Nanomaterials

EU MDR - Nanomaterials

Presented by:
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Claigan

Overview - Agenda - Nanomaterials and EU MDR

- Intro
- Nanomaterials
  - EU MDR
  - Other regulations
  - Definition and Guidance
- Nanomaterials risks
  - Biocides
  - Additives
- Practice compliance approaches
  - Statement
  - Leachables
  - Content Testing / Eng Eval.
- Q&A

Webinar is 50 minutes with 10 minutes of Q&A
(hopefully)

Claigan - What do we need to quote?

- **Laboratory testing**
  - Email us picture or weblink of product to info@claigan.com

- **Monthly / Quarterly Updates**
  - Email us at info@claigan.com

- **SCIP Web Demonstration and Template**
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Nanomaterial - EU MDR

- Nanomaterials are regulated under EU MDR

- 10.6
  - Devices shall be designed and manufactured in such a way as to reduce as far as possible the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention shall be given to nanomaterials.

The More Familiar (not nano) EU - CMRs and EDCs

- 10.4.1 - Design and manufacture of devices
- Devices, or those parts thereof or those materials used therein that:
  - are invasive and come into direct contact with the human body,
  - (re)administer medicines, body liquids or other substances, including gases, to/from the body, or
  - transport or store such medicines, body fluids or substances, including gases, to be (re)administered to the body,
- Require to justify and label
  - Carcinogens, Mutagens, Reproductive Toxins (CMR) & Endocrine Disrupting Chemicals (EDCs)
  - >0.1% w/w

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- 7.6. Rule 19
  - All devices incorporating or consisting of nanomaterial are classified as:
    - class III if they present a high or medium potential for internal exposure;
    - class IIb if they present a low potential for internal exposure; and
    - class IIa if they present a negligible potential for internal exposure.

Nanomaterials in Other Regulations

- Currently regulated in
  - EU Biocides Directives
  - EU Food Contacting
- Future regulation of specific nanomaterials expected in
  - RoHS
  - REACH

RoHS Recast

- Nanomaterials addressed
- In order to review and amend Annex II, the Commission shall take special account of whether a substance, **including substances of very small size or with a very small internal or surface structure**, or a group of similar substances:

(a) could have a negative impact during EEE waste management operations,

(b) could give rise to uncontrolled release into the environment

(c) could lead to unacceptable exposure of workers involved in the waste EEE collection or treatment processes;

Guidance on Nanomaterials

- Opinion on "Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices "
  - 6 January 2015
  - https://ec.europa.eu/health/sites/health/files/scientific_committees/emerging/docs/scenihr_o_045.pdf

Non-Invasive Devices

- 3.5.2.1 Non-invasive medical devices

- These are devices in contact with intact skin. Released nanosized components have a low potential to penetrate through the skin.

- ie. low risk

Invasive Devices - Part I

- 3.5.2.2 Invasive medical devices

- All classes of invasive devices may potentially generate nanoparticles.
- For invasive devices, the released nanoparticles have a direct port of entry into the body depending on the localisation of the device used.
- Products consisting of free nanomaterials lead to high potential for systemic exposure
- Whether a high systemic exposure occurs depends on the actual use of the medical device and the route of exposure, i.e. the location where the medical device is used

Invasive Devices - Part 2

- 3.5.2.2 Invasive medical devices (cont.)

- Nanomaterials in products used in surgery are generally **embedded inside** or coated on larger products. The duration of contact with the patient is relatively short. Local exposure to the bound nanomaterials at the site of treatment will, therefore, be high in all cases, whereas systemic exposure potential to free nanomaterials is likely to be very low.

- Local exposure to the fixed nanomaterials at the site of treatment will therefore be high in all cases, whereas systemic exposure potential to free nanomaterials may be considered low, provided there is only slow generation of wear particles.

Nanomaterial - EU MDR

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- Definition of nanomaterial
  - "'nanomaterial' means 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 1-100 nm;"

Nanomaterial definitions

- Definitions
  - ‘particle’, for the purposes of the definition of nanomaterial … means a minute piece of matter with defined physical boundaries;
  - ‘agglomerate’, for the purposes of the definition of nanomaterial … means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components;
  - ‘aggregate’, for the purposes of the definition of nanomaterial … means a particle comprising of strongly bound or fused particles;

Nanomaterial Types

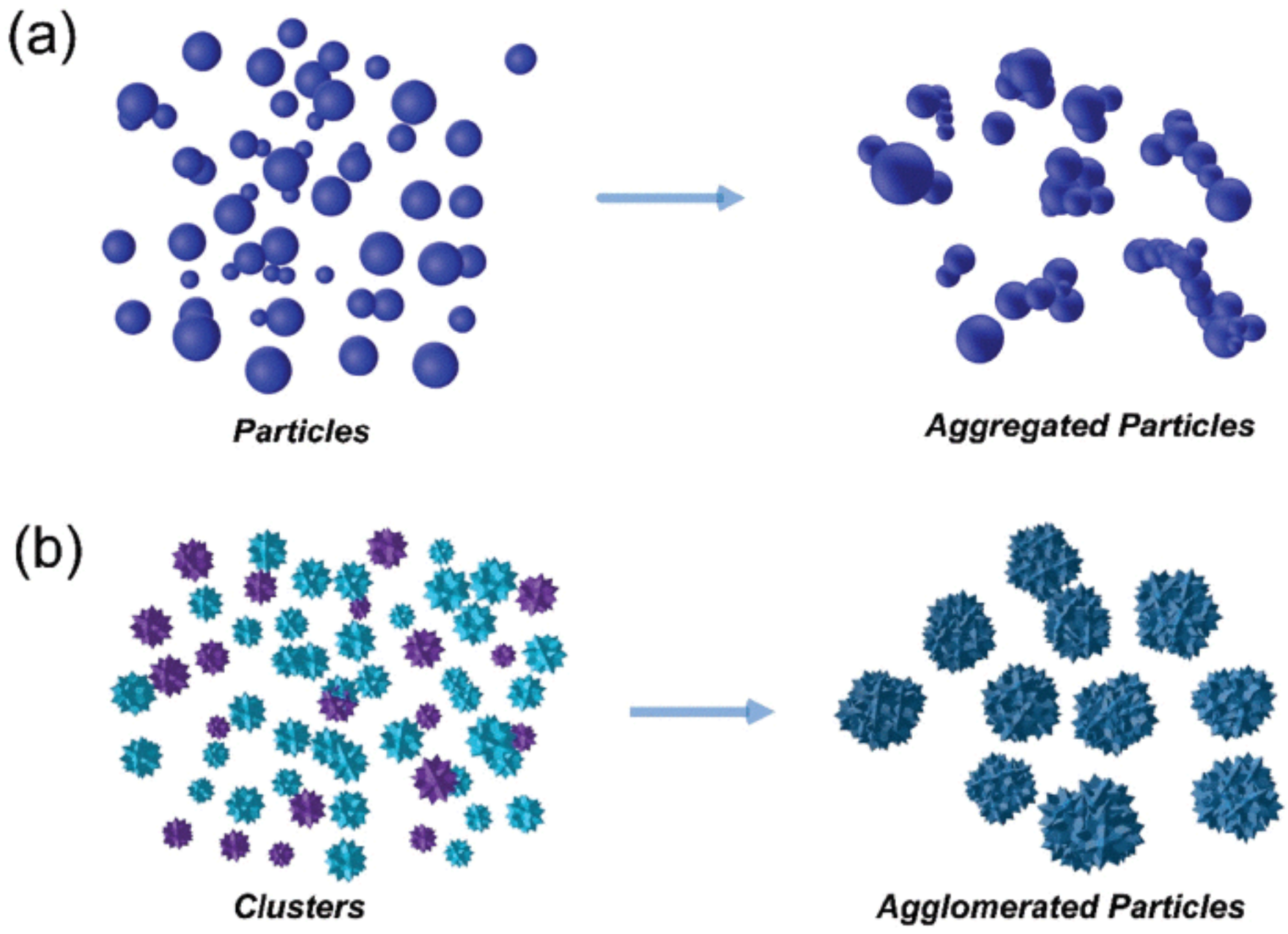


Fig. 1 Schematic illustration of the mechanism difference between (a) aggregation, and (b) agglomeration.

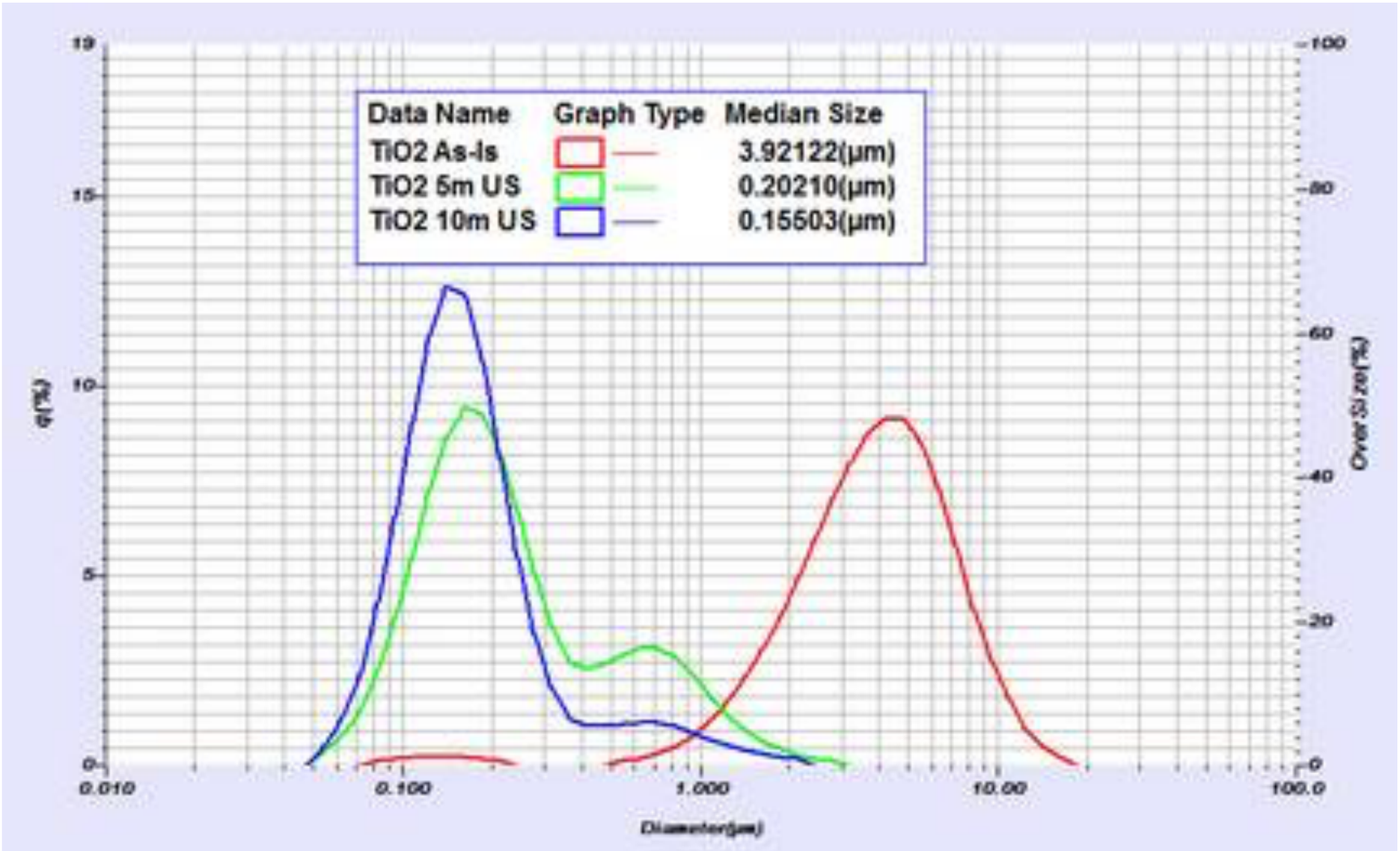
Common Nanomaterials in Medical Devices

- Inorganic additives to plastics
  - Colourants (TiO_2)
  - Fillers ($CaCO_3$)
  - Inorganic flame retardants (SbO_3)
  - Heat stabilizers (~~Pb~~, Sn, Ba, ~~Cd~~ and Zn)

- Can be nanomaterials
- But often are not.
  - (not a very helpful statement :-)

Colourants

- TiO2
  - Averages ~200nm, but can be below 100nm

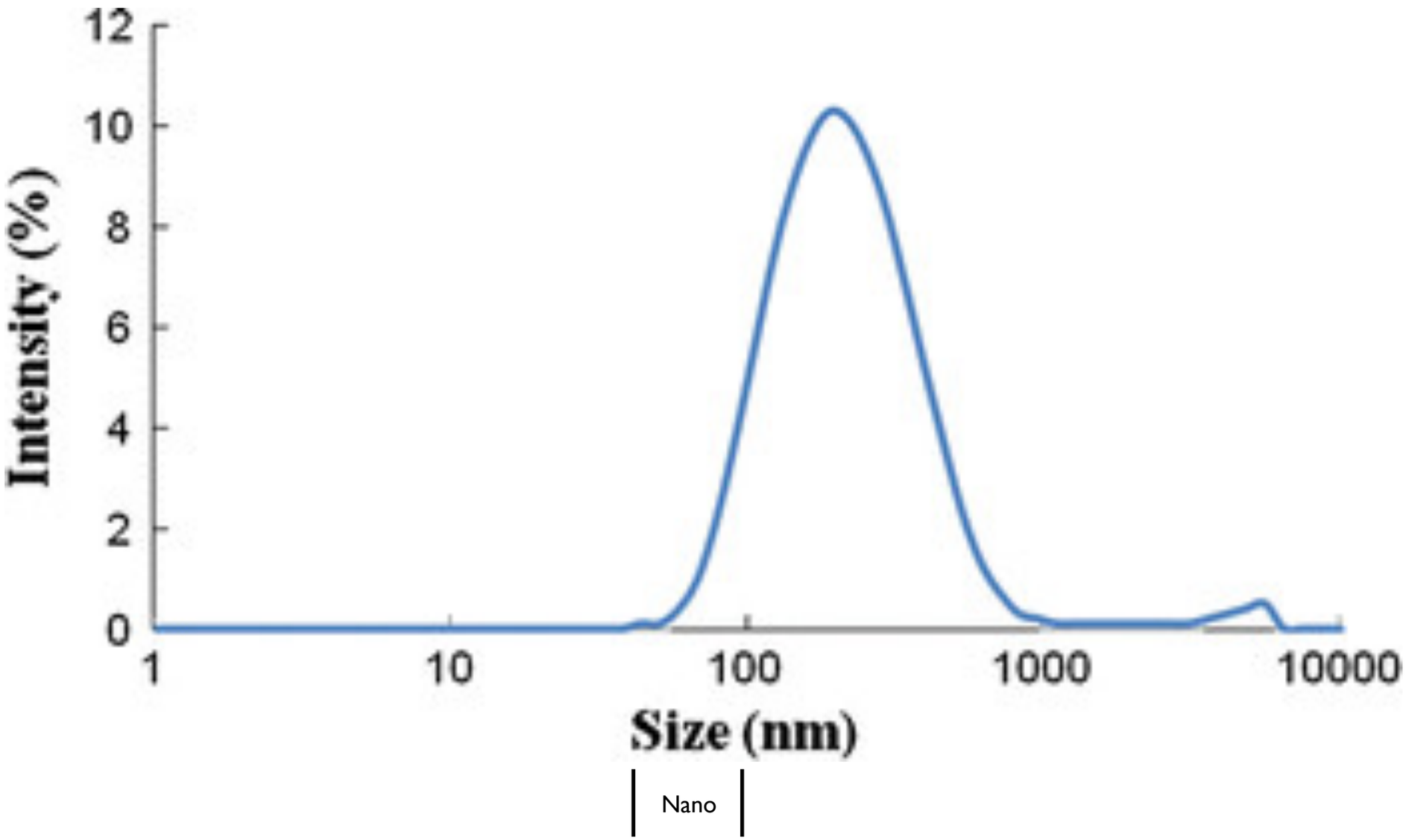


Nano

- Horiba Scientific

Colourants

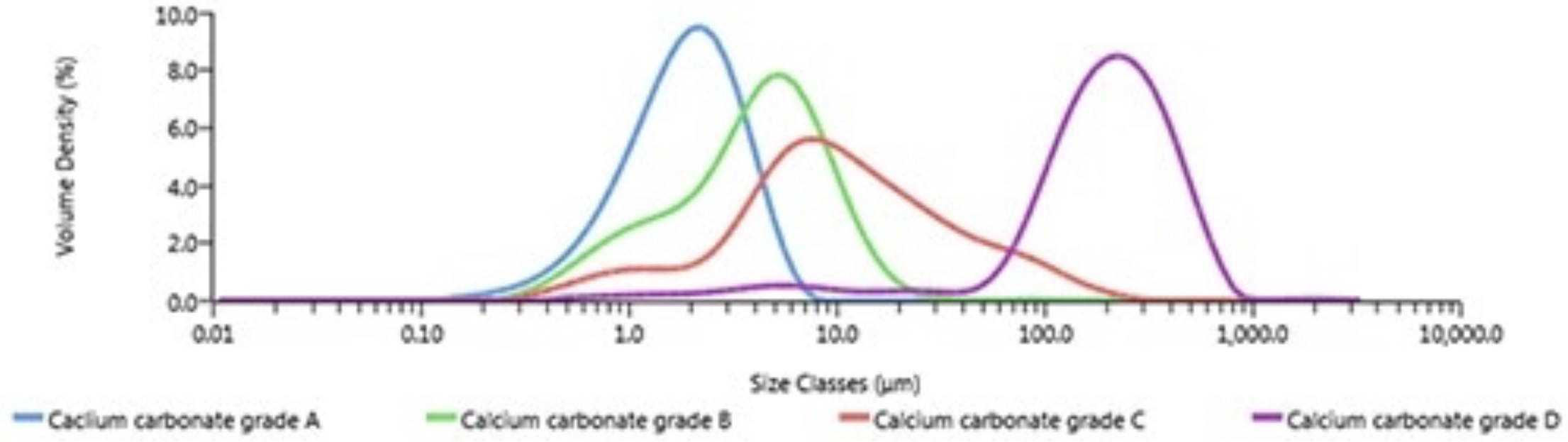
- ZnO2
  - Averages ~200nm, but can be below 100nm



- Horiba Scientific

Fillers

- Calcium Carbonate
  - Averages ~1,000nm
    - Rarely below 100nm



Nano

- Azo Materials

Antimony Trioxide Synergist

- Antimony trioxide
  - Averages ~1,000nm
    - Can be below 100 nm

	ITEMS	Sb2O3 Grades					
Chemical Properties	Sb2O3 >	99.50%	99.80%	99.9% FB	99.9% FA	99.9% W	99.9% N
	PbO <	0.080%	0.050%	0.010%	0.005%	0.004%	0.004%
	As2O3 <	0.080%	0.050%	0.010%	0.005%	0.004%	0.004%
	CuO <	0.006%	0.002%	0.002%	0.002%	0.002%	0.002%
	Fe2O3 <	0.006%	0.002%	0.002%	0.002%	0.002%	0.002%
	Se <	0.003%	0.001%	0.001%	0.001%	0.001%	0.001%
Physical Properties	Whiteness >	95	95	96	96	90	97
	Particle Size(um)	0.5-1.2	0.5-1.2	0.5-0.8	0.5-0.8	2.0-3.5	0.05-0.15

Nano

- Lin Chemicals

Stabilizers

- Stabilizers in plastics
  - Zinc stearate
  - Calcium stearate

- Average size
  - ~5 um (~5,000 nm)

- Generally soluble
  - Usually free Zn or Ca in the plastic
  - Not nanomaterial

Biocides

- Biocidal coatings
  - TiO_2
  - SnO_2
  - Ag

- Almost always nanomaterials

Nanomaterials Compliance

- That was cool and all…
- So what now?

Nanomaterials Compliance Key Items

- Objective evidence

- What do I put in my technical file to address nanomaterials?

- Or more specifically,
  - what do I put in my technical file to prove that I have addressed nanomaterials?

Nanomaterials
Practical Approach Part 1 - Statement

- General statement on risk of nanomaterials

  - No intentionally added biocides
  - No intentionally added nanomaterials
  - Address that additives are unlikely to be 1 to 100 nm
  - Identify that additives are embedded in plastics
    - And make up less than 50% of plastic

- Downside
  - Not all reviewers are keen on the lack of objective data

Nanomaterials
Practical Approach Part 2 - Leachables

- Leachables
  - Review leachables for
    - Cu, Sb, Ag, Co, Ni, Ba, Zn, Ti, Ca
  - If any detected, identify the source and identify cannot be nano materials
    - Examples
      - Nickel - dissolved from steel. Not nanomaterial
      - Ti - confirmed TiO2 colourant is not nanomaterial

Nanomaterials
Practical Approach Part 3 - Content Testing

- Testing product for additives
  - Test for
    - Cu, Sb, Ag, Co, Ni, Ba, Zn, Ti, Ca
    - In plastics
  - Confirm that the related potential nanomaterials are below 50% of plastic
  - Normally combined with engineering review of product and materials

- One of the most common approaches

Advantages of Content Testing

- Easy addition to CMR and EDC testing for medical devices

- CMR and EDC compliance medical devices
  - Testing is the most common approach to compliance
  - Straight forward to add the potential nanomaterials elements to testing to verify concentration

Recap - Compliance Approaches Nanomaterials in Medical Devices

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1. Statement on risk of nanomaterials
2. Reviewing leachable testing for potential nanomaterials
3. Testing for elements that could be nanomaterials to confirm embedded potential nanomaterials are below 50% of the plastic

How Can Claigan Help?

- General statement
  - Expert opinion regarding risk
  - Provides risk opinion

- Testing
  - Content testing of potential nanomaterials
  - Provides test data

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Q&A