# EU chemical regulations and nanomaterials

IACM

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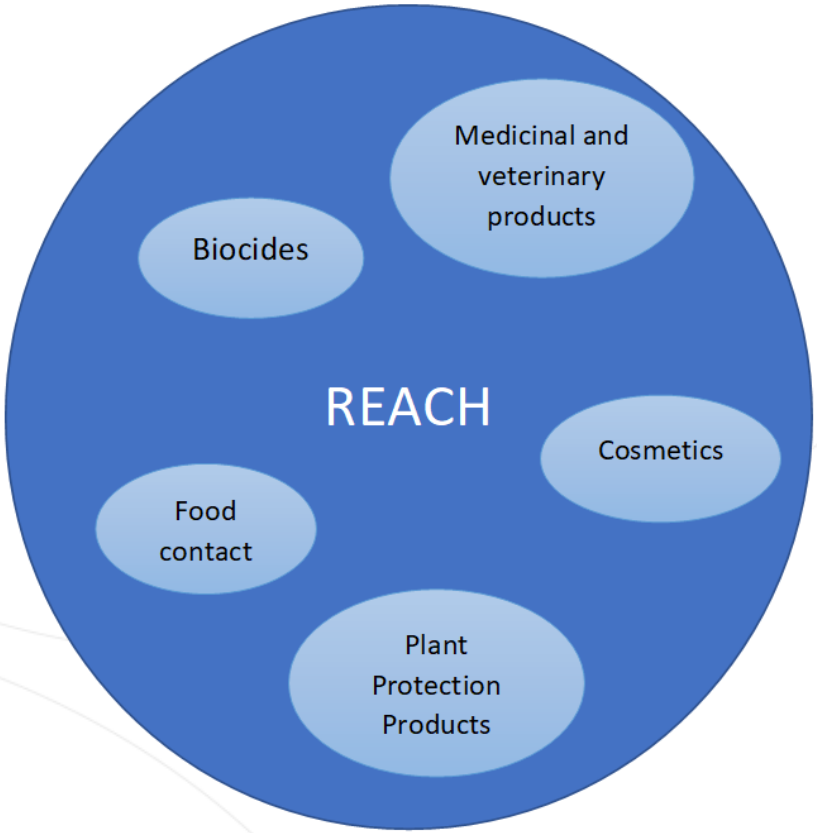
Business through Science

## Contents

- Definition of nanomaterials
- REACH
  - Past and Present
  - Future
- Food and Food Contact Materials
- CLP – Titanium Dioxide
- Brexit – What might change?

# Regulatory framework for chemicals in the EU




- Regulations are largely 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

# Definition of nanomaterial

- 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.*"

# Revision of definition and other definitions

- Revised definition under consultation
  - Largely unchanged from draft
  - May introduce more detail – e.g. SSA < 5 $m^2/cm^3$ to define a non-nanomaterial
- Unlikely to be in place before revision of REACH in 2020.
- Applicable to REACH and BPR.
- Different definitions in other regulations
  - Cosmetics – Specifies insoluble particles
  - Plastic Food Contact Materials – Specifies deliberately manufactured particles

# REACH and Nanomaterials – Past and Current

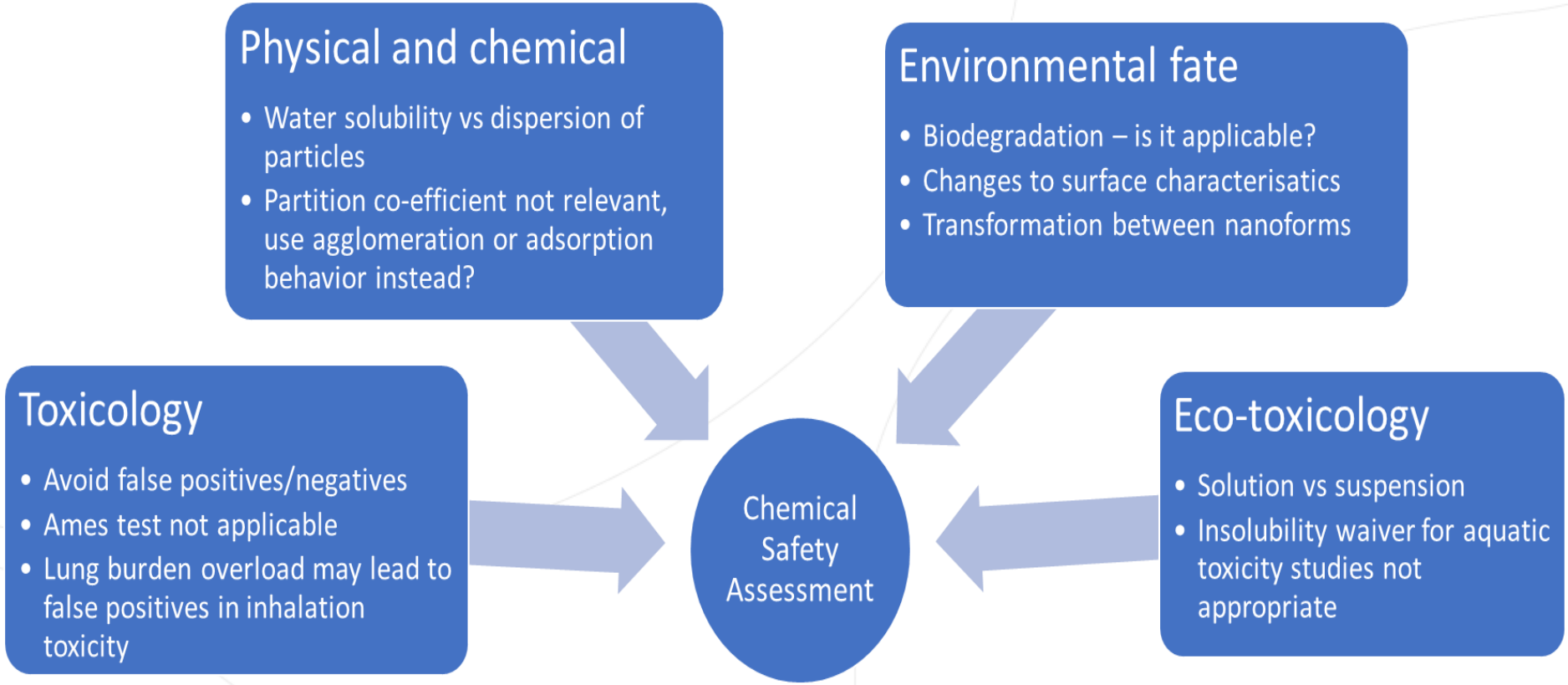
- Each registrant should characterise their substance to ensure that the hazard/exposure/risk assessment in the dossier applies to their product.
- Some substances may be further identified by other parameters (Guidance for identification and naming of substances, Section 4.2.3)
  - Particle size mentioned 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.

# Difficulties around identification and characterisation of nanomaterial

- Definition based on:
  - Primary particle size
  - Distribution by number distribution
  - Shortest dimension
- Many analytical methods do not measure these parameters
- Group of methods will be required
- Good sample preparation will be essential

EU Regulations on nanomaterials

# Hazard endpoint testing



# 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.

# Revision of REACH

- Proposed revision of Annexes of REACH under consultation
- Will introduce “nanoform” and “set of similar nanomaterials” into regulation
- Expected to be in place in January 2020

# Key points in proposed revision to REACH – 'Nanoform'

- Nanoform
  - Meets the definition of nanomaterial but differ by physical or chemical parameters
    - Size/shape/surface functionalisation/other parameter
  - Intentional different parameter = new nanoform
  - Inter-batch variability with a grade does not constitute a new nanoform
- Set of similar nanoforms
  - Different phys/chem parameters BUT same toxicological and ecotoxicological profile
  - Only one set of chemical characterisation and hazard endpoints required for a set
    - Limits must be scientifically justified
  - Read across to other sets encouraged but must be scientifically justified

## Key points in proposed revision to REACH - Characterisation

- Particle characterisation will become compulsory for each set of nanoforms. It will require as a minimum
  - Particle size distribution
  - Surface functionalisation
  - Shape/aspect ratio/other morphological features
  - Surface area
- Will probably be needed for ALL powders including historically registered substances
  - Dossier updates would be required

# Key points in proposed revision to REACH – Endpoint testing

- Required endpoints depends on tonnage of substance
  - Sum of all nanoforms and bulk forms
- Value for each endpoint required for each similar set of nanoforms
- Grouping and read-across will be essential to reduce testing and cost

## Key points in proposed revision to REACH – other impacts

- Safety Data Sheets
  - Might require SDS to include information on different nanoforms
  - Exposure Scenarios for nanoforms could be needed
- Downstream Users
  - Downstream users who functionalise nanomaterials (e.g. oxidise MWCNT) might need to do their own risk assessments

# Proposal for harmonised classification by French CA

- Harmonised classification of Carcinogen 1B, H350i proposed in May 2016
- Justification
  - Registration dossier makes no distinction between crystal forms and particle size
  - 4 studies (2 inhalation + 2 installation) showed tumour formation
  - Existing IARC classification as Carc 2B
  - Mode of Action relevant to all forms identified

# Response from Industry

- 514 responses during consultation
- Much disagreement with proposal
  - Substance has been used since 1923 with no epidemiological adverse results
  - Toxicity studies were limited and of poor quality
  - Interspecies (rat to human) extrapolation unjustified
  - Classification based on the non neo-plastic effects (inflammation) should be applied instead
  - Adverse effect is not substance related

# Committee for Risk Assessment Opinion

- Recommended classification of Carc 2 (H350i)
- Proposed that a note be applied that forms with particle shape or surface coating could have a more severe classification or be classified through an additional route of exposure

# Committee for Risk Assessment Opinion

- Why not Carc 1B?
  - Some studies invalid due to excessively high doses
  - No positive epidemiological studies
  - Some tumours seen are from mechanisms unique to rats

# Committee for Risk Assessment Opinion

- Why still classify as carcinogen?
  - Epidemiological studies would probably not detect cases possibly caused by titanium dioxide exposure
    - BMD10 = 5 – 25 mg/$m^3$; Exposure = 0.7 mg/$m^3$ = 0.3 – 1.4 % increase risk
    - Lung cancer occurrence = 5 – 7 %; increased risk would not be detected.  Cannot overrule animal studies
  - Guidelines recommend that studies include dose that delays clearance
  - Results are not unique to rats
    - Evidence can only be discounted if MOA conclusively determined not to be relevant to humans

# Activities since RAC Opinion

- CARACAL deferred decision
- Notes to classification through Annex VI suggested (and rejected by others)
- Suggestion of Annex II labelling derogation for liquid suspensions (non-inhalable products).
- More discussions!
- Next CARACAL meeting End of Nov

# Further impacts from classification

- Mode of action suggested
  - Low solubility/biopersistency → pulmonary inflammation → Reactive Oxygen Species → secondary cytotoxicity/cell proliferation → tumour
- Mode may be common to all PSLT (Poor Solubility Low Toxicity) substances
- Will all PSLT substances by classified the same?
  - E.g. Talc, carbon black, zirconium dioxide
- Could be difficult to prove and raise many legal issues

# Impact of Classification change

- Carc. 1B
  - Mixtures containing > 0.1 % must be classified as Carc 1B
  - Substance listed on Annex VI of CLP are restricted from use in consumer products
- Carc. 2
  - Mixtures containing > 1 % must be classified as Carc. 2
  - Restriction on use in consumer products does not apply

# Other EU regulations

- Food related (see next slides)
- 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.
- Medical devices
  - Degree of risk assessment required depends on likelihood of release of nanomaterials from the device.

# Feed Additives

- EFSA decide if feed additive is safe based on a submitted technical dossier
- Dossier should contain
  - Conditions of Use
  - Additive and active substance characterisation
  - Stability and homogeneity
  - Speed of degradation in digestive tract key aspect of risk assessment and testing strategy – Use bulk data
  - Inhalation by animal and worker safety must be assessed
- No application for nano-additive has yet been made

# Novel foods regulation (2015/2283)

- Different definition to recommended REACH definition
  - May include substances > 100 nm
- Novel food – any food not used for human consumption to a significant degree before 15 May 1997 inc. food or vitamins/mineral/other consisting of engineered nanomaterials
- No advice regarding different nanoforms….yet!

# Provision of food information to consumers

- Same definition as novel food regulation
- Ingredients present as engineered nanomaterial must be labelled with “(nano)” following the name in the list of ingredients.

# Food Contact Materials Regulations

- Plastic Food Contact Materials
- Active and Intelligent Food Contact Material
- Common aspects
  - Definition includes a reference to “deliberate” manufacture.
  - Substances on Union list can be used as active substance or authorisation can be sought from EFSA (not yet established!).
  - Nanoparticles must have an authorisation on a case by case basis.
- No reference to different nanoforms but coating has been including in the name of coated substances in the Union list.
- The functional barrier derogation does not apply to nanomaterials

# French ban on use of E171 in foods

- Jun 2016 – EFSA state that $TiO_2$ is safe for use but highlights datagaps
- Jan 2017 – INRA publish report indicating development of non-malicious, pre-tumorous damages in the colon of rats fed with $TiO_2$ nanoparticles
- May 2018 – French announces that the use of E171 (titanium dioxide) in food products will be suspended
- June 2018 – EFSA re-evaluate TiO2 based on 4 new studies.  Concluded that opinion did **not** need to change

# Impacts of Brexit on chemical regulations

- Still no idea what is going to happen!
- Potential outcomes
  - “Chequers Plan” – Government’s preferred option
  - No deal
  - Brexit delayed or postponed
  - Alternative plan (after Chequers rejected or after general election)

# Impact of Chequers on chemical regulation

- Regulations still apply during Withdrawal period
- UK maintains links with ECHA and REACH still applies in UK
- Not clear whether regulatory divergence could occur
- EU do not think links with ECHA easy to maintain (but they are looking to have links with third-parties)
- Impacts on new trade agreements

# Impact of No Deal on chemical regulation

- All UK registrations/authorisations will no longer exist
- New registrations will be required for new UK regulations
- Initially UK REACH will mirror REACH
- Regulatory divergence possible
  - Impacts of conflicting trade agreements

# Impact of other Brexit directions

- Brexit delayed/postponed
  - Everything stays the same?
  - Will EU allow this?
- Other outcomes
  - UK REACH will mirror REACH initially
  - Beyond that….who knows?!?

# Thank you!

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