



12 March 2015, Venice, Italy.
EU-US Bridging NanoEHS Research Efforts

Risk Management & Control Breakout Group

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What are nanomaterials?

Natural systems include functional nanomaterials



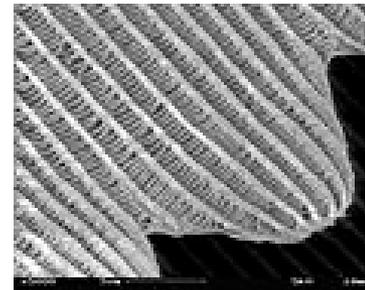
silica spheres in opal



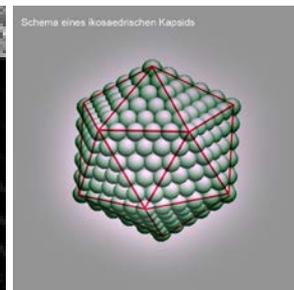
Wax surface of a lotus leaf



Spatulae on a Gecko foot

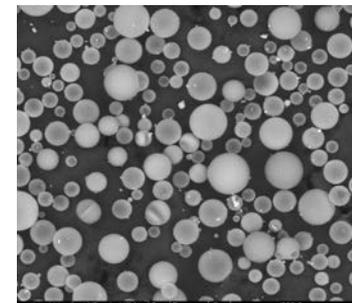


Wing of a butterfly



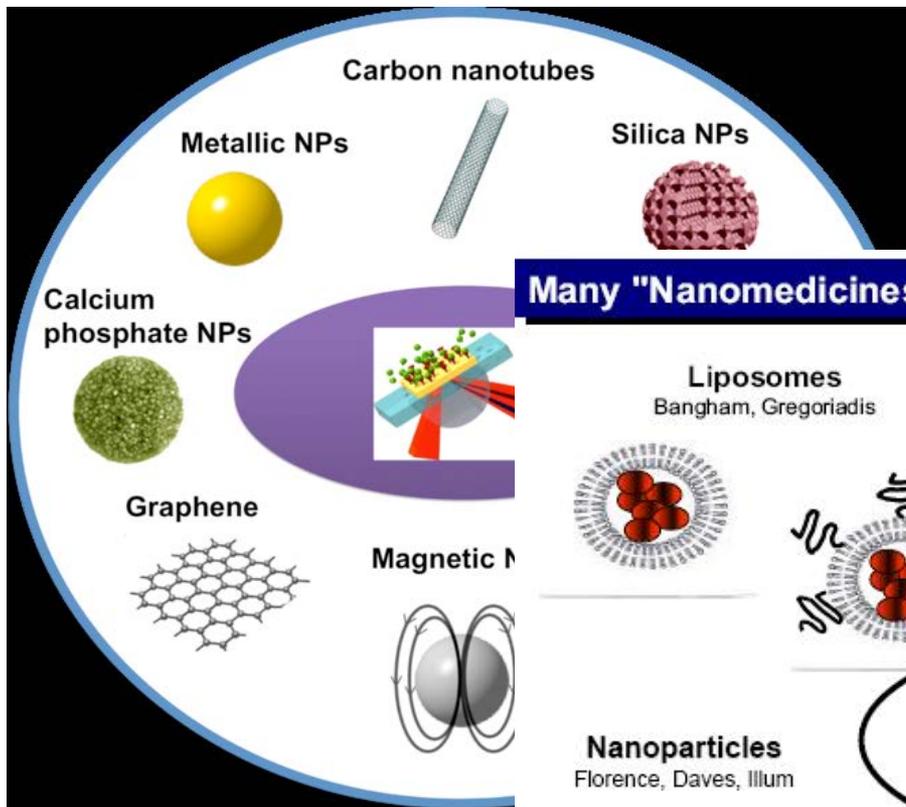
Viruses and viral capsids

Materials that have been used for many years where a proportion of the material happens to be in nanoform



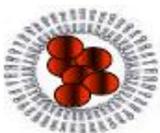


Engineered nanomaterials



Many "Nanomedicines" are already in routine clinical use

Liposomes
Bangham, Gregoriadis



Antibodies and their Conjugates
Celltech-UCB



Viruses as viral vectors for gene therapy
Seymour

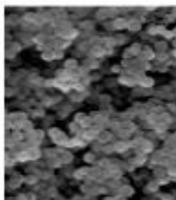


polymer micelles



Nanomedicines

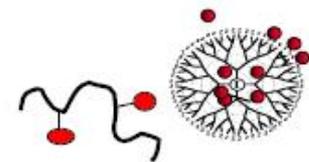
Nanoparticles
Florence, Daves, Illum



Polymer-protein conjugates



Unimolecular Polymeric Drugs and Conjugates
Duncan





Differential Benefits of Nanoform vs Chemical Substance

Nanoscale structures possess different properties from smaller soluble chemical 'substance' or microscale forms

e.g.

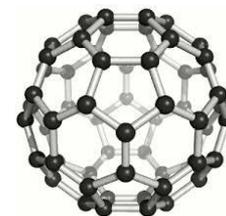
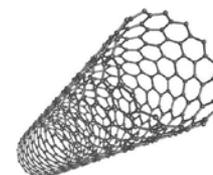
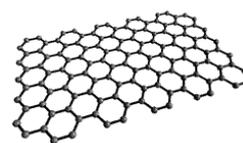
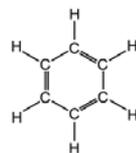
high tensile strength

low weight

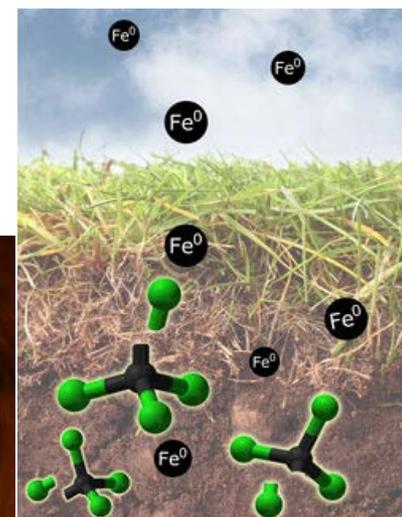
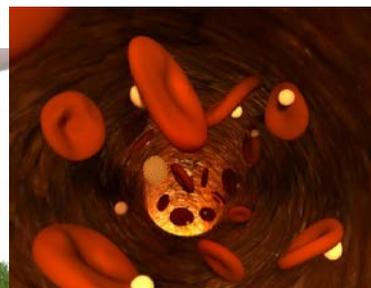
high electrical and thermal conductivity

unique optical, electronic and mechanical properties

molecular and cell level targeting of drugs



→ The exploitation of functional benefits across all types of product innovations





The Scale of Nanomaterials Manufacturing in EU

Based on published studies:

- between 500 and 2000 nanomaterials are currently placed on the EU market. Most (around 80%) of the manufacturers and/or importers of nanomaterials are micro companies or SMEs [1]
- the estimated total number of European nanomaterials manufacturers is between 200 and 300 [2]

1. Risk & Policy Analysts Limited. (2012). Impact Assessment of the REACH Implementation Project on Substance ID for Nanomaterials. Norfolk.

2. Kauhanen, L., Rissanen, J., & Crawley, T. (2011). Study on REACH contribution to the development of emerging technologies.



Differential Benefits of Nanomaterials → Differential Risks of Adversity?

Nanoscale materials can possess different health and eco-toxicological properties than simple chemical

Who do we need to protect from any potential adverse effects:

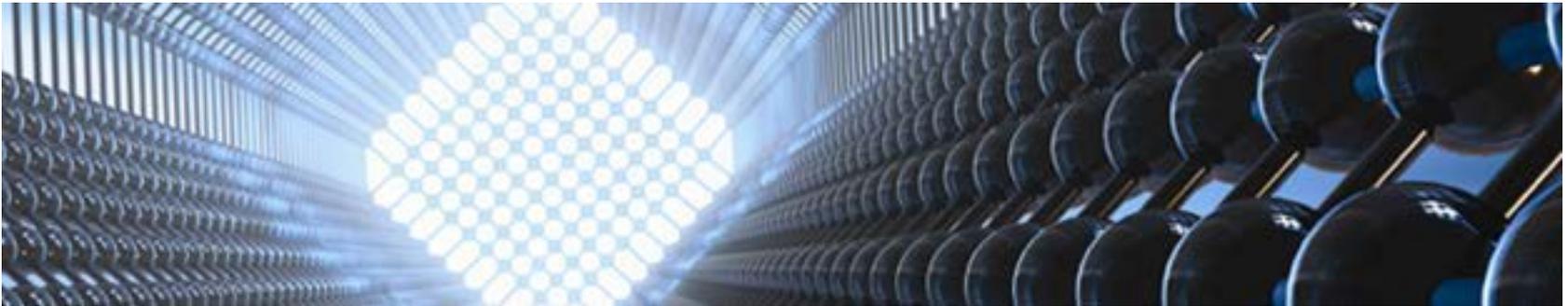
- Workers in manufacturing
- Consumers directly exposed
- General public – air emissions, drinking water etc.
- Environment – flora & fauna, air & water quality

A nanoform may change in different environments
e.g. as a product is manufactured through to end use and disposal

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Differences & Similarities in EU & US Nanomaterials Regulations





Regulatory Definition of 'Nanomaterial'

European Commission

On *18 October 2011* the European Commission adopted the Recommendation on the definition of a nanomaterial.

*'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**.*

*In **specific cases** and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.*

*By **derogation** from the above, fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions below 1 nm should be considered as nanomaterials.'*



Regulatory Definition of ‘Nanomaterial’

European Commission

‘*Nanomaterials are not intrinsically hazardous per se* but there may be a need to take into account specific considerations in their risk assessment.

Therefore one purpose of the definition is to *provide clear and unambiguous criteria* to identify materials for which such considerations apply.

It is only the *results of the risk assessment* that will determine whether the nanomaterial is hazardous and whether or not further action is justified.’



Regulatory Application

EU REACH & CLP Regulation

Manufacturers, importers and downstream users have to ensure that their nanomaterials do not adversely affect human health or the environment.

This includes nanomaterials and nanoforms of bulk substances.

European Commission (EC), member states and CASG Nano (a stakeholder group of experts on nanomaterials), prepares advice on how to manage nanomaterials under the REACH and CLP Regulation

A *technical manual and video* providing guidance on how to include information on nanomaterials in registration dossiers prepared in the International Uniform Chemical Information Database (IUCLID) was released in 2010, and subsequently updated in 2013

<https://www.youtube.com/watch?v=6disirpXxx4&feature=youtu.be>

European Commission launched a public consultation on the *modification of the REACH Annexes on nanomaterials*, which was open for input from 21 June 2013 until 13 September 2013



Regulatory Application

EU Cosmetics Regulation No 1223/2009

The first regulation to make specific consideration of nanomaterials & currently incorporates a specific *Definition of a Nanomaterial*

‘an insoluble or biopersistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm’.

Scientific Committee on Consumer Safety (SCCS) published in 2012 *‘Guidance on the Safety Assessment of Nanomaterials in Cosmetics’*

11th January 2013, obligation of *‘Responsible Person’* to notify to the EC, via the Cosmetic Products **Notification Portal**, all cosmetic products containing nanomaterials, **six months prior to placing them on the market**. Labelling of ingredients as (nano) on the product.

Data for risk assessment → SCCS



Regulatory Application

EU Novel Foods Regulation EC 258/97

European Parliament in July 2010 debated a draft update which included a stipulation to ban nanoscale ingredients from food until the risks posed are better understood.

All-night conciliation talks to update the Novel Foods Regulation broke down without agreement after Council refused a final compromise offer relating to the labelling of cloned-derived products from the European Parliament. This means that the current Novel Foods Regulation, adopted in 1997, will remain in force.

As an indirect consequence - There will continue to be no special measures regarding nanomaterials in food



Regulatory Application

EU Biocidal Products Regulation No 528/2012

The Biocidal Product Regulation (BPR) is the first piece of EU legislation to implement the European Commission definition on nanomaterials.

A dedicated *risk assessment* is needed when a nanomaterial form of an active or non-active substance is used in a biocidal product. Such biocidal products must also be **labelled** and indicate the name the nanomaterial followed by the word "nano" in brackets.

The approval of the 'active substance' does not cover the nanomaterial form except where explicitly mentioned.

A separate dossier with all data requirements for the nanoform must be provided.



Regulatory Application

US-EPA & TSCA

In 2008, EPA declared that CNT was different from graphene and other carbon forms covered in TSCA

EPA is developing a proposal to establish reporting and recordkeeping requirements under the Toxic Substances Control Act (TSCA) for chemical substances when manufactured, imported or processed as nanoscale materials.

Premanufacture notification

TSCA requires manufacturers of new chemical substances to provide specific information to the EPA for review prior to manufacturing chemicals or introducing them into commerce

EPA may take action to ensure that those chemicals that pose an unreasonable risk to human health or the environment are effectively controlled and use limited.



Regulatory Application

US-EPA & TSCA

Significant New Use Rules (SNUR) require that manufacturers, importers and processors of certain substances notify EPA at least 90 days before beginning any activity that EPA has designated as a "significant new use."

August 2013 – CNTs were included in a SNUR on the Federal Register

Information gathering

Requires reporting and recordkeeping under TSCA section 8(a), that persons who manufacture nanoscale materials notify EPA of certain information including

- production volume
- methods of manufacture and processing
- exposure and release information
- available health and safety data.



Regulatory Application

US-EPA & TSCA

Test rule

Under TSCA section 4, EPA is to propose a rule to require testing for certain nanoscale materials that are already in use.

Focus on classes of nanoscale materials not already being tested by other Federal and international organizations.

Aim: understand potential health and environmental effects of nanoscale materials and establish a correlation between the chemical/physical properties and the effects of the nanoscale form

Over time, EPA will evaluate the information and consider whether appropriate action needs to be taken under TSCA to reduce any risk to human health or the environment.



Regulatory Application

US FDA – latest report 2012

FDA is maintaining a product-focused and science-based regulatory policy to appropriately regulate products using this emerging technology.

Final Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology

‘The guidance does not establish a regulatory definition of the term "nanotechnology" or any related vocabulary.’

‘The final guidance also encourages industry to consult with the FDA early in the product development process to address questions related to the safety, effectiveness, or other attributes of nanotechnology products, or to address questions about regulatory status of the products.’



Regulatory Application

US FDA – latest report 2012

Final Guidance for Industry: Safety of Nanomaterials in Cosmetic Products

‘The framework currently in use for assessing safety of cosmetics is appropriate for cosmetics containing nanomaterials.

However, data needs and testing methods should be evaluated in light of the properties, behaviours, and/or effects that may be exhibited by nanomaterials used in cosmetic products’

Final Guidance for Industry: Assessing the Effects of Significant Manufacturing Process Changes, including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that are Color Additives

→ consult with FDA regarding a significant change in manufacturing process for a food substance already in the market



Differences & Similarities EU-US

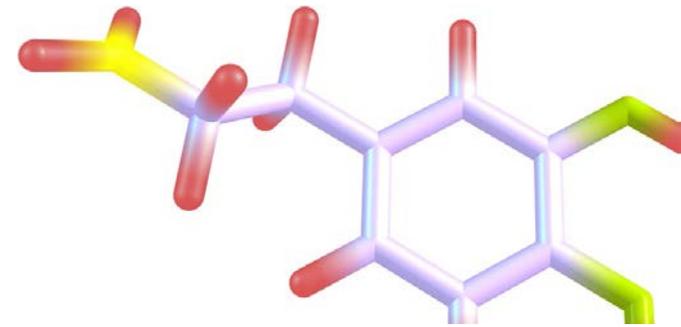
	Type of definition	Distribution threshold	Intentionally manufactured	Size	Novel properties
European Commission	Advisory	50% by number	No	1-100nm	No
EC Cosmetics	Regulatory	None	Yes	1-100nm	No
EC Biocides	Regulatory	50% by number	No	1-100nm	No
US EPA	Advisory	10% by weight	Yes	1-100nm	Yes
US FDA	Advisory	None	Yes	1-100nm and up to a micron	Yes

Can or should a harmonised Definition be developed?
What are the implications to industry of the current status?



Controlling Exposure & Reducing Risk

- require the use of PPE e.g. impervious gloves and respirators – worker setting
- Impose testing requirements to generate health and environmental effects data – characterize hazards
- limit human exposure - based on risk assessment
- limit environmental releases - based on risk assessment
- limit uses of new nanoscale materials
 - potentially large socio economic impacts?



Thank You for Listening

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