Current legislative framework for nanomaterials: supporting REACH regulation

NanoMONITOR 1st Stakeholder's Day

Dr Neil Hunt

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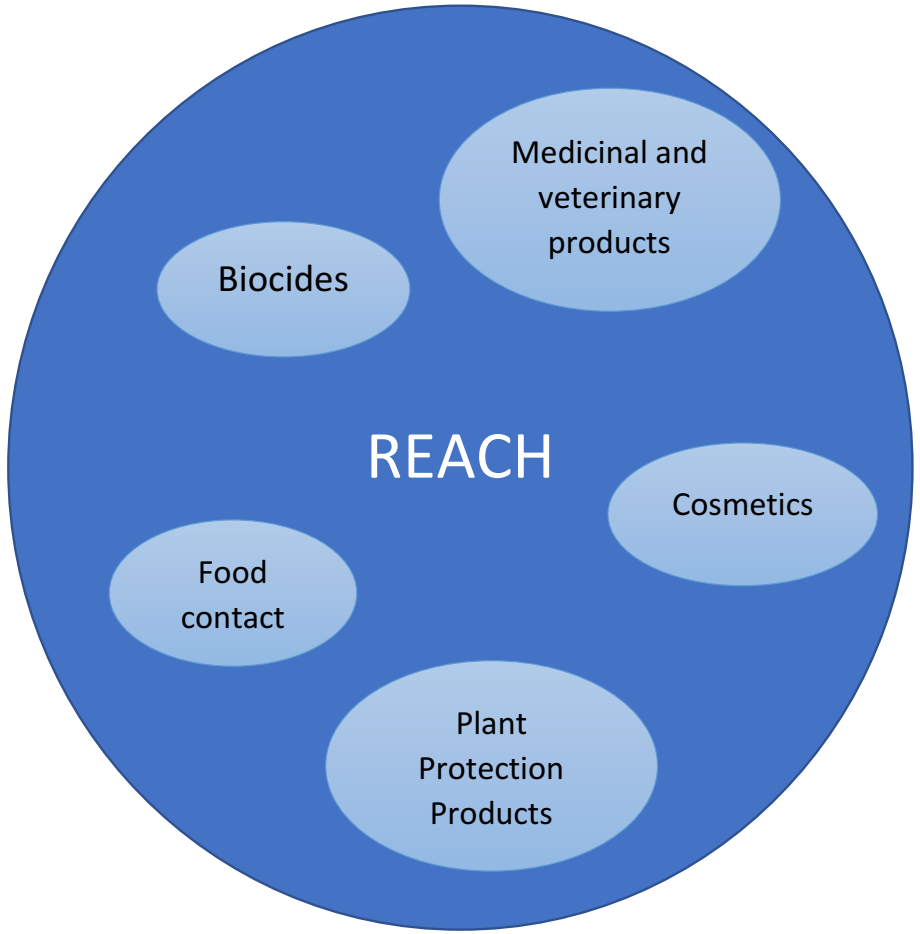
Regulatory framework for chemicals in the EU



- Regulations are use based.
- REACH covers all uses not covered by other regulations.
- No nano-specific regulation.
- Each regulation may require nanomaterials to be assessed differently to bulk forms

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Useful definitions

- Nanomaterial (draft):
  - *A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100* nm.

- Nanoform (ECHA, RIVM, JRC (2016))
  - *The term ……. to distinguish forms of a substance that fulfil the EC Recommendation on the definition of the term 'nanomaterial' but differ with regard to size distributions, shape and/or surface chemistry*."

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Revised definition of nanomaterial

- A revised definition is being discussed.
- Largely the same but with some important changes.
  - Clarification that it does not cover individual molecules (macromolecules, dendrimers).
  - Not clear whether particles with a dimension of < 1 nm will remain nanomaterials or not.
  - Specific Surface Area of < 5 m^2/cm^3 may be used to define substance that are not nanomaterials.
  - The 50 % by number size distribution may be regarded as indicative and other values might be more relevant in certain situations.
- Lots of debate and discussion, so these might change!
- Hopefully will be in place before any revision of Annex XIV to avoid replication of work for registrants.

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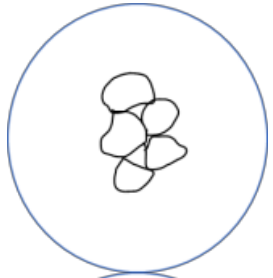
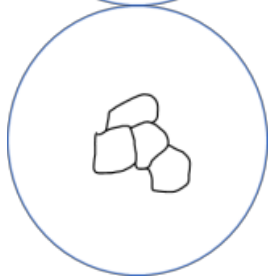
Definition of nanomaterial – Key points

Primary particles in unbound state



Primary particles as an agglomerate



Primary particles as an aggregate

- *"particles, in an unbound state or as an aggregate or as an agglomerate".*
  - Definition based on dimensions of primary particles
  - Agglomerate can be relatively easily broken, but aggregates are not easy to break into their constituent primary particles without damaging particles.
  - Is primary particle or agglomerate/aggregate size key for risk assessment?

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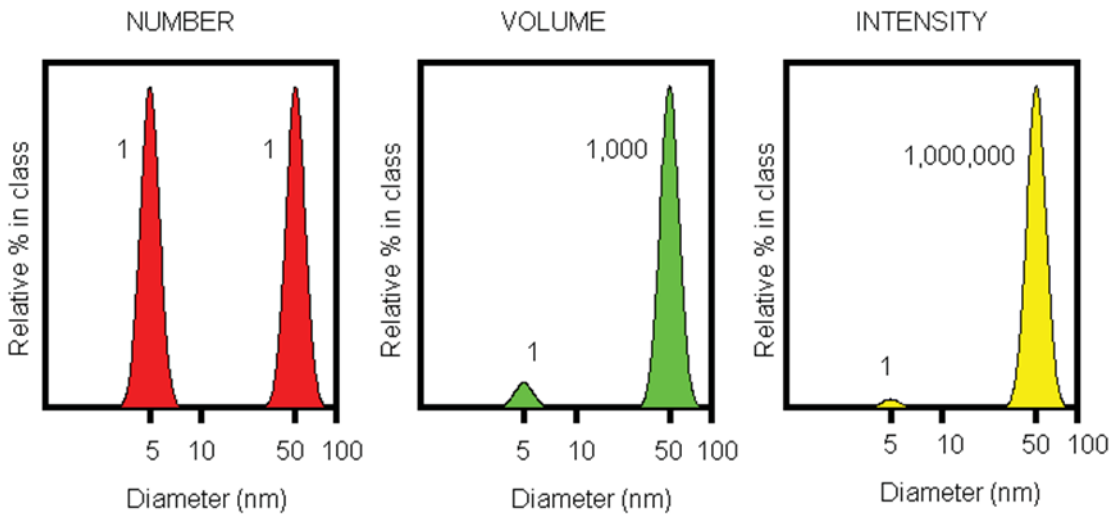
Definition of nanomaterial – Key points



- *50 % or more of the particles in the number size distribution*
  - Modal average of number distribution
  - Can analytical methods measure number distribution?
  - Number distribution will look different to volume or response distributions.
  - Are a lot of powders going to fall under the definition unexpectedly?

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Definition of nanomaterial – Key points

- *One or more external dimensions is in the size range 1 nm - 100 nm.*
  - Particles, rods, needles and plates can all be nanomaterials.
  - Shortest dimension is the key parameter.
  - Do analytical methods measure this dimension?
  - Nanoscale pores and spaces do not define a nanomaterial.

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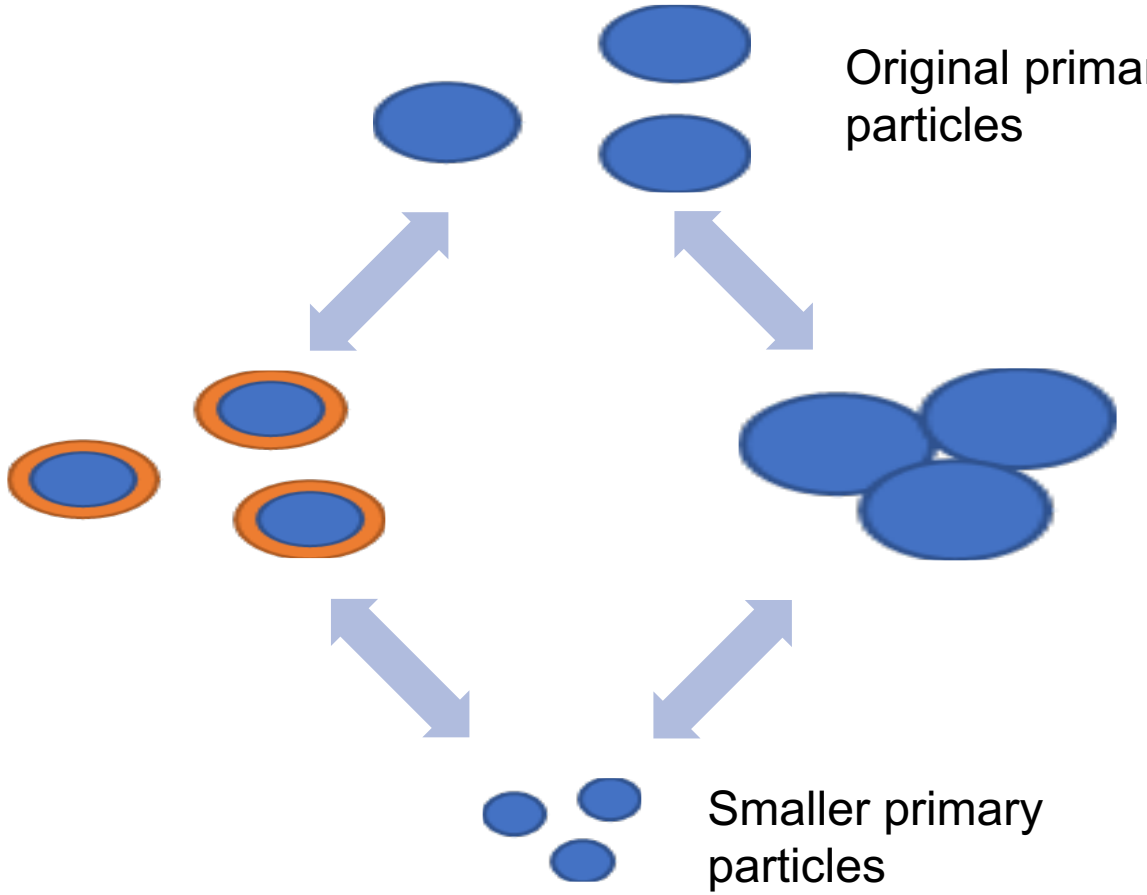
Nanoforms – Interconvertibility



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Nanoforms – Difficulties in Lifecycle Assessment

- Organic liquid substance
  - Only change of state is between solid, liquid and gas.
  - Hazards are intrinsic to the substance.
  - Changes in state mainly affect exposure.
- Nanomaterial powder
  - Different nanoforms of the same substance may display different toxicological profiles.
  - Different nanoforms of the same substance may display different exposure behaviours.
  - Which form exists at each point in the lifecycle?
  - Is the hazard, exposure and risk assessment appropriate for the nanoform?

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Key aspects of REACH

The hazards and risks arising from a substance should be known, and the appropriate risk management measures communicated, for substances manufactured in or imported to the EU.

Toxicological / Ecotoxicological / Physical Chemical Hazards identified by one entity (Lead Registrant)

Other registrants should receive permission to use this data in their registration dossier and ensure that it is relevant to the substance that they place on the market

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Nanomaterials and REACH

- Aspects of REACH apply to nanomaterials as to other forms of a substance.
  - The same inclusion and exclusion criteria (polymers, mixtures, exemptions).
  - Timetable is the same.
  - Same basic information requirements based on production volumes of the registrants.
  - Information in the registration dossier should apply to the substance placed on the market.
  - Testing should be adapted to the properties of the substance.

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Substance identification – General points in REACH

- All substances should be identified by their chemical composition.
  - Require identification and quantification of constituents
- Some substances may be further identified by other parameters (Guidance for identification and naming of substances, Section 4.2.3)
  - Particle size mentioned as a possible parameter.
  - Whether or not a substance is a nanomaterial is a possible parameter.
- Substance identification should be sufficient to assess whether the data in the registration dossier is applicable.

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Impact of recent Board of Appeal decision

ECHA decision

- Registrants of titanium dioxide should include details of all nanoforms as part of substance characterisation.

Industry (Registrants) Appeal

- This would mean nanoforms of a substance had additional requirements to bulk forms. This is not in line with Annex VI of REACH.

Board of Appeal (BoA) Decision

- BoA found in favour of registrants BUT it was highlighted that it should be shown that data in the dossier is applicable to the substance placed on the market.

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Revision of Annex VI of REACH

- Annex XVI states the characterisation requirements for REACH.
- Currently particle characterisation is an option not an obligation. Key issue in recent BoA decision.
- Absence of particle characterisation makes dossier and substance evaluation difficult.
- REACH revisions currently estimated to be officially in place in 2020.
- It is currently expected that particle characterisation to identify nanomaterials and nanoforms will be more prominent in Annex XVI.
- This will apply to all powders not only deliberately manufactured nanomaterials.

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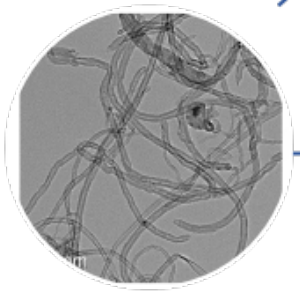
Particle characterisation to identify nanomaterials



Primary particles

- Many techniques measure particle size as they exist.
- Size of agglomerates or aggregates are measured

Shortest dimension

- Many techniques measure dimensions of swept area of a particle as it tumbles
- Longest dimension of hydro(aero)dynamic radius measured

Distribution by number

- Simple methods measure distribution by mass or volume
- Mathematical corrections needed to give distribution by number.

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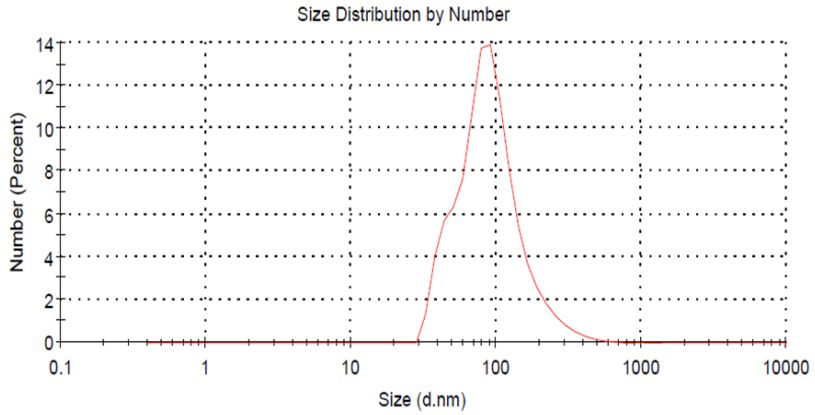
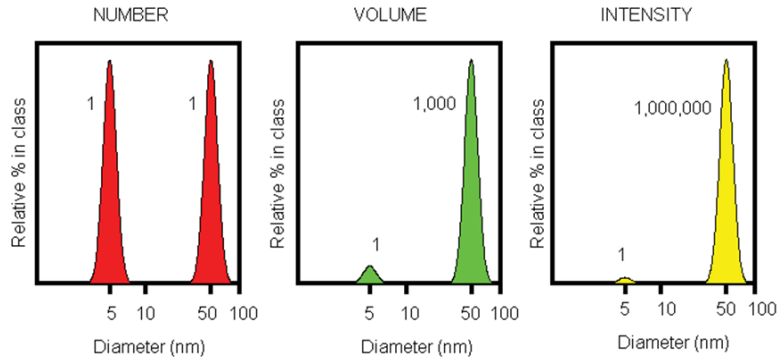
Dynamic Light Scattering



Peak diameter (nm)	% number	Standard deviation (nm)	Z Average (nm)	Polydispersity index
99.36	100.0	62.60	231.2	0.337



- Uses fluctuations in scattered light caused by a particle to determine how fast the particle moves in a suspension through Brownian Motion.
- Advantages:
  - Relatively cheap and easy to use
  - Measures a statistically significant distribution of particle size relatively rapidly
- Disadvantages
  - Distribution measured by signal intensity or volume NOT number
  - Does not distinguish agglomerate/aggregates from primary particles
  - Measures hydrodynamic radius
- Conclusion
  - Good screening tool.
  - If DLS indicates a sample is a nanomaterial, it almost certainly is!
  - Should not be used in isolation

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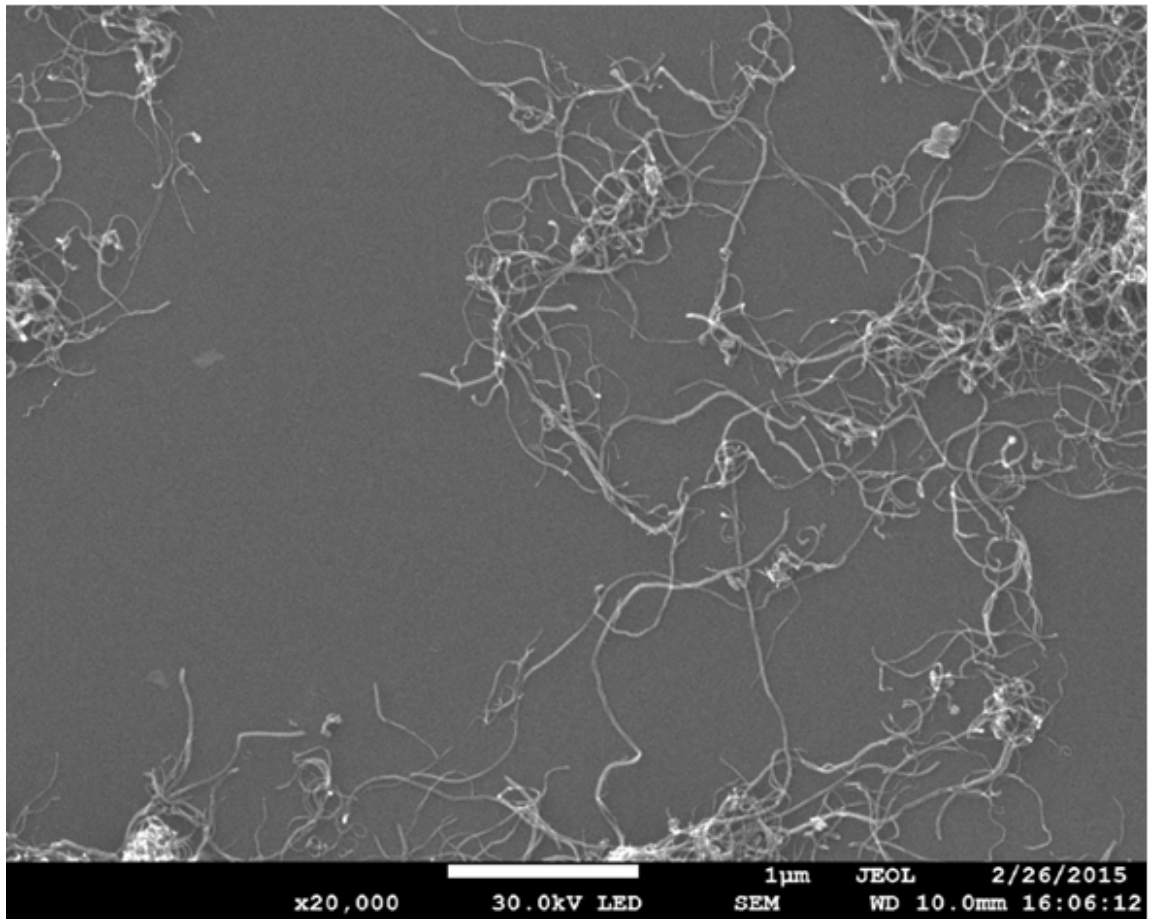
Electron Microscopy (Scanning or Transmission)



- Use electron beams to visualise particles at magnifications that cannot be achieved using optical microscopy.
- Advantages
  - Primary particles can be distinguished from agglomerates/aggregates
  - Particle size and shape can be measured
  - Shortest dimension can be measured
- Disadvantages
  - Multiple images needed to give a statistically significant sample size
  - Probably requires operator input and judgement to identify primary particles
  - Gives a 2-D image of 3-D object
- Conclusion
  - Essential tool for particle characterisation
  - Can be used to check whether results from other methods can be used to measure primary particle size distribution.

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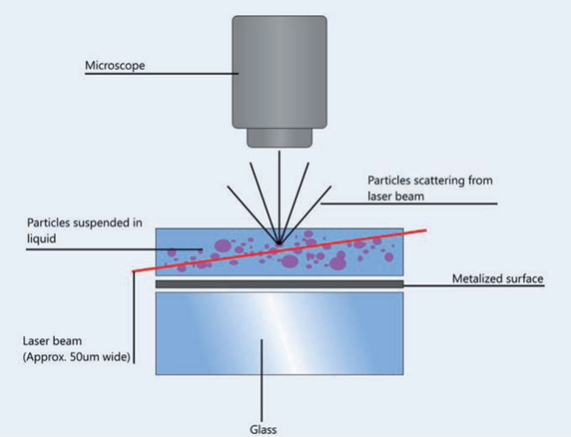
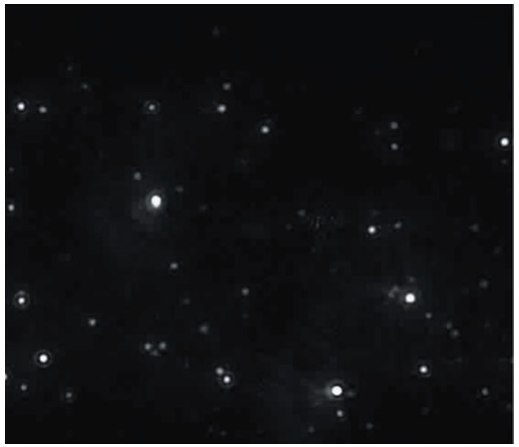
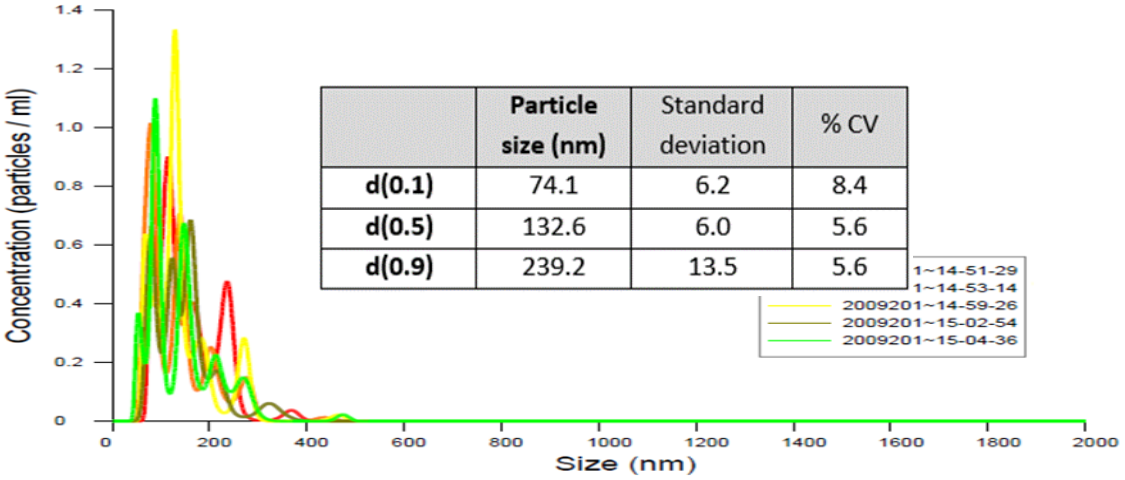
Particle Tracking Analysis







	Particle size (nm)	Standard deviation	% CV
d(0.1)	74.1	6.2	8.4
d(0.5)	132.6	6.0	5.6
d(0.9)	239.2	13.5	5.6

- Tracks scattered light patterns caused by individual particles. Uses velocity through a medium to calculate particle size.
- Advantages
  - Measures number distribution
  - Relatively low cost
  - Can be used with low concentration samples
- Disadvantages
  - Measures hydrodynamic radius
  - Cannot distinguish primary particles from agglomerates/aggregates
- Conclusion
  - Useful tool to directly measure number distribution of particles
  - Needs microscopy to confirm exactly what is being measured.

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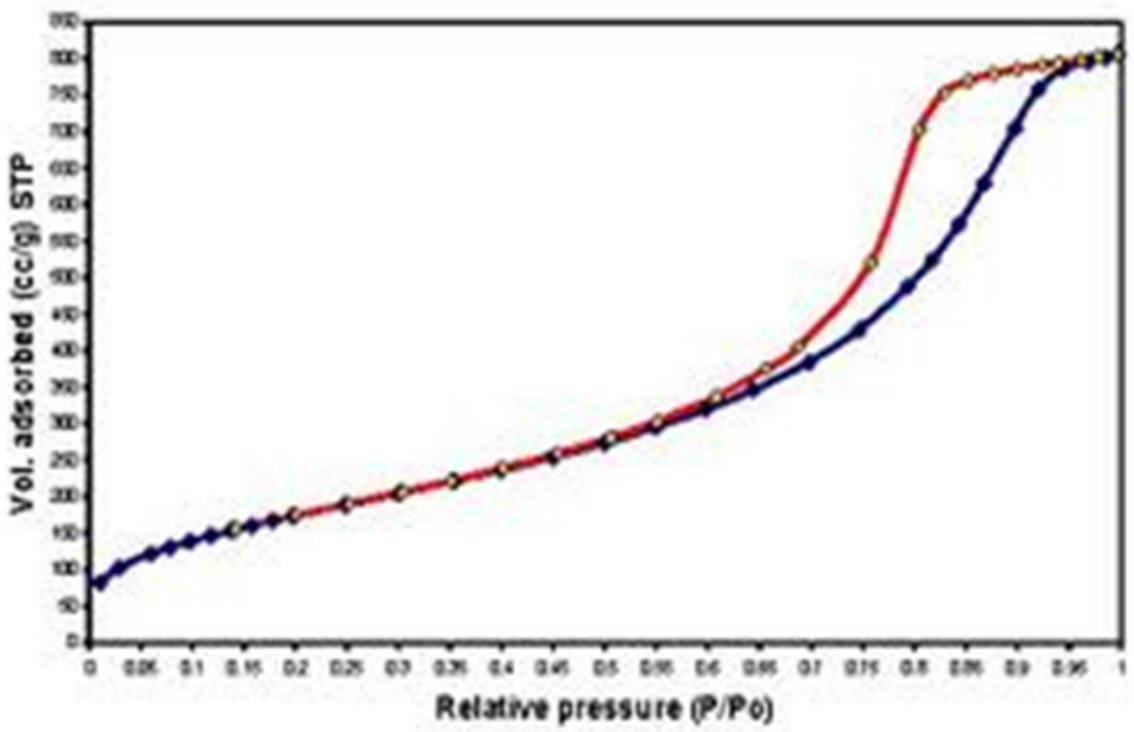
Specific Surface Area (SSA) by Brunauer Emmett Teller (BET) analysis



- Calculates SSA by measuring amount of a gas that can be adsorbed onto the surface of the sample.
- SSA > 60 m^2/cm^3 regarded as indicating a nanomaterial.
- SSA < 5 m^2/cm^3 may be a cut of for not being a nanomaterial (new definition of nanomaterial).
- Advantages
  - Well known method with many providers. Standard methods available.
- Disadvantages
  - Not a measurement of primary particle size distribution.
  - Internal structures (pores, tube interiors) can bias towards higher values.
  - Knowledge of density is required.
- Conclusion
  - Cannot be used in isolation but is very useful to support conclusions.

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Sample Preparation

- Sample preparation key to measuring what you think you are measuring.
- How are agglomerates broken?
- Are additives required to keep primary particles unbound?
- Is the substance soluble/stable in the technique medium?
- Ensure primary particles are not damaged during treatment.

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Particle Characterisation

- In many situations , no single method can be used to prove a substance a substance is a nanomaterial according to the current definition.
- Techniques should be appropriate to the substance.
- Different techniques might be appropriate for risk assessment (measuring particle size as it exists).
- Must be aware of exactly what is being measured.

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REACH and Hazard Assessment

- Testing requirements based on the tonnage per annum of the substance manufactured in or imported into the EU.
- Clearly defined in Annexes VII to X of REACH.
- Waivers for some studies available.
- Read-across, QSAR and grouping are all permitted but must be scientifically justified.

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REACH Hazard Assessment of Nanomaterials

- Same endpoints required as for other substances.
- Endpoint methodology might need to be altered to account for characteristics of nanomaterials.
- Some waivers might not be appropriate to use.
- Comprehensive guidance given by ECHA in Annexes to guidance documents

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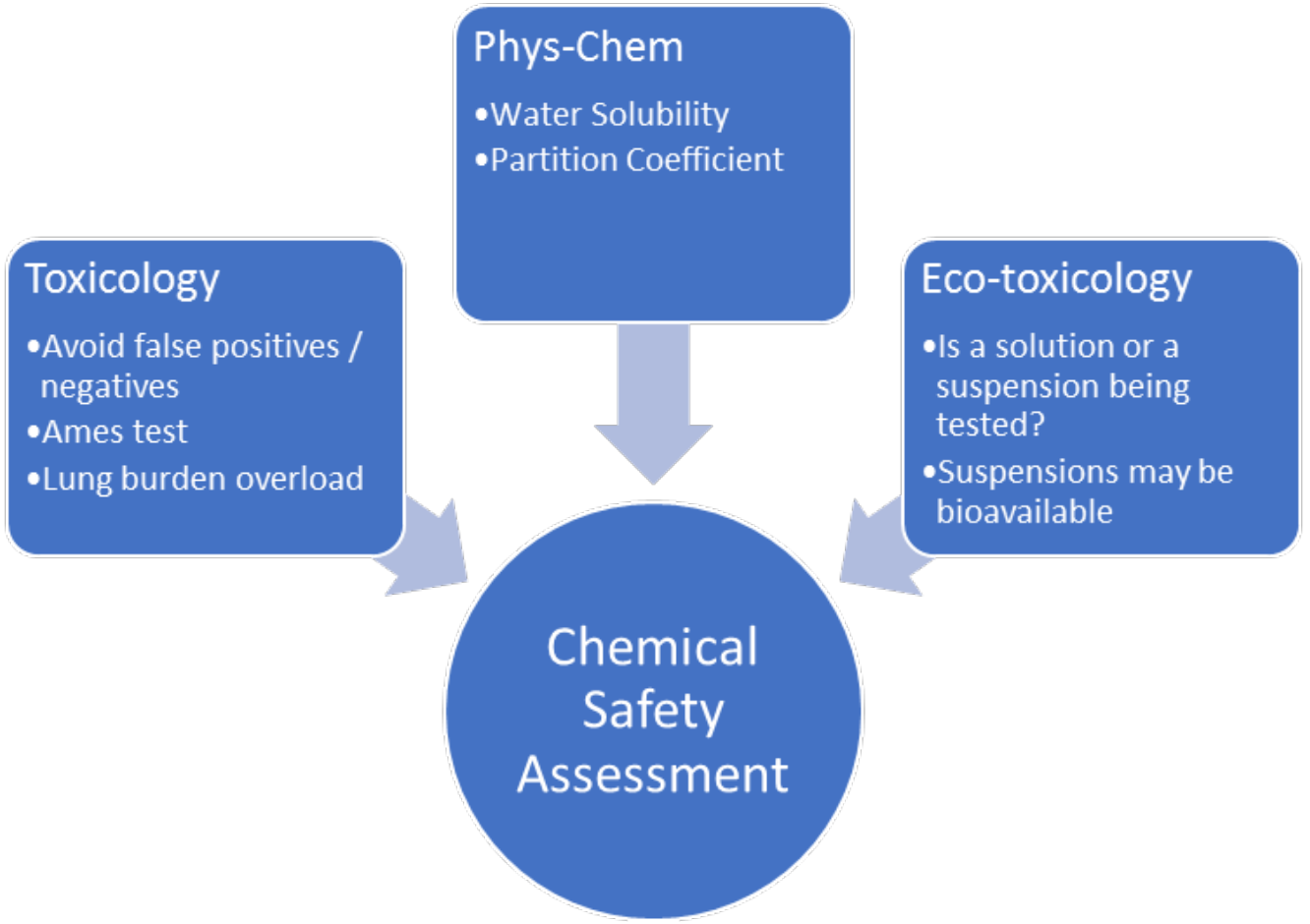
REACH endpoint modifications



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Intelligent testing strategies for nanomaterials – REACH and beyond

- In vitro, in silico, QSAR and read-across will be vital to avoid large scale animal testing.
- Research ongoing
  - EU funded projects (MARINA, NanoReg, SUN etc.)
- Risk assessment should account for changes to nanoform through the lifecycle.
- Proper characterisation both before and during studies essential

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REACH and Exposure Assessment

- All REACH registrations require communication of the uses of a substance.
- If the substance is hazardous and is registered at over 10 t/a, exposure scenarios must be included in a Chemical Safety Report.
- Exposure is often estimated using established occupational and environmental fate modelling tools.
- The registrant must choose the appropriate tool.

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Exposure Assessment and Nanomaterials

- Choose the correct nanoform for the lifecycle stage.
- Can standard tools be applied to nanomaterials?
  - Possibly for worker exposure if read-across to bulk forms can be proved.
  - Unlikely for environmental exposure as most tools use partition co-efficient as a key parameter.
- Some nano-specific tools available
  - Nano module of Stoffenmanger
  - SimpleBox4nano
- EU funded projects should improve the choice and quality of models.
- The models will need to be validated against measured data.
  - NanoMONITOR

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REACH, Risk Assessment and Communication

- Risk is measured by ensuring exposure via a given route is lower than a calculated “safe” value.
- If risk is not acceptable, appropriate risk management measures should be implemented.
- The measures required to ensure acceptable risk from a substance must be communicated in exposure scenarios found in the annex of an Extended Safety Data Sheet (eSDS).
- Any recipient of an eSDS must implement the measures stated or prove that alternative methods are equivalent or superior.
- Measurement can also be used to prove compliance.
  - NanoMONITOR

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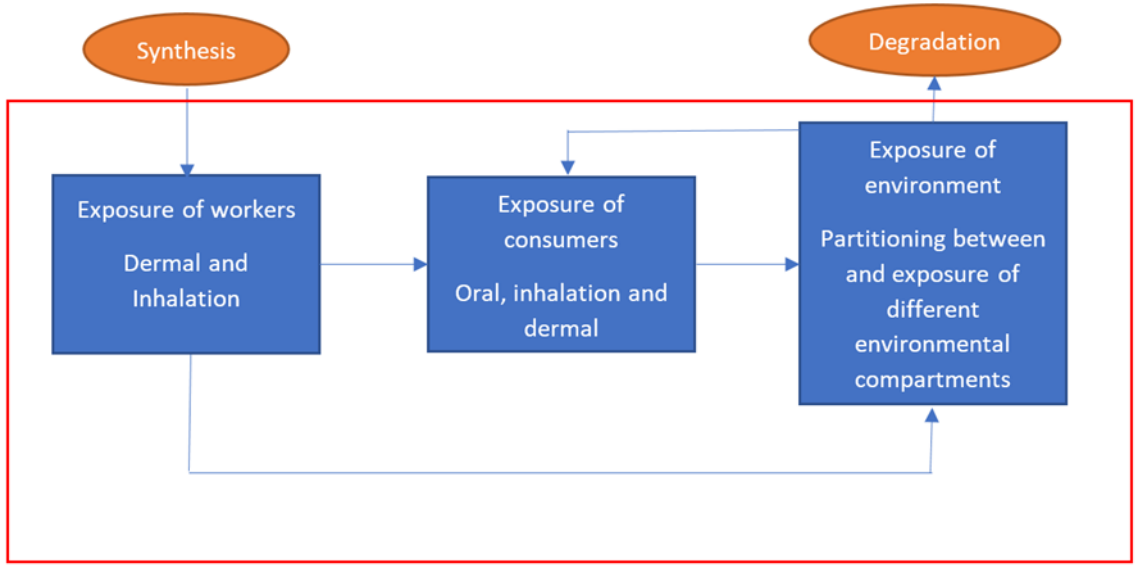
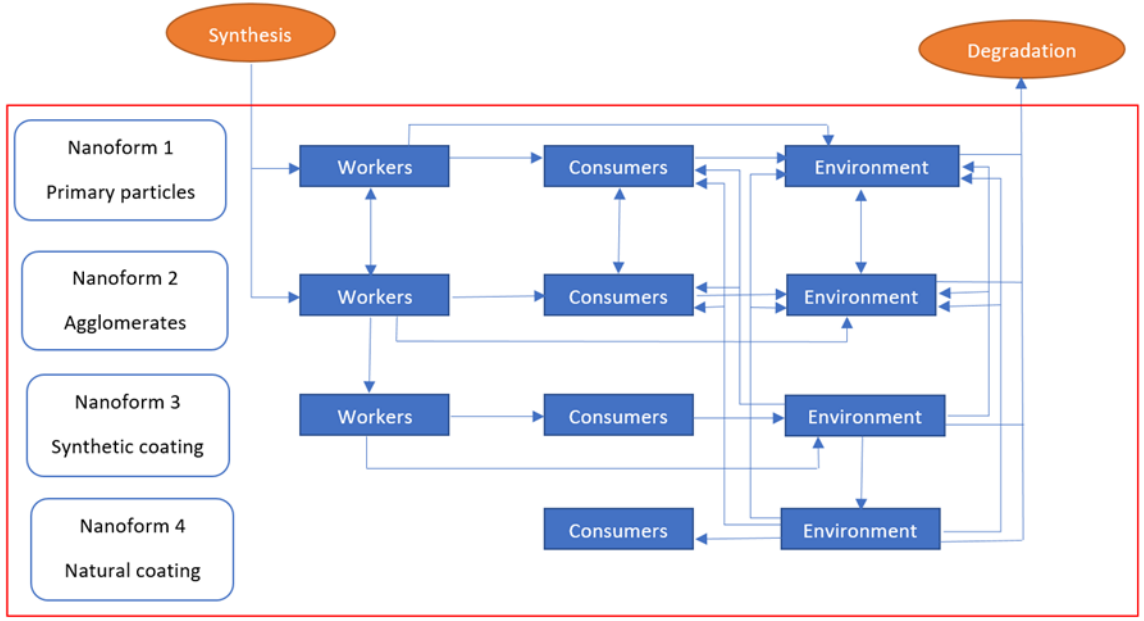
Risk Assessment and Nanomaterials

- Risk Assessment of bulk substance.



- Interconversion and different (eco)-toxicological profiles of nanoforms make risk assessment more complex.



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Risk Assessment and Nanomaterials

- Hazard of a nanomaterial is not intrinsic due to different nanoforms.
- Hazard can be reduced by Safe Design of the nanomaterial.
  - See SUN project.
- Risk management measures should be appropriate to nanomaterial.
  - Face masks should use appropriate fine filters.
  - Settling tanks with humates might be useful for on-site remediation of waste waters.
- Exposure scenarios for nanomaterials uncommon.
  - See MARINA project (or ask me!).

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Nanomaterials and other EU regulations

- Biocidal Products Regulation
  - An active substance in a nanoform must be authorised separately to the same substance in the bulk form.
- Cosmetics Regulation
  - Nanomaterials as cosmetic ingredients must be assessed separately to bulk forms of the same substance if they perform certain roles in the cosmetic.
  - The ingredients list must show that a substance exists as a nanomaterial.
- Food Contact Materials
  - A nanoform of a substance cannot be regarded as being on the Union List of authorised substances even if the bulk form is on the list.
  - Assessment and authorisation is made on a case by case basis.

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Nanomaterials and other regulations

- Medical devices
  - Degree of risk assessment required depends on likelihood of release of nanomaterials from the device.
- US
  - One off reporting scheme to EPA.
- Australia
  - NICNAS revised, may introduce new hazard symbol for “nanohazard”.
  - May require new nanospecific hazard statements.

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National Registries and Voluntary Notification Schemes

- There is no EU-wide notification scheme.
- Some countries have implemented reporting schemes for nanomaterials used or placed on the market in that country.
- Each scheme has different targets and requirements.

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Belgian Scheme

- Mandatory reporting scheme
- Notification of any nanomaterial manufactured on over 100 g if it is placed on the market for professional use.
- Decree to notify articles and complex objects containing a nanomaterial whose release cannot be excluded and is present at > 0.1 mass % has been postponed.
- Proposed inclusion of mixtures in scheme has been postponed.

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French Scheme

- Mandatory reporting scheme
- Manufactured nanomaterials produced, imported or distributed in France to professional users in over 100g, where the nanomaterial is a substance, part of a mixture or in an article where release would be foreseeable under normal conditions.

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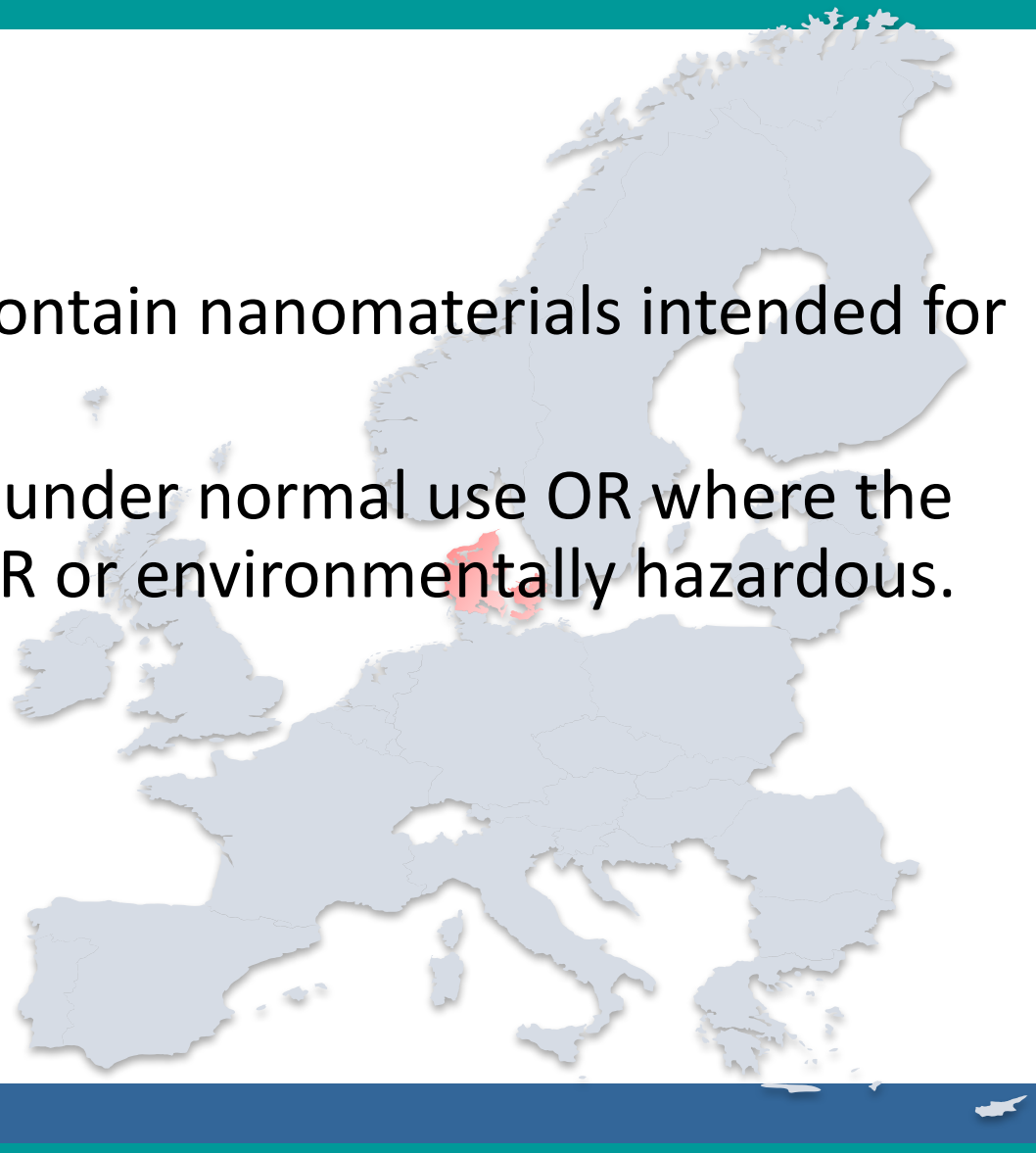
Danish Scheme

- Mandatory reporting scheme
- Notification of mixtures and articles that contain nanomaterials intended for sale to the general public.
- Either where the nanomaterial is released under normal use OR where the nanomaterial is not released but it is a CMR or environmentally hazardous.
- No mass threshold.
- Many exemptions.



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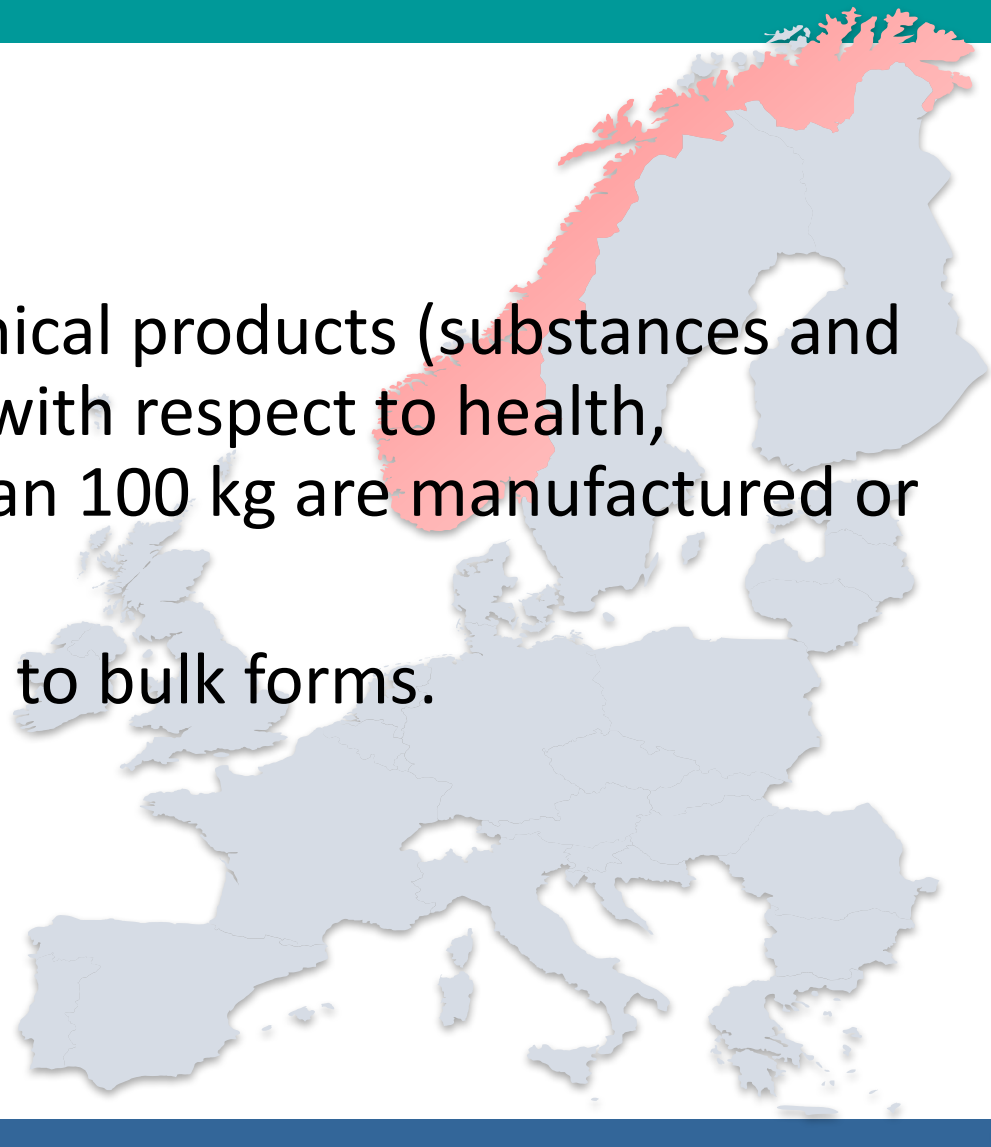
Norwegian Scheme

- Mandatory reporting scheme
- Falls within the current register of all chemical products (substances and mixtures) that are classified as hazardous with respect to health, environment or fire/explosivity, if more than 100 kg are manufactured or imported.
- Nanomaterials are now reported distinctly to bulk forms.



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Swedish Scheme

- Similar scheme to French.
- Due to be active in 2019.

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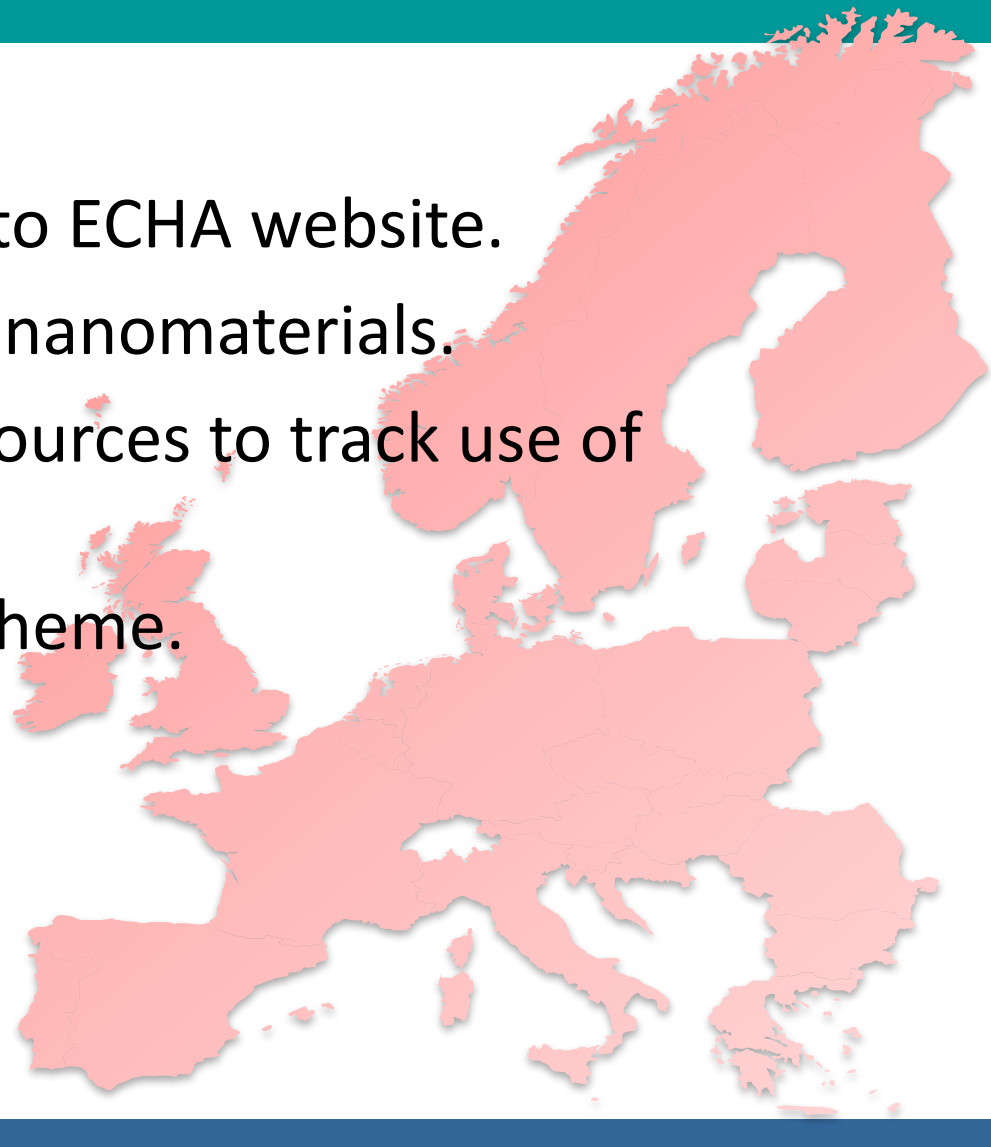
Observatory for Nanomaterials

- To be set up by ECHA but will be separate to ECHA website.
- Intended to improve transparency around nanomaterials.
- Will use nation state registries and other sources to track use of nanomaterials in EU.
- Not intended to be obligatory reporting scheme.



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Summary

- There are no nano-specific regulations in the EU.
- Current chemical regulations can be applied to nanomaterials.
- Some modification of individual studies might be required within a regulation.
- Particle characterisation is not an obligation under Annex VI of REACH, but a registrant should be able to prove data in the dossier is applicable to their product throughout its lifecycle.
- Individual countries may have reporting procedures.

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