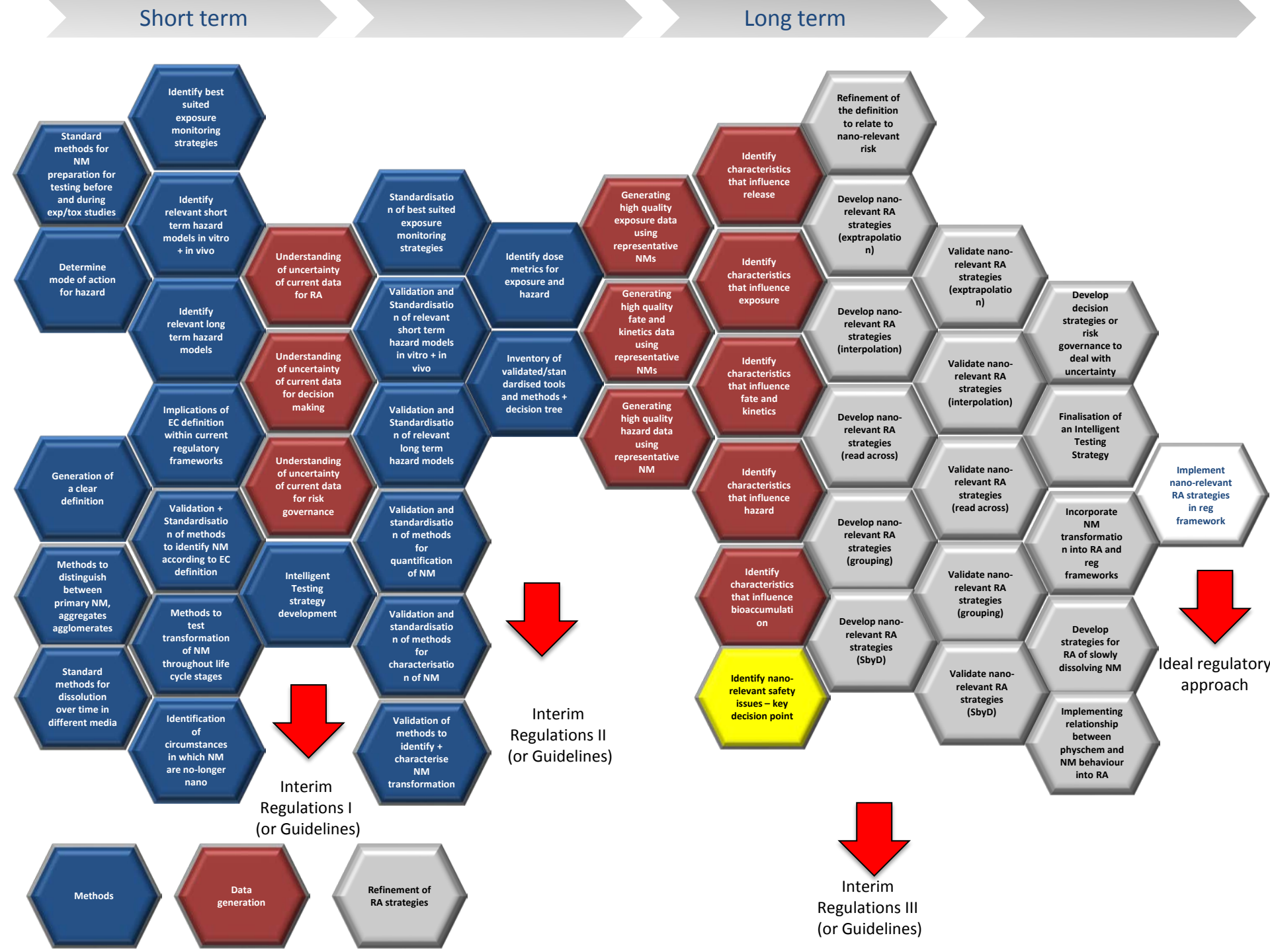
Diagrams also generated for Hazard ID and Exposure ID

ITS NANO

ITS-NANO hexagon approach

The Plan

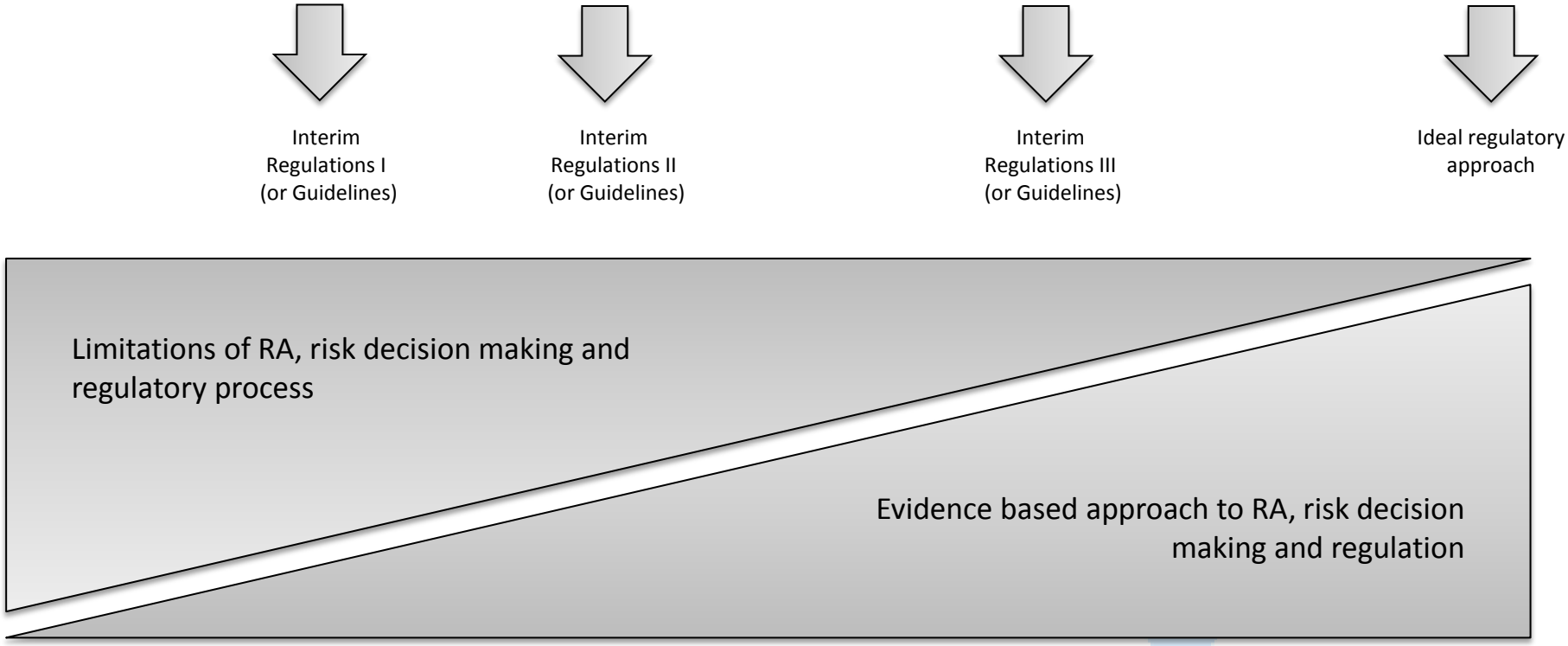
- Convert NANoREG Regulation Research Gap analysis into a hexagon diagram.
- Colour code the hexagons by identifying which research priorities are relevant or common to both road maps.
- Interrogate the diagram using the Regulatory Questions from NANoREG and edit as appropriate.
- Interrogate the diagram 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
Identify best suited exposure monitoring strategies
Standard methods for NM preparation for testing before and during exp/tox studies
Identify relevant short term hazard models in vitro + in vivo
Determine mode of action for hazard
Identify relevant long term hazard models
Implications of EC definition within current regulatory frameworks
Generation of a clear definition
Validation + Standardisation of methods to identify NM according to EC definition
Methods to distinguish between primary NM, aggregates agglomerates
Methods to test transformation of NM throughout life cycle stages
Standard methods for dissolution over time in different media
Identification of circumstances in which NM are no-longer nano
Understanding of uncertainty of current data for RA
Understanding of uncertainty of current data for decision making
Understanding of uncertainty of current data for risk governance
Intelligent Testing strategy development
Standardisation of best suited exposure monitoring strategies
Validation and Standardisation of relevant short term hazard models in vitro + in vivo
Validation and Standardisation of relevant long term hazard models
Validation and standardisation of methods for quantification of NM
Validation and standardisation of methods for characterisation of NM
Validation of methods to identify + characterise NM transformation
Interim Regulations I (or Guidelines)
Identify dose metrics for exposure and hazard
Inventory of validated/standardised tools and methods + decision tree
Interim Regulations II (or Guidelines)
Generating high quality exposure data using representative NMs
Generating high quality fate and kinetics data using representative NMs
Generating high quality hazard data using representative NM
Identify characteristics that influence release
Identify characteristics that influence exposure
Identify characteristics that influence fate and kinetics
Identify characteristics that influence hazard
Identify characteristics that influence bioaccumulation
Identify nano-relevant safety issues – key decision point
Refinement of the definition to relate to nano-relevant risk
Develop nano-relevant RA strategies (exptrapolation)
Develop nano-relevant RA strategies (interpolation)
Develop nano-relevant RA strategies (read across)
Develop nano-relevant RA strategies (grouping)
Develop nano-relevant RA strategies (SbyD)
Validate nano-relevant RA strategies (exptrapolation)
Validate nano-relevant RA strategies (interpolation)
Validate nano-relevant RA strategies (read across)
Validate nano-relevant RA strategies (grouping)
Validate nano-relevant RA strategies (SbyD)
Develop decision strategies or risk governance to deal with uncertainty
Finalisation of an Intelligent Testing Strategy
Incorporate NM transformation into RA and reg frameworks
Develop strategies for RA of slowly dissolving NM
Implementing relationship between physchem and NM behaviour into RA
Implement nano-relevant RA strategies in reg framework
Ideal regulatory approach
Interim Regulations III (or Guidelines)
Methods
Data generation
Refinement of RA strategies

RRR diagram so far

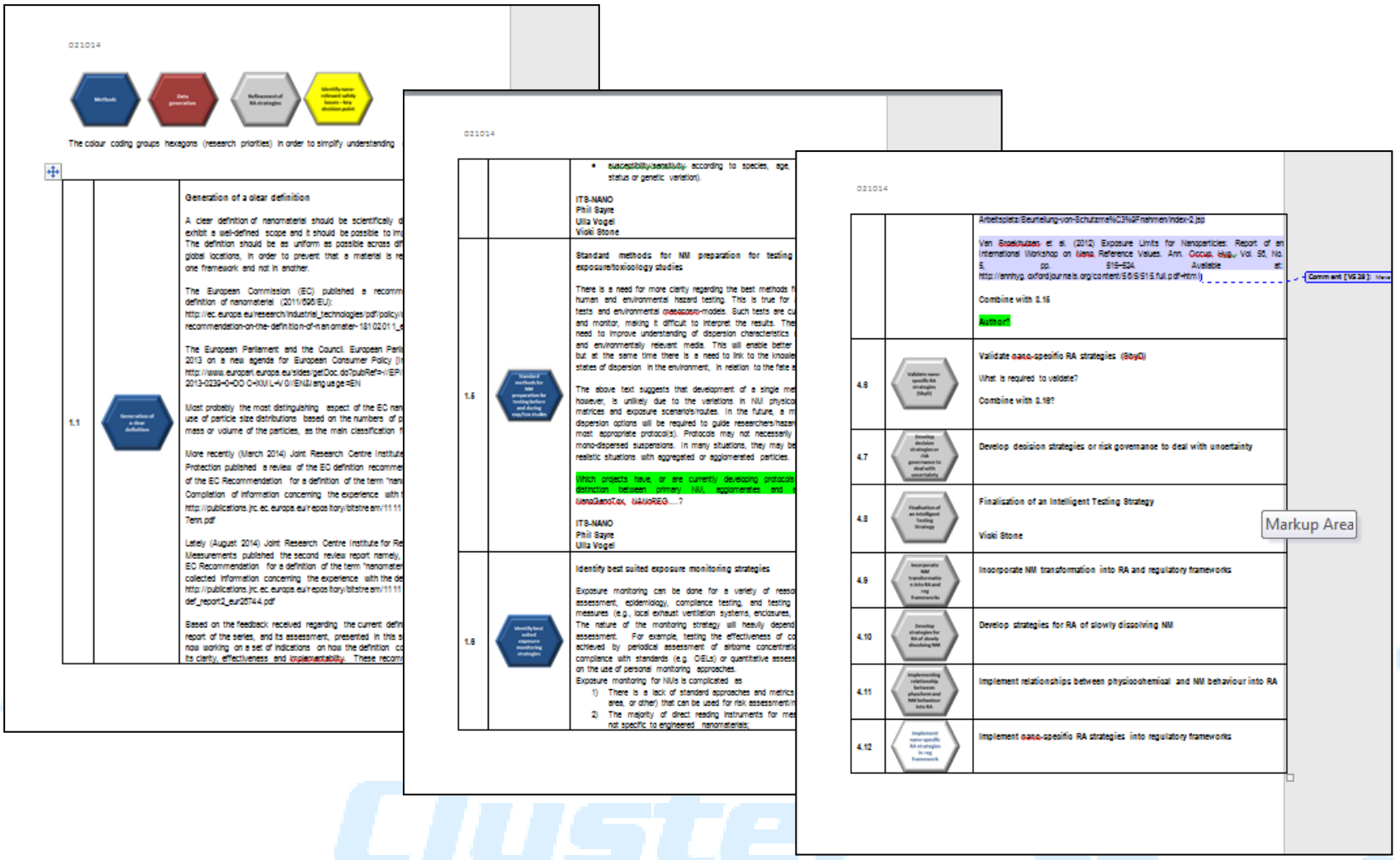
- 50 Research priority hexagons identified
- 21 methods
- 11 data generation
- 16 Refinement of RA strategies
- 1 Identify nano-relevant safety issues – key decision point
- 1 implement nano-specific RA strategies in regulatory frameworks
- 3 interim regulations generated over time lead to a final fourth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



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.

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

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.

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

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