The Regulatory Science Framework in nanomedicine: how science could improve the implementation of regulation?

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What are the opportunities of innovative nanotechnology based health products?

Medicinal products
- Increased stability and blood circulation
- Improved transport across the barriers

Medical devices
- Lighter, Stronger Implantable Devices
- Alter or enhance adhesion properties

Are the current regulatory frameworks suitable for nanotechnology based products?
• Working Group on Nanomedicines of the International Pharmaceutical Regulators Programme (IPRP) established in 2009
• 1st International Workshop on Nanomedicines in 2010 (EMA)
• Release of Reflection Papers 2013-2015 (CHMP EMA)
• Global Summit on Regulatory Science (GSRS) workshops in 2015, 2016 and 2019!
• "Bridging communities in the field of nanomedicine" JRC workshop in 2017
Aim:

Improve the risk-benefit assessment of nanotechnology based materials used in health products

Dec. 2017 - Nov. 2021

European Union’s Horizon 2020 Research and Innovation Programme Grant Agreement No 761104
Identification of regulatory needs
Integrated testing strategies/ DSS
Biodistribution: in vitro, in vivo, in silico
Biological response to NBMs
Quality and standardisation
Community bridging

Literature
Scientific state of art
Method development
Knowledge exchange
Identification of regulatory challenges

**Input:**
- Regulatory documents
- Reflection papers
- Guidance documents
- Peer-reviewed publications
- Standards

**Regulatory challenges**

**Harmonisation needs**

**Methodologies**

**Purpose:**
- Guide the consortium towards the development of relevant methods
- Inform the stakeholders on regulatory challenges
- Find the synergies with other sectors
Is the existing guidance sufficient for assessing innovative nanomedicines?

No or only initial guidance is available.

Do nanomedicines require additional safety and quality assessments?

Uncertainty for product developer.

Characterisation of nanomedicine for regulatory purposes might be insufficient.

Lack of robust datasets.

How can we break the cycle?

- Text-mining tools to monitor the scientific literature
- Real world databases to analyse safety issues
- Proactive pharmacovigilance with rapid reporting on adverse effects

Do nanomedicines require additional safety and quality assessments?
Are there any nano-specific adverse effects of nanomedicines that require regulatory awareness?

Scientific literature is growing fast, impossible to monitor
Text mining tools might help to identify weak signals

**Step 1**
Identify all reported safety issues related to nanomaterials in scientific literature using text mining tools

**Step 2**
Map against safety issues already identified in regulatory documents

Uncovered adversities
How to regulate nanotechnology based products cutting across regulatory frameworks?

Classification into medicinal products and medical devices according to legal definitions can be challenging.

Strengthen the collaboration between medicines regulators and medical devices regulators.

Combination products

Borderline products

Development of a common regulatory path?
How to assess the bioequivalence of follow-on nanomedicines?

- Expiry of patents of first generation nanomedicines
- Development of generics ("nanosimilar")
- Regulatory initiative allowing to assess the bioequivalence to the innovator product

*Ehmann et al; Next-generation nanomedicines and nanosimilars: EU regulators’ initiatives relating to the development and evaluation of nanomedicines* Nanomedicine (2013) 8(5), 849–856
Are standardised methods available to assess nanomedicines?

Different nanomedicines require different tools

- Limited reliability for heterogeneous samples
- Material dependent applicability
- Measurements in biological environment
- Nanomaterial interference with assay
- Reliability of constantly new developed instrumentations
Mapping in REFINE

Gap analysis is ongoing

- **Step 1**: Compilation of the Regulatory Library
- **Step 2**: Extraction of the information needs
- **Step 3**: Categorisation of the information needs
- **Step 4**: Mapping against available methods
Preliminary methodological gap analysis

- Drug loading and drug release
- Surface analysis
- Kinetic properties in biological media
- Evaluation of the interaction with the immune system
- ADME and biodistribution

Halamoda B. et al (2018); Mapping of the available standards against the regulatory needs for nanomedicines. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, Volume 11, Issue 1*
Why do we need to harmonise the terminology?

- A clear and transparent communication among stakeholders
- An effective review for policy making and research granting,
- Information retrieval: patent searching, clinical trials, etc
- A harmonised regulatory governance,
- Standardisation of tests for quality, safety & efficacy assessments


78% of these terms in 1 article
2% present in 10 documents
13084 author keywords from 7000 publications
REFINE aims to address regulatory challenges for nano-enabled health products

Several regulatory challenges have been identified in the REFINE's White paper

The White paper will be presented to involved communities to gather their feedback

Relevant methods will be developed in experimental workpackages of REFINE

Refine will also develop a Decision Support System providing assistance to the preclinical characterisation of nano-enabled health products

Knowledge and methods available in other sectors will be used for the cross-fertilisation strategy
Feedback on the White paper

Dissemination and survey on the REFINE website
http://refine-nanomed.com/

Global Summit on Regulatory Science 2019
Nanotechnology and Nanoplastics

SAVE THE DATE!
24-26 September 2019
Visit to the EC Joint Research Centre in Ispra - 27.09.2019
Lago Maggiore, Italy

Co-Organised by
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More information on
THANKS FOR YOUR ATTENTION

QUESTIONS?

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