



IMDRF International Medical
Device Regulators Forum

Definition and regulation in terms of mechanism of action and intended use

- 1 - Nanomaterial-containing medical devices
- 2 - (Ingestible) medical devices composed of substances

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German Medicines Manufacturers' Association

Bundesverband
der Arzneimittel-
Hersteller e.V. **B.A.H**

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Nanomaterial-containing medical devices

European Commission's Proposal for a Medical Devices Regulation (MDR)

(...) In order to ensure a high level of health protection, free movement of goods and legal certainty for manufacturers, it is necessary to introduce a **uniform definition for nanomaterials** based on **Commission Recommendation 2011/696/EU** of 18 October 2011 on the definition of nanomaterial, with the **necessary flexibility to adapt** this definition to scientific and technical progress and subsequent **regulatory development at Union and international level**. (...)

COMMISSION RECOMMENDATION of 18 October 2011 on the definition of nanomaterial (2011/696/EU)

'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 nm-100 nm**. (...)

Nanomaterial-containing medical devices

-> *All products that contain pigments or filler materials are affected !!!*

- Examples: powdered medical gloves, pigmented compression or anti-thrombosis stockings, superabsorber-containing dressing materials, tubes for ventilation, plastic syringes and many other products
 - Many dental materials are affected: impression materials, adhesives, prostheses or artificial teeth.
(These products contain powder, e.g. porcelain powder, glass powder, pyrogenic silicas, pigments or other basic substances that meet the definition of nanomaterials according to recommendation 2011/696/EU.)
 - In many cases MD are “nano” because grinding or other crushing processes were involved in their manufacture.
- > Nano is not part of the intended use or mechanism of action
- > Often occurs accidentally
- > MD with a long history of safe use
- > Actually regulated as low risk-MD (class I or IIa)
- > Many natural substances like sand, dusts or milk are “nano” – human exposure since thousands of years!

Nanomaterial-containing medical devices

BAH position:

- Additional requirements **specific** for nanomaterials (e.g. additional specific **risk assessment** and **biological studies - ISO 10993**), based on the respective product in question, potential risks of such products can be evaluated as part of the conformity assessment procedure.
- Products that do not bear nanomaterial intentionally but **can release** nanoparticles due to their application => proof required that no nanoparticle is released during the use of the medical device in question (e.g. due to abrasion). **Not possible to prove a zero-release!**
- It should be considered if the specific nanomaterial has a **long history of safe use** within the particular group of products (e.g. most dental materials for decades)
- It should be considered if MD were assessed by appropriate European **scientific bodies** such as the Scientific Committee on Consumer Safety (SCCS) or the European Food Safety Authority (EFSA) with regard to their safe use.
- Europe / MDR: deletion of **rule 19**

Nanomaterial-containing medical devices at the IMDRF

Purpose

In view of the global medical device industry a single definition for the term "nanomaterial" is necessary. Therefore we propose to develop a **globally harmonized definition of nanomaterials**.

Rationale

A broad range of innovative and established MD is concerned by the divergence in the definition of "nanomaterial" resulting in **different risk classifications and regulatory requirements**.

Therefore a global approach is needed to ensure **consistency of MD regulation in terms of intended use and mechanism of action** as well as an appropriate risk-based assessment of nanomaterial-containing MD.

Issues to be addressed

- 1) **Definitions and relevant terms regarding the characterization of nanomaterial in MD**: bound and unbound stage, zero-release of particles, occurring incidentally or through manufacturing, added intentionally, abrasion etc.
- 2) **Standards**, measuring methods
- 3) Consideration of nanomaterial-containing MD with a long history of safe use (e.g. many dental materials)
- 4) Conformity assessment of nanomaterial-containing MD

Opportunities for regulatory convergence

- 1) Find a globally harmonized definition of nanomaterial and an appropriate classification and regulation on the concerned MD
- 2) Create appropriate essential requirements (specific biological evaluation and risk assessment) for nanomaterial-containing MD

Medical devices composed of substances

- eye drops / nose drops / products for humidification of the skin (dexpanthenole)
- lozenges against sore throat
- flushing solutions (sodium chloride)
- products against flatulencies / accumulation of gas in the stomach (simeticone=polyethylenglycole)
- laxatives

Many of those regulated now as low risk (class I) self-care devices!

Medical devices composed of substances

European Commission's Proposal for a Medical Devices Regulation (MDR):

“Devices that are composed of substances or combination of substances
intended to be ingested, inhaled or administered rectally or vaginally
and
that are absorbed by or dispersed in the human body”

Absorption - movement of a **drug** into the bloodstream (pharmacokinetics)

Absorption = Blood uptake = “entrance into the body” -> Dispersion / Distribution

Possible routes for absorption: ingestion, inhalation, dermal absorption, injection

Ingestion does not automatically mean absorption!

Medical devices composed of substances

For the purpose of clarification we propose the following change :

“Devices that are composed of substances or combination of substances intended to be ingested, inhaled or administered rectally or vaginally and that are absorbed by or **and** dispersed in the human body **to achieve their intended purpose** shall comply, by analogy, with the relevant requirements laid down in Annex I to Directive 2001/83/EC.” = medicinal products directive

Rationale:

- Substances that are unintentionally absorbed in trace amounts by the body are already evaluated as part of the **risk assessment**
- High requirements should only apply to products whose **intended purpose in accordance with the mode of operation** requires an absorption and distribution of a substance in the body
- **Requirements specific for medicinal products** such as studies on the pharmacodynamics are **not applicable** to medical devices that are not absorbed by the body and distributed to achieve their intended purpose
- Substance passes the gastrointestinal tract and is excreted without being changed

*Europe / MDR: deletion of **rule 21***

Medical devices composed of substances at the IMDRF

Purpose / Issues to be addressed

- 1) Secure the global approach of **defining the scope of products within the medical devices regulations in terms of the intended use and the mechanism of action** as developed by the former Global Harmonization Task Force,
- 2) Have an international concordance in **risk classification** .

Rationale

Develop technical documents that would appropriately address the specifics of this group of medical devices at both national/regional and international level.

Opportunities for regulatory convergence

- 1) Discuss the appropriate risk classification of self-care medical devices
- 2) Harmonize the Unique Device Identification approach concerning this type of devices.

Relevant existing documents at IMDRF or GHTF and national level, as well as in international bodies

New Work Item Proposal

” Nanomaterial-containing medical devices - definition of “nanomaterial”

- 1) Definition of the Terms ‘Medical Device’ and ‘In Vitro Diagnostic (IVD) Medical Device’ (SG1 N071:2012)
- 2) Principles of Medical Devices Classification (SG1 /N077:2012)
- 3) Commission Recommendation of 18 October 2011 on the definition of nanomaterial (Text with EEA relevance) (2011/696/EU)
- 4) Council Directive 93/42/EEC of 14 June 1993 concerning medical devices
- 5) ISO/TS 27687:2009: Nanotechnologies - Terminology and definitions for nano-objects - Nanoparticle, nanofibre and nanoplate
- 6) ISO/TC 194: Biological evaluation of medical devices - WG17 Nanomaterials
- 7) ISO/TR 15499:2012: Biological evaluation of medical devices - Guidance on the conduct of biological evaluation within a risk management process
- 8) Harmonized Standard EN ISO 10993: Biological evaluation of medical devices
- 9) Harmonized Standard EN ISO 14971: 2012: Medical devices - Application of risk management to medical devices
- 10) Harmonized Standard EN ISO 13485: 2012: Medical devices - Quality management systems - Requirements for regulatory purposes

New Work Item Proposal

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- 4) Harmonized Standard EN ISO 10993: Biological evaluation of medical devices
- 5) Harmonized Standard EN ISO 13485: 2012: Medical devices - Quality management systems - Requirements for regulatory purposes

Thank you very much for your attention!