Global Regulatory Landscape for Nanomaterials in Healthcare

- European Union
  - Medicinal Products
  - Medical Devices
- United States of America
  - Drug products, biological products and medical devices
- Australia
  - Therapeutic Goods
- Canada
- OECD global overview

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EU Regulation of Medicinal Products

- Directive 2001/83/EC relating to medicinal products for human use

Any substance or combination of substances presented for treating or preventing disease in human beings.

Any substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings is likewise considered a medicinal product.

- Second Regulatory Review on Nanomaterial 2012/0572

'The Commission takes the view that current legislation on medicinal products allows an appropriate risk/benefit analysis and risk management of nanomaterials.'

- European Medicines Agency (EMA)
  - Innovation Task Force
  - Scientific Guidelines

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EU Regulation of Medicinal Products

European Medicines Agency (EMA) scientific guidelines

- *Data requirements for intravenous iron-based **nano-colloidal products** developed with reference to an innovator medicinal product (2015)*
- *Data requirements for intravenous **liposomal products** developed with reference to an innovator liposomal product (2013)*
- *Development of **block-copolymer-micelle** medicinal products (2014)*
- *Surface coatings: general issues for consideration regarding parenteral administration of **coated nanomedicine products** (2013)*

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EU Regulation of Medical Devices

Regulation on Medical Devices - 2017/745 - Definitions

*'**medical device**' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:*

— diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,

— investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,

— providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations,

*'**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;*

Fullerenes, graphene flakes and single-wall carbon nanotubes with one or more external dimensions below 1 nm shall also be deemed to be nanomaterials

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EU Regulation of Medical Devices

*‘**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.’*

‘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 Regulation on Medical Devices comes into force in 2020

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EU Regulation of Medical Devices

SCENIHR Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices

- safety evaluation and risk assessment on the use of nanomaterials in medical devices that should be considered in conjunction with the ISO 10993-1:2009 standard
- Phased approach:
  1. particle release,
  2. particle distribution and persistence,
  3. hazard assessment (toxicological evaluations)
  4. risk characterisation/risk assessment
- *'the potential risk from the use of nanomaterials in medical devices is mainly associated with the possibility for release of free nanoparticles from the device and the duration of exposure'*

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EU Regulation of Medical Devices

ISO/TR 10993-22:2017 Biological evaluation of medical devices -- Part 22: Guidance on nanomaterials

- characterization of nanomaterials;
- sample preparation for testing of nanomaterials;
- release of nano-objects from medical devices;
- toxicokinetics of nano-objects;
- biological evaluation of nanomaterials;
- presentation of results;
- risk assessment of nanomaterials in the context of medical device evaluation;
- biological evaluation report;
- nanostructures on the surface of a medical device, intentionally generated during the engineering, manufacturing or processing of a medical device.

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EU Regulation of Medical Devices

- Competent Authorities on Medical Devices charged the European Commission New and Emerging Technologies Working Group – Special Interest Group on Nano with the development of **Information and guidance on classification for MDs (changes on classification rules).**

- The main issue is the clarification of high, medium, low and negligible internal exposure.

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United States Regulatory Framework for Nanomaterials in Healthcare

- Federal Food, Drug, & Cosmetic Act (FD&C Act)
- Food and Drug Administration
- **Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology**
  - Drugs, biological products, medical devices
  - No regulatory definition of a nanomaterial
  - Points to consider:

*1. Whether a material or end product is engineered to have at least one external dimension, or an internal or surface structure, in the **nanoscale range** (approximately 1 nm to 100 nm);*

*2. Whether a material or end product is engineered to exhibit **properties or phenomena,** including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer (1,000 nm).* [6]

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US FDA Consultation

- **NIA Member Consultation on US FDA Draft Guidance on Drug Products, Including Biological Products, that Contain Nanomaterials**
- US FDA's current thinking on the topic
- Federal Food, Drug, & Cosmetic Act (FD&C Act) and Public Health Service Act(PHS Act)
- Deadline **19 March 2018**

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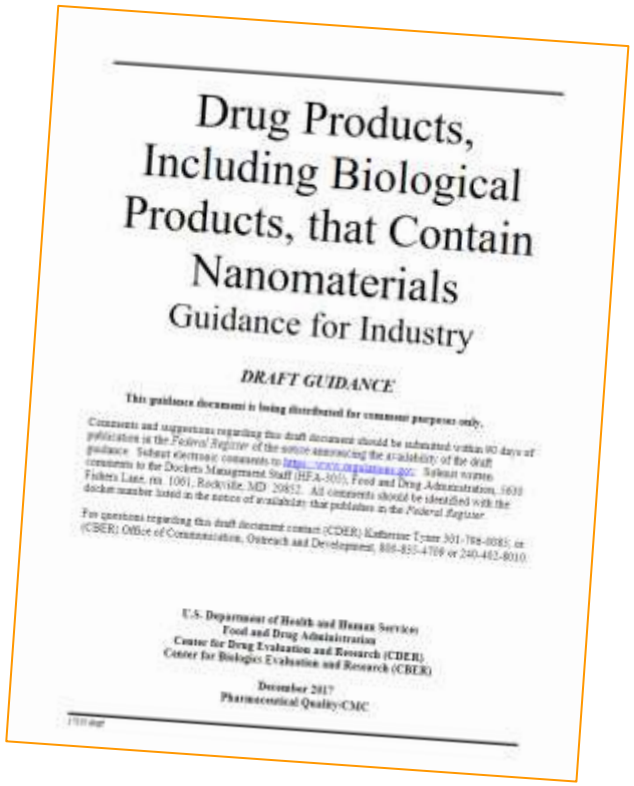
US FDA Consultation

- Recommendations for the content of regulatory applications
- Broad scope for a nanomaterial :
  - approximately **1 nm to 100 nm**
  - **properties or phenomena** that are attributable to dimensions of the material (up to 1micrometer)
- **Risk-based approach** for nanomaterials
- Para-regulatory text
- Scientifically comprehensive document
- NIA to ask for globally harmonised definitions



Drug Products, Including Biological Products, that Contain Nanomaterials

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2017
Pharmaceutical Quality/CMC

Members input by 6 March to Guillaume Flament
Document accessible via Members Area/Open Consultations

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Australia Therapeutic Goods Regulation

2011 - Australian regulatory guidelines for medical devices (ARGMD)

*'The European Commission has endorsed the precautionary principle in relation to medical devices containing nanomaterials**.** As an example, some dental materials may contain nanomaterials. The manufacturer should therefore incorporate the precautionary principle into their risk-management system for these devices. This would require explicit consideration of the uncertainty associated with the potential hazards posed by nanomaterials and the limits of current scientific knowledge.*

> *The TGA position is consistent with that of other Australian Government agencies and with the EU position.* ***The precautionary principle is consistent with the Australian approach to nanomaterials, and with the requirement.'***

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Health Canada

- Health Canada
- Health Products and Food Branch (HPFB)
- Policy Statement on Health Canada's Working Definition for Nanomaterial
  - ‘Nanoscale’ means 1 to 100 nm, inclusive
  - ‘Nanoscale properties, phenomena’
- **Applies to the Food and Drugs Act covering:**
  - Cosmetic Regulations
  - Food and Drug Regulations
  - Medical Devices Regulations
  - Natural Health Products Regulations
  - Safety of Human Cells, Tissues and Organs for Transplantation Regulations
- Health Canada my require information on:
  - Intended use, manufacturing methods, Characteristics, and physical chemical properties Toxicological, eco-toxicological, metabolism and environmental fate data that may be both generic and specific to the nanomaterial if applicable; and, Risk assessment and risk management strategies, if considered or implemented.

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OECD - Regulatory Frameworks for Nanotechnology in Foods and Medical Products

- 2013 publication
- Further identification of regulatory activities in:
  - France
  - Japan
  - Russian Federation

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Thank you

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