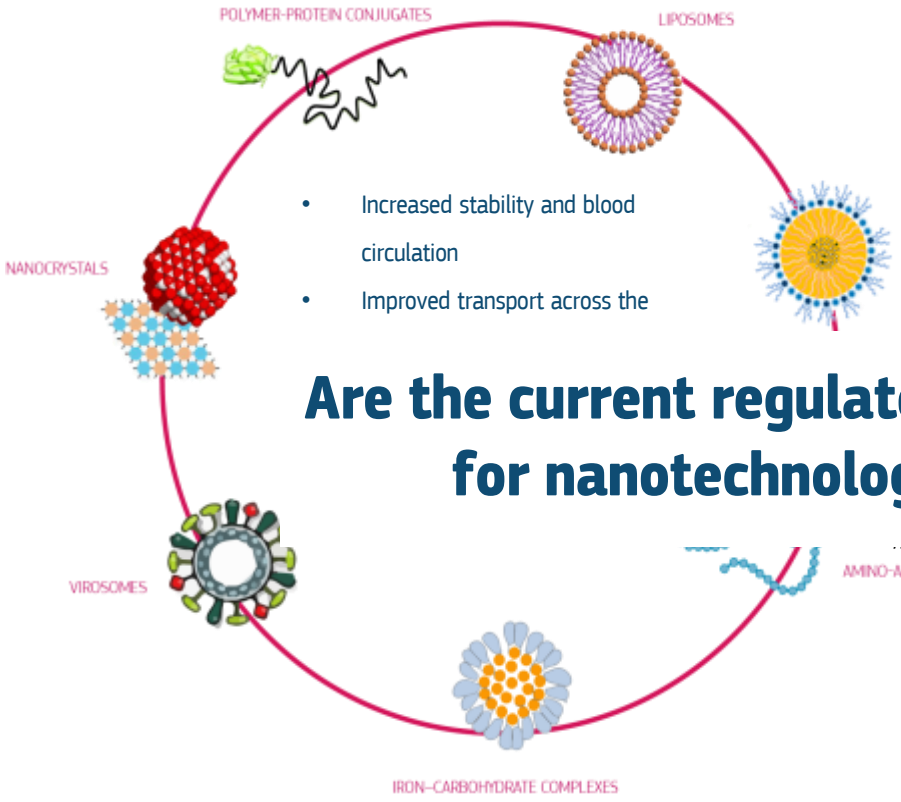
The Regulatory Science Framework in nanomedicine: how science could improve the implementation of regulation?

Blanka Halamoda Kenzaoui
EC Joint Research Centre

EuroNanoForum 12-14 June 2019

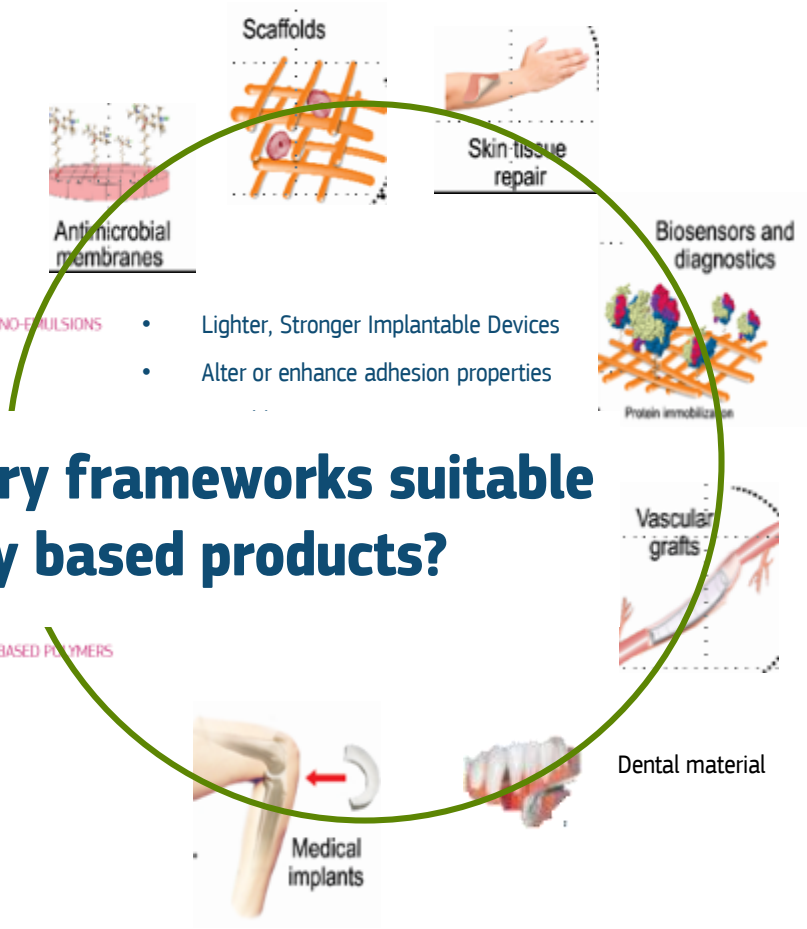
What are the opportunities of innovative nanotechnology based health products?

Medicinal products



- Increased stability and blood circulation
- Improved transport across the

Medical devices



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

Are the current regulatory frameworks suitable for nanotechnology based products?

Regulatory science activities

- 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

Regulatory Toxicology and Pharmacology

Bridging communities in the field of nanomedicine

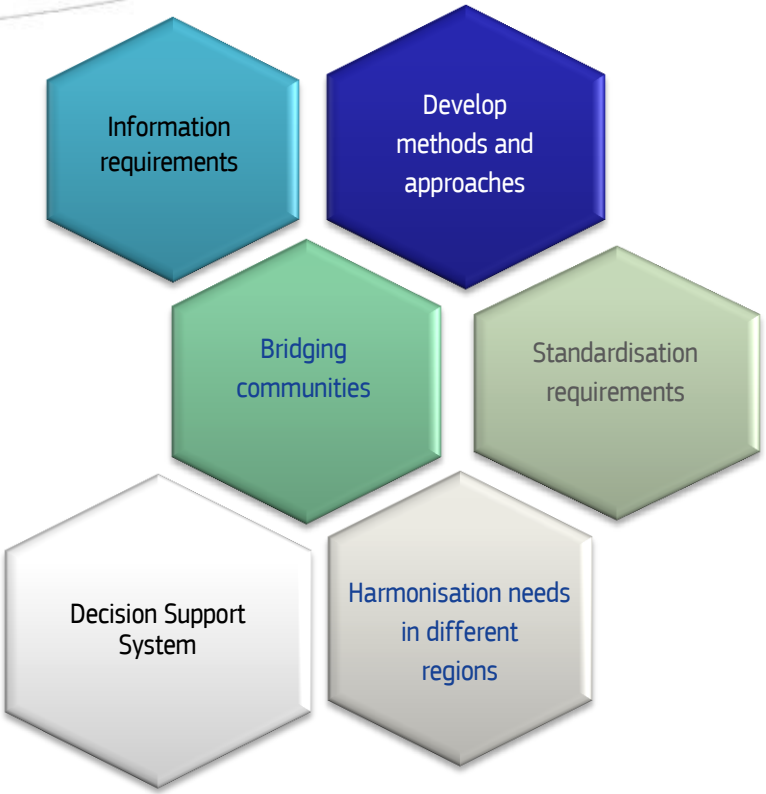
REFINE Regulatory Science Framework for Nano(bio)materials based Medical Products and Devices

Aim:

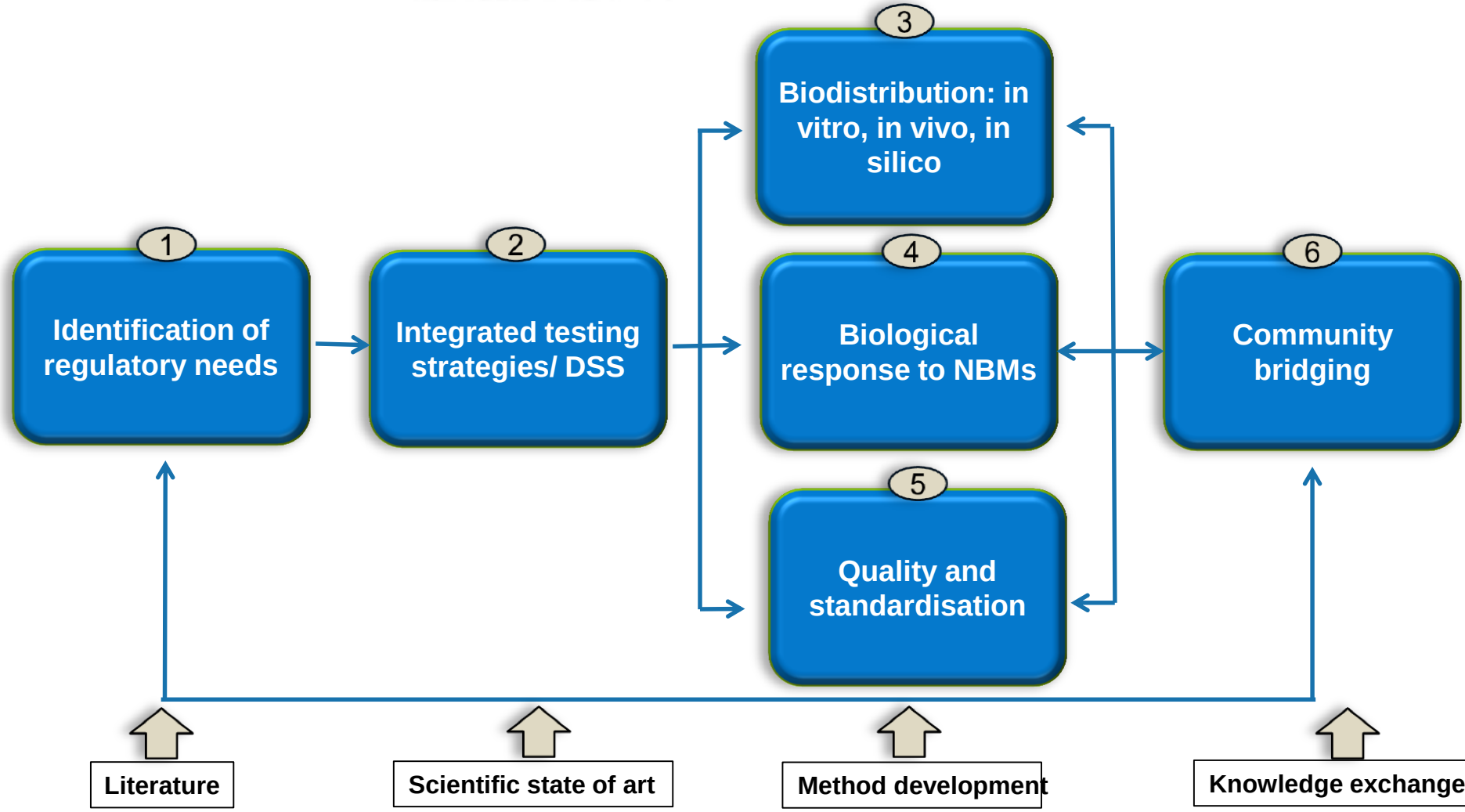
Improve the risk-benefit assessment of nanotechnology based materials used in health products

Dec. 2017- Nov.2021

European Union's Horizon 2020
Research and Innovation Programme
Grant Agreement No 761104



REFINE structure



Identification of regulatory challenges

Input:

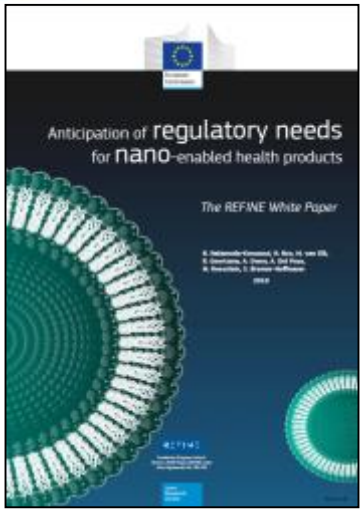
- Regulatory documents
- Reflection papers
- Guidance documents
- Peer-reviewed publications
- Standards

Regulatory challenges

Harmonisation needs

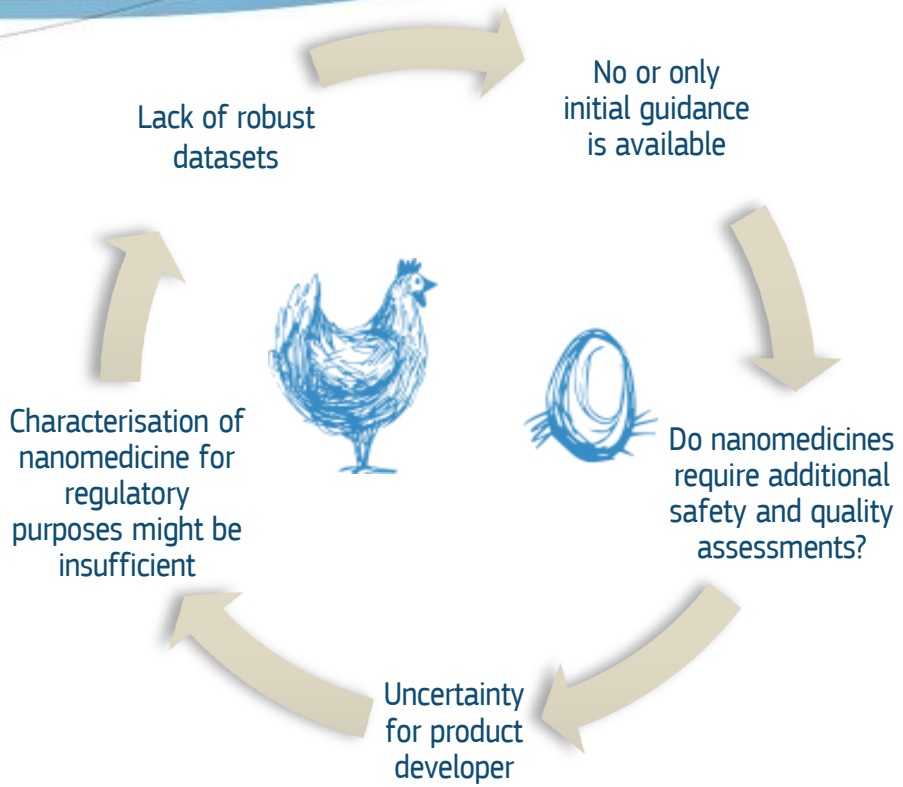
Methodologies

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?



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

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

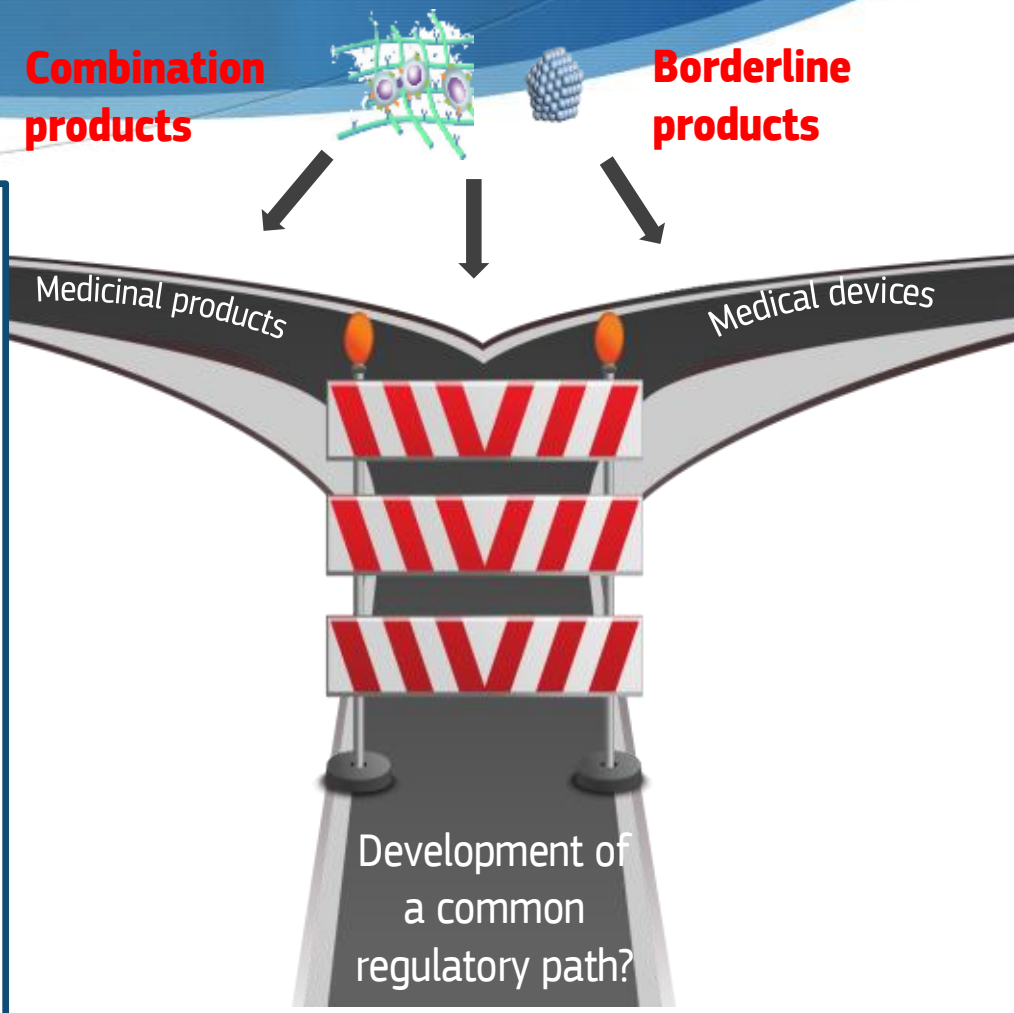
Map against safety issues already identified in regulatory documents

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



How to assess the bioequivalence of follow-on nanomedicines?

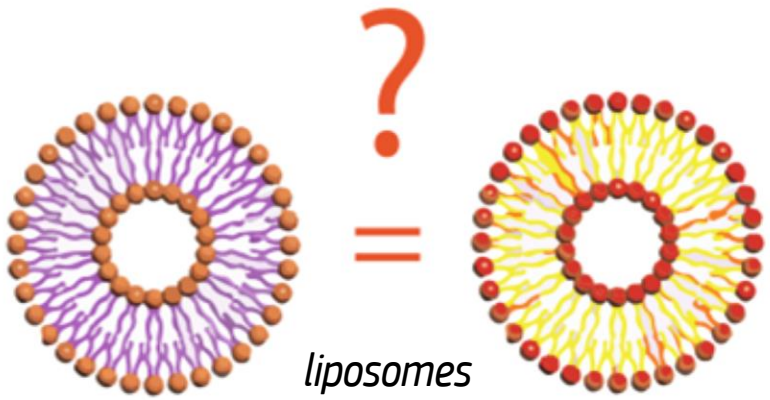
Expiry of patents of first generation nanomedicines

↓

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

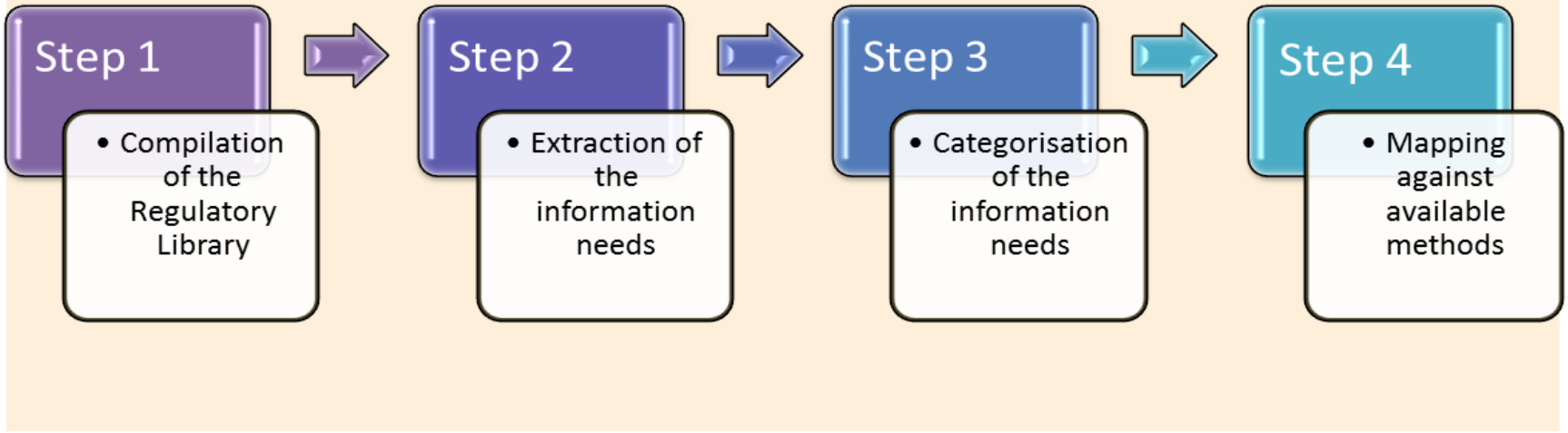
Material dependent applicability

Measurements in biological environment

Nanomaterial interference with assay

Reliability of constantly new developed instrumentations

Mapping in REFINE



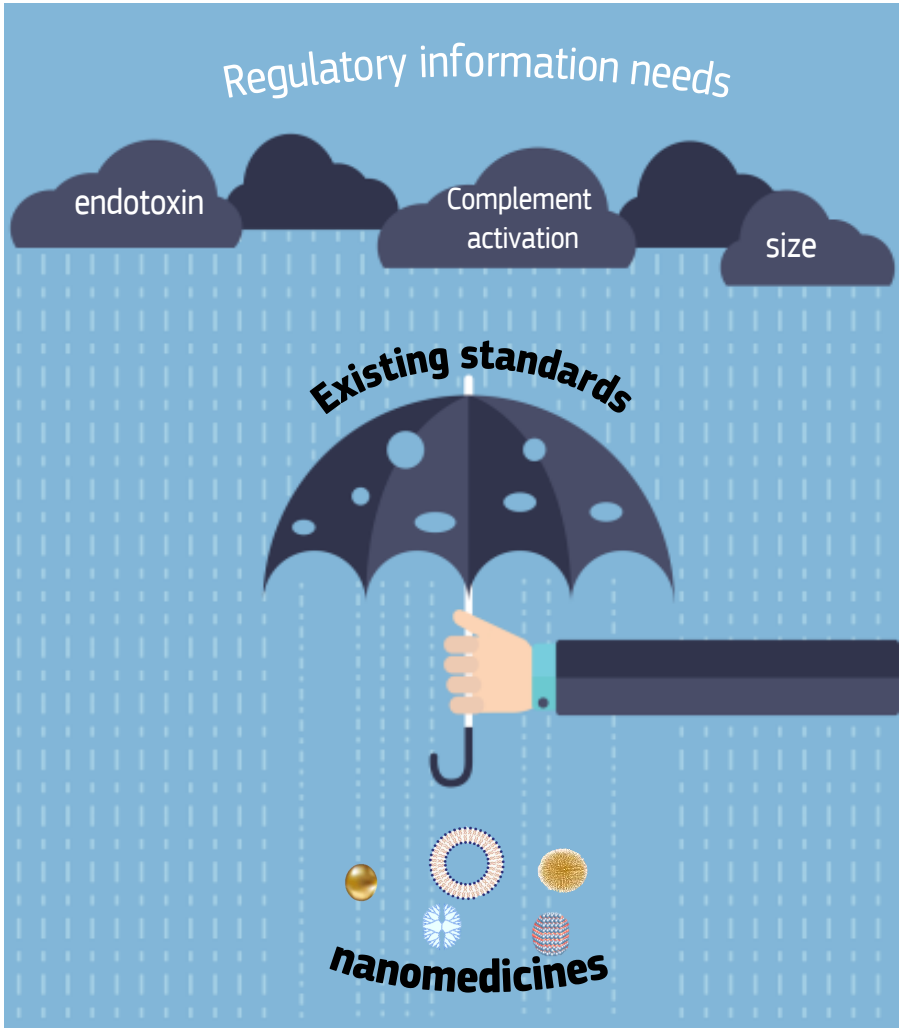
Gap analysis is ongoing

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**

REFINE

WP3 WP4



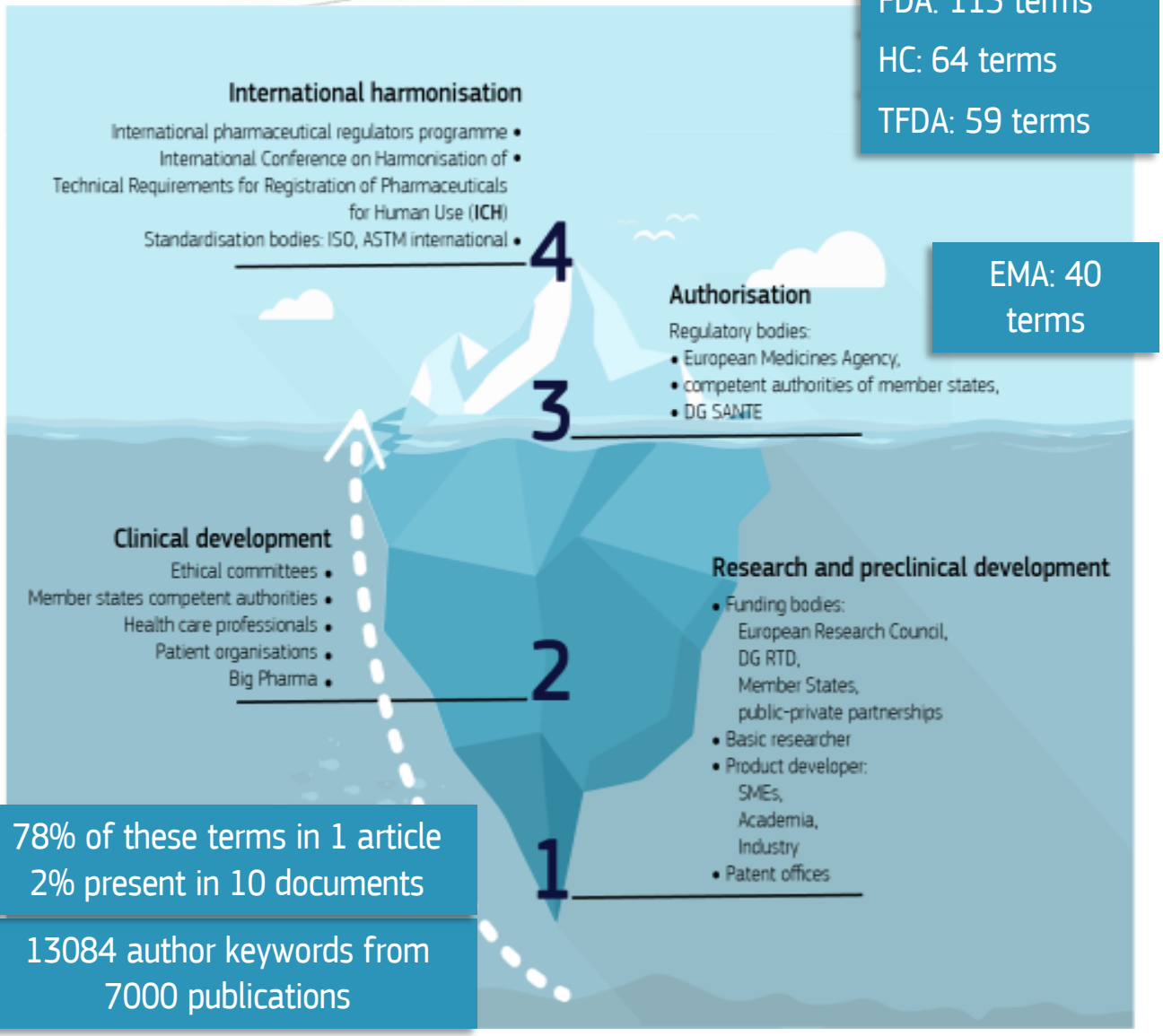
Halamoda B. et al (2018); Mapping of the available standards against the regulatory needs for nanomedicines. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, Volume 11, Issue 1

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

IPRP working group on "Nanomedicines"

Quirós Pesudo, L., *Mapping Nanomedicine Terminology in the Regulatory Landscape*, EUR 29291 EN;



FDA: 115 terms

HC: 64 terms

TFDA: 59 terms

EMA: 40 terms

78% of these terms in 1 article
2% present in 10 documents

13084 author keywords from 7000 publications

Summary

REFINE aims to address regulatory challenges for nano-enabled health products

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

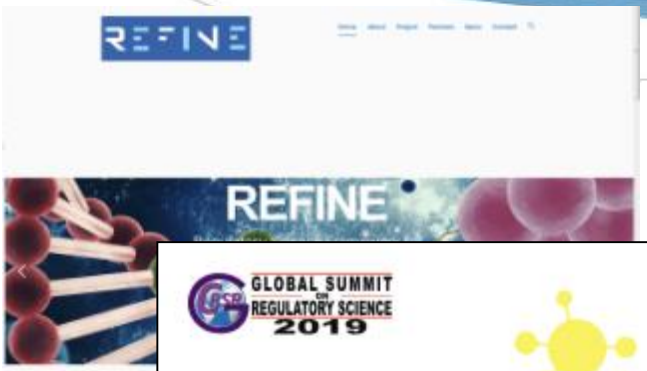
The White paper will be presented to involved communities to gather their feedback

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/

THANKS FOR YOUR ATTENTION

QUESTIONS?

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 761104