Safety and Sustainability Assessment in Safe-by-design in NanoReg2

EURONANOFORUM 2019
Bucharest, 12|06|2019

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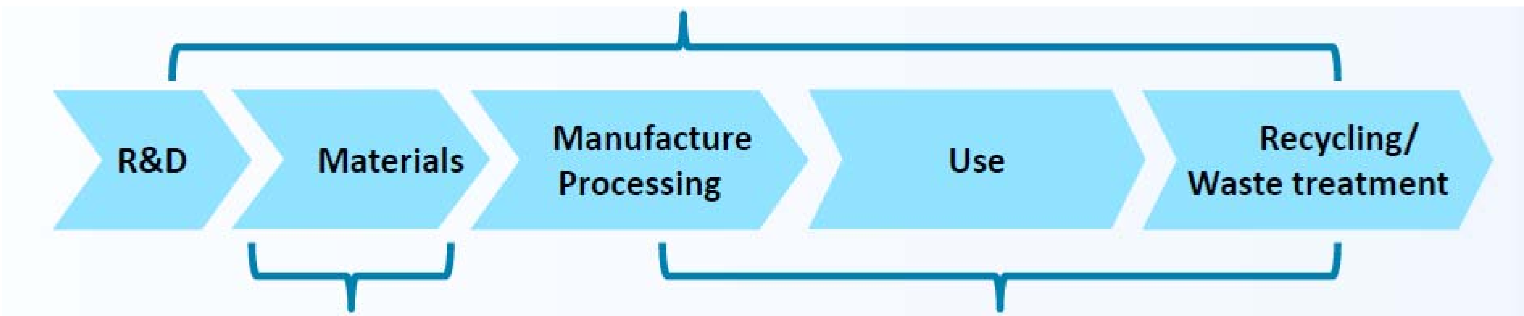
What is Safe-by-design. NanoReg2 concept.

SbD aims at reducing uncertainties and risks of human and environmental safety of nanotechnology, starting as early as possible during the innovation process, on the basis of mandatory and voluntary safety and efficacy compliance requirements.



It covers:

- All the value chain. Three pillars Safe products, safe production, safe use.
- Reduces costs
- Flexible, it anticipates future nanosafety demands

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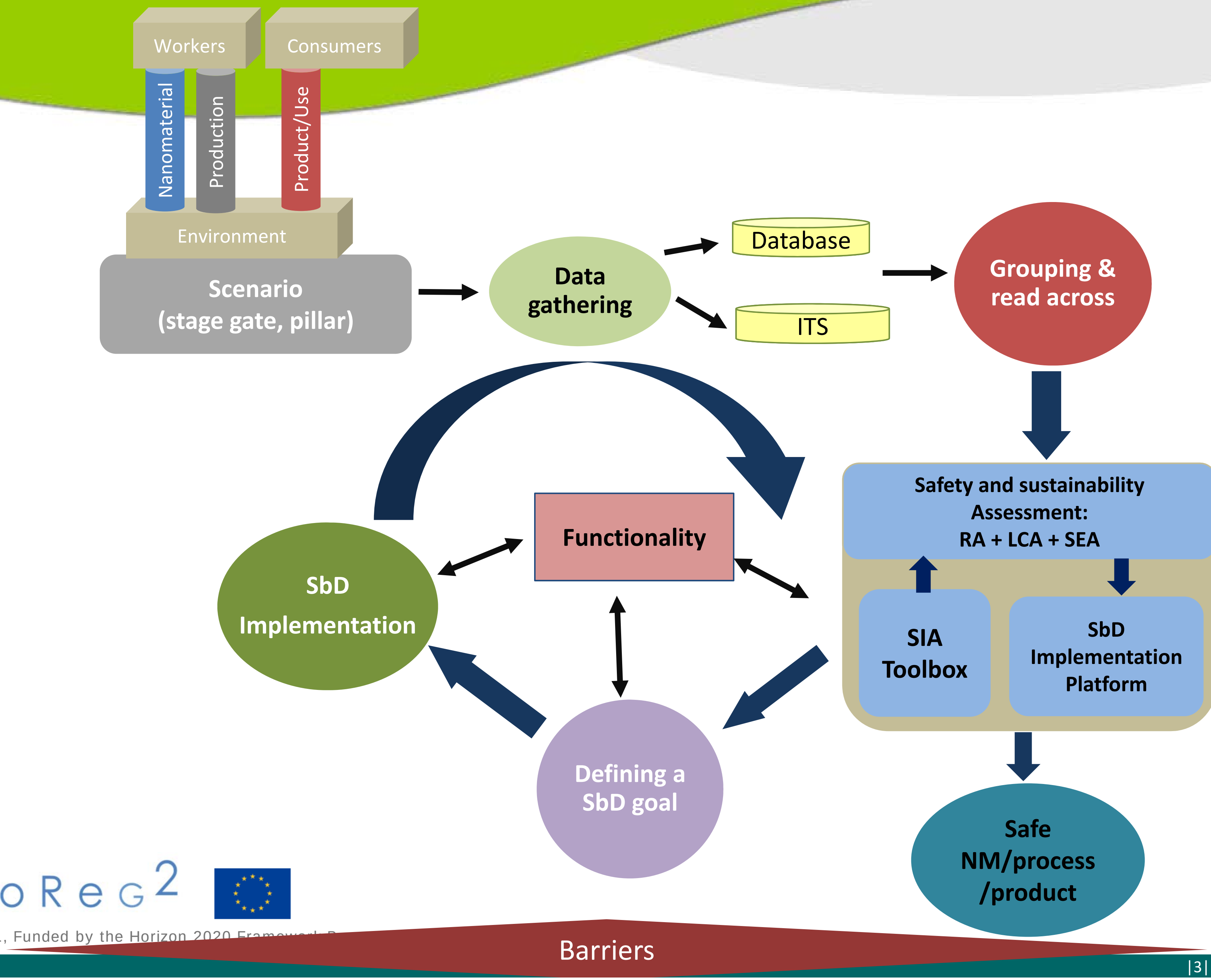
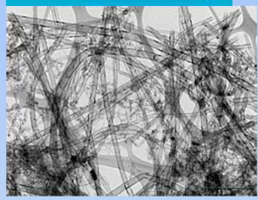
SAFE-BY-DESIGN. NANOREG2 CONCEPT

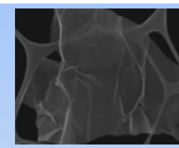


NanoReG2



CNF for automotive applications

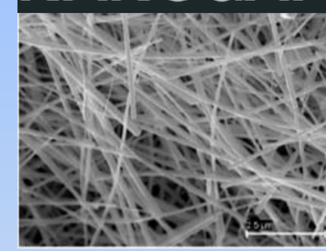
Si based NMs for batteries



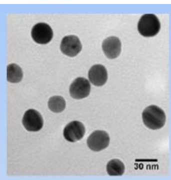
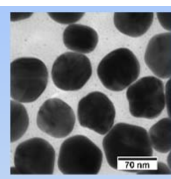
Graphene for coatings & paint applications

Industrial Case Studies

Dye doped nanoSiO_2 for biosensors



Ag nanowires for electronic products

Ag NPs for antibacterial coatings

Nano SiO_2 for resins applications

Industrial case studies

Demonstration:

1. Toxicity SOPs
2. First full comparison RA tools with industrial case studies

Method development:

1. Adaptation of LCA to NMs
2. SEA application to an industrial case study
3. Data integration RA, LCA & SEA for SbD
4. SbD practical guidance

Industrial impact:

1. Behaviour change towards a SbD approach
2. In-depth knowledge of the toxicity, exposure and risk of their NMs & process.
3. Change in production processes
4. Selection of safer NM for upscale & market production
5. Awareness of main barriers and incentives for SbD.

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Safety and sustainability Assessment. Overall concept

Understand the value chain demonstrator and draw a first «grainy» picture

Screening Risk Assessment

1. Risk assessment plan
2. Hot spots and targets
3. General data gaps

Evaluate the SbD implementation by RA, LCA and SEA indicators

Comparative Assessment

1. SbD evaluation
2. Tools applicability

Safety and sustainability Assessment. Overall concept

Risk Assessment (RA)

- Control banding tool for preliminary RA: identification of hot spots and data gaps.
- Semi-quantitative or quantitative models for comparative risk assessment . Evaluation of the SbD

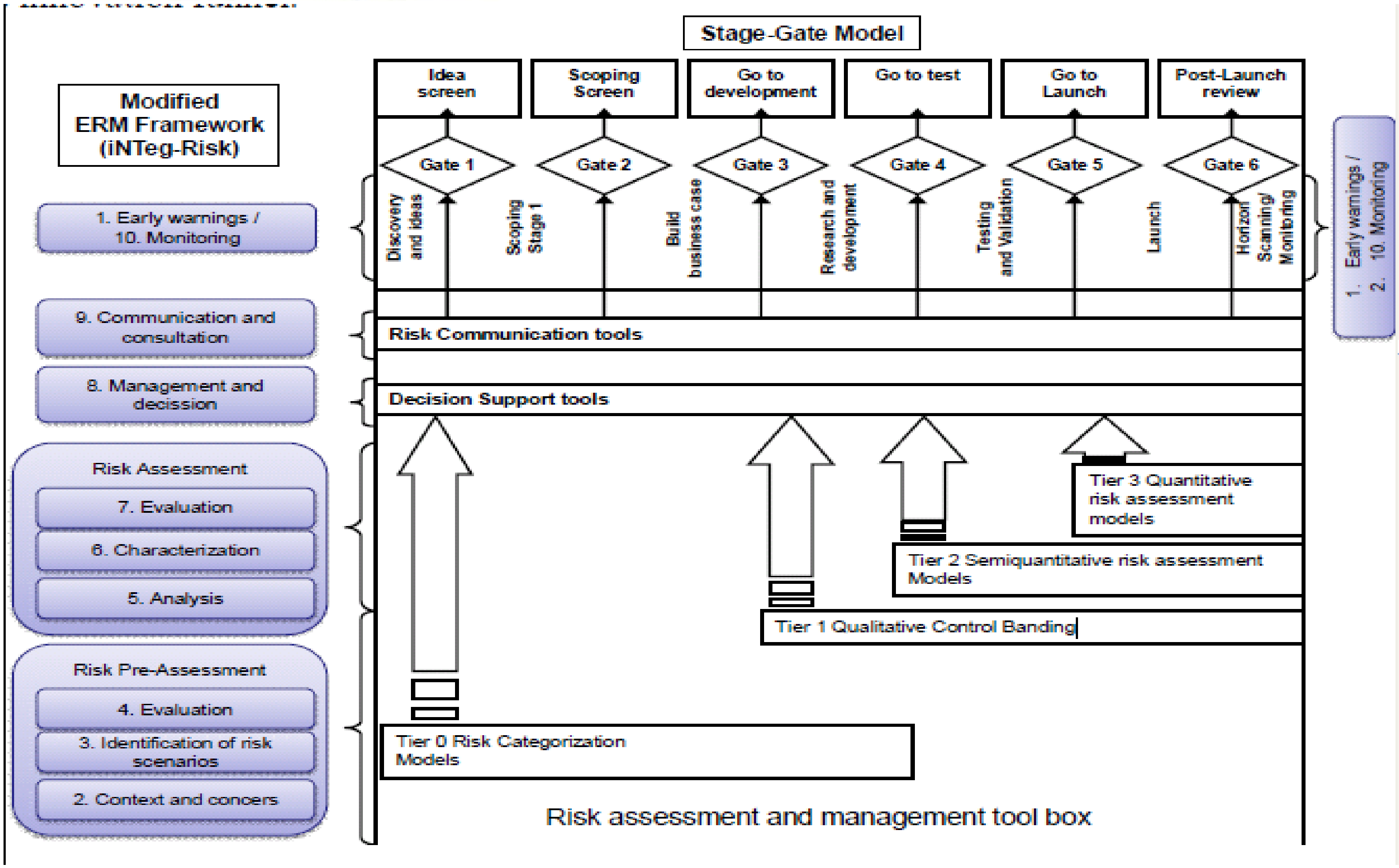
Life Cycle Assessment (LCA)

- Established & standardised method. Evaluates potential impacts on ecosystems, human health and resources.
- Limitations when applied to nanomaterials. Development needed: impact assessment of releases of nanoparticles & data on production.
- LCA can be applied even in the design stages to manage/ control the (out-coming-future) potential impacts.
- Different scenarios can be evaluated.

Socio-Economic Analysis (SEA):

- Socio-Economic Analysis is a decision support approach for evaluation of regulation, regulatory proposals, projects…
- Methodological comparison of pros and cons of alternative situations
- Take into account : environmental, health and economic impacts

Safety and sustainability assessment. RA



Safety and sustainability assessment. RA

Model	Scope	Target group	# parameters	Outcput
CB Nanotool	Risk ass. and man.	Researchers	45	Risk Level + general recommendation
Swiss Precautionary Matrix	Source identification and risk reduction	Workers, consumers and the environment	28	Need for action/no action
Stoffenmanager Nano	Prioritize health risks implementation of control measures.	Workers	47	Risk priority bands. Ranking priority of needed actions
NanoSafer	Precautionary risk assessment	Workers	29	Risk Level (RL). Recommendation and actions to be taken into consideration
NanoRiskCat	Risk assesment	Professional end users, consumers, environment	16	Exposure and hazard potential
ISO/TS 12901-2:2014	Prioritize health risks and implementation of control measures.	Workers		Risk Level (RL). Recommendation and actions to be taken into consideration

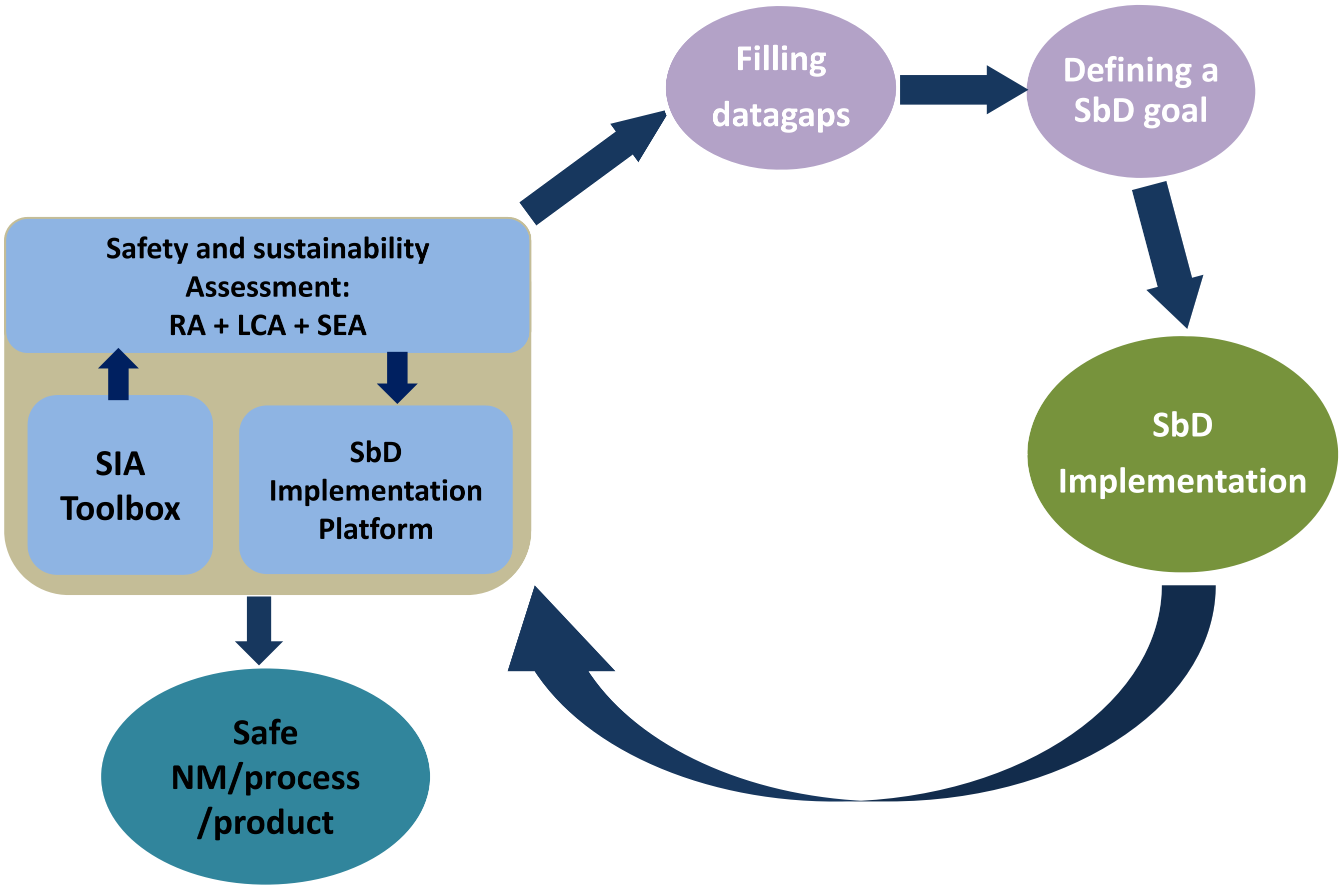
Safety and sustainability assessment. SOPs

- Physico-chemical and (eco) toxicological characterisation of NM:
  - Dustiness, zeta potential, Hydrochemical reactivity, dissolution, stability
  - Genotoxicty, cytotoxicity, instillation assay, ROS, inlfammation, eye irritation, dermal irritation
  - In vitro cytotoxicity on fish cell lines, mussels cell lines
  - In vivo test on mussels, algae and microinvertebrates

- Existing SOPs have been used in most cases for the characterisation of industrial NMs:
  - OECD guidelines
  - NANoREG SOPs
  - Nanogenotox dispersion protocol

- Development of new SOPs:
  - *In vitro* lung clearance using lung epithelium: ALI system and analysis with cytometry and ELISA

Safety and sustainability assessment. RA



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Safety and sustainability assessment. RA

SUNDS. It is a powerful tool to carry out a risk assessment of different scenarios (i.e. before and after SbD) but it requires the calculation of a benchmark dose (BMD), i.e. a dose of no toxic effect. Only possible with an *in vivo* assay.

Weight of Evidence (WoE) approach. Combines the available data (evidences) into hazard and exposure classes through a system of weights and algorithms. Weights are defined to give to each data their relevance for the risk assessment and the data quality in the integration process. Online tool was developed.

Last two models were applied with the help of GreenDecision, srl and colaboration with the caLIBRAte project

Safety and sustainability assessment. RA

Demonstration. First full comparison RA tools using industrial case studies

	Antolin	Avanzare	HiqNano	Nanogap	Nanomakers	Nanocomposix
RA tools	SPM	SPM	SPM	SPM	SPM	SPM
	NanoSafer	NanoSafer	CB Nanotool	NanoSafer	NanoSafer	NanoRiskCat
				NanoRiskCat	NanoRiskCat	
	SUNDs/WoE	SUNDs/WoE	WoE		Literature based RA SUNDs /WoE	Literature based RA SUNDs/WoE

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Safety and sustainability assessment. RA

	Control banding tools	Comparative tools
Characteristics	▪ Simple ▪ Easy to use ▪ Qualitative ▪ Few data needs: default values, worse case scenarios ▪ Highly conservative.	▪ More complex. More expertise required ▪ More information needed ▪ Semiquantitative or quantitative
When to use	▪ Initial picture ▪ Identify gaps, hot spots, raise red flags ▪ Comparison of very different situations ▪ Early stages	▪ Comparison of different situations ▪ Later stages when more information is available

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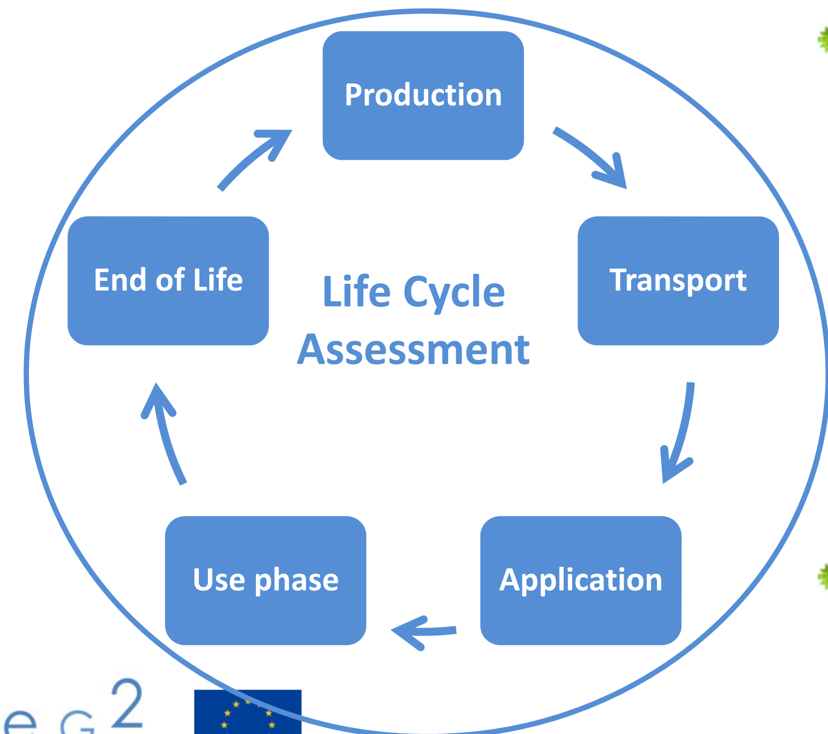
Safety and sustainability assessment. LCA

IN COMMON WITH RA

- Assessment of the use (phase) of the substance
- Where can release take place?
- Which would be the target media?
- Which would be the damage?



SPECIFIC TO LCA

- Covers entire life cycle, from extraction of resources to final disposal
- Addresses also additional impacts, such as for example “Global Warming”
- Assesses respective impacts related to all material and energy consumption along the life cycle
- More relative results: comparison among materials or processes.

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Safety and sustainability assessment. LCA

LCA inventories → inputs and outputs of the system (material/energy consumption and substance emission), being basis in order to calculate Indicators for Impact categories

(i.e. Global Warming Potential, Human Toxicity, Ecotoxicity, Eutrophication potential…)

From inventory to indicators: Characterization Factors (CFs);

Releases of the substance are multiplied with these factors → their relative contribution to an impact

Key Impact Categories for ENMs: Toxicity and Ecotoxicity

Reference methodology:
- USEtox™ model (Rosenbaum et al. 2008)
- Fate-exposure-effect model to calculate CFs
  - Human toxicity
  - Ecotoxicity

Safety and sustainability assessment. LCA

Adaptation of LCA to NMs

USEtox

Reduce compexity

Get consistency

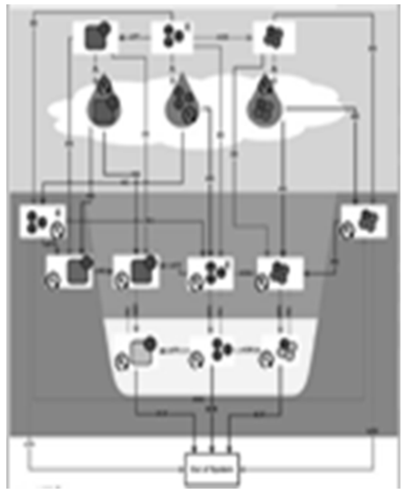
Fate

X

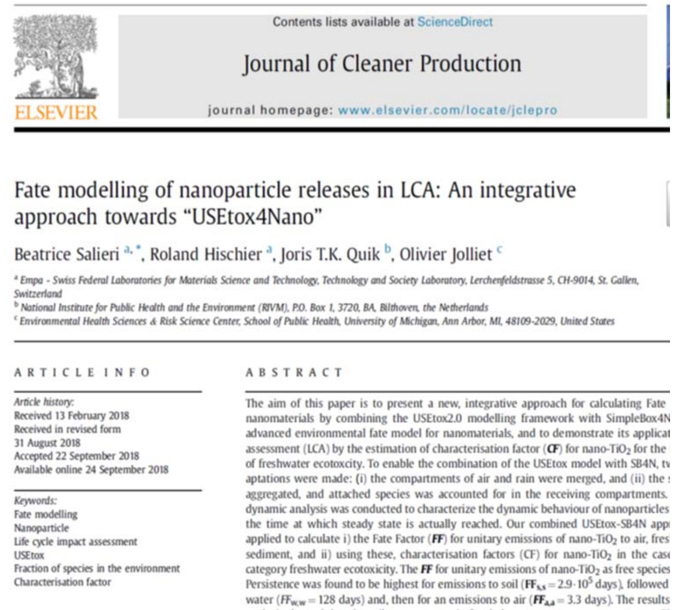
Exposure

X

Effect



Simplebox4Nano



Contents lists available at ScienceDirect

Journal of Cleaner Production

journal homepage: www.elsevier.com/locate/jclepro

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Fate modelling of nanoparticle releases in LCA: An integrative approach towards "USEtox4Nano"

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ARTICLE INFO

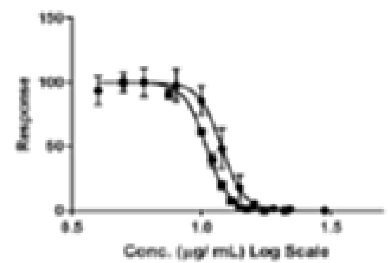
Article history:
Received 13 February 2018
Received in revised form
31 August 2018
Accepted 22 September 2018
Available online 24 September 2018

Keywords:
Fate modelling
Nanoparticle
Life cycle impact assessment
USEtox
Fraction of species in the environment
Characterisation factor

ABSTRACT

The aim of this paper is to present a new, integrative approach for calculating Fate nanomaterials by combining the USEtox2.0 modelling framework with SimpleBox4N advanced environmental fate model for nanomaterials, and to demonstrate its applicat assessment (LCA) by the estimation of characterisation factor (**CF**) for nano-TiO_2 for the of freshwater ecotoxcity. To enable the combination of the USEtox model with SB4N, tv aptations were made: (i) the compartments of air and rain were merged, and (ii) the aggregated, and attached species was accounted for in the receiving compartments. dynamic analysis was conducted to characterize the dynamic behaviour of nanoparticles the time at which steady state is actually reached. Our combined USEtox-SB4N app applied to calculate i) the Fate Factor (**FF**) for unitary emissions of nano-TiO_2 to air, fres sediment, and ii) using these, characterisation factors (CF) for nano-TiO_2 in the case category freshwater ecotoxicity. The **FF** for unitary emissions of nano-TiO_2 as free species Persistence was found to be highest for emissions to soil ($FF_{s,s} = 2.9 \cdot 10^5$ days), followed water ($FF_{w,w}$ = 128 days) and, then for an emissions to air ($FF_{a,a}$ = 3.3 days). The results

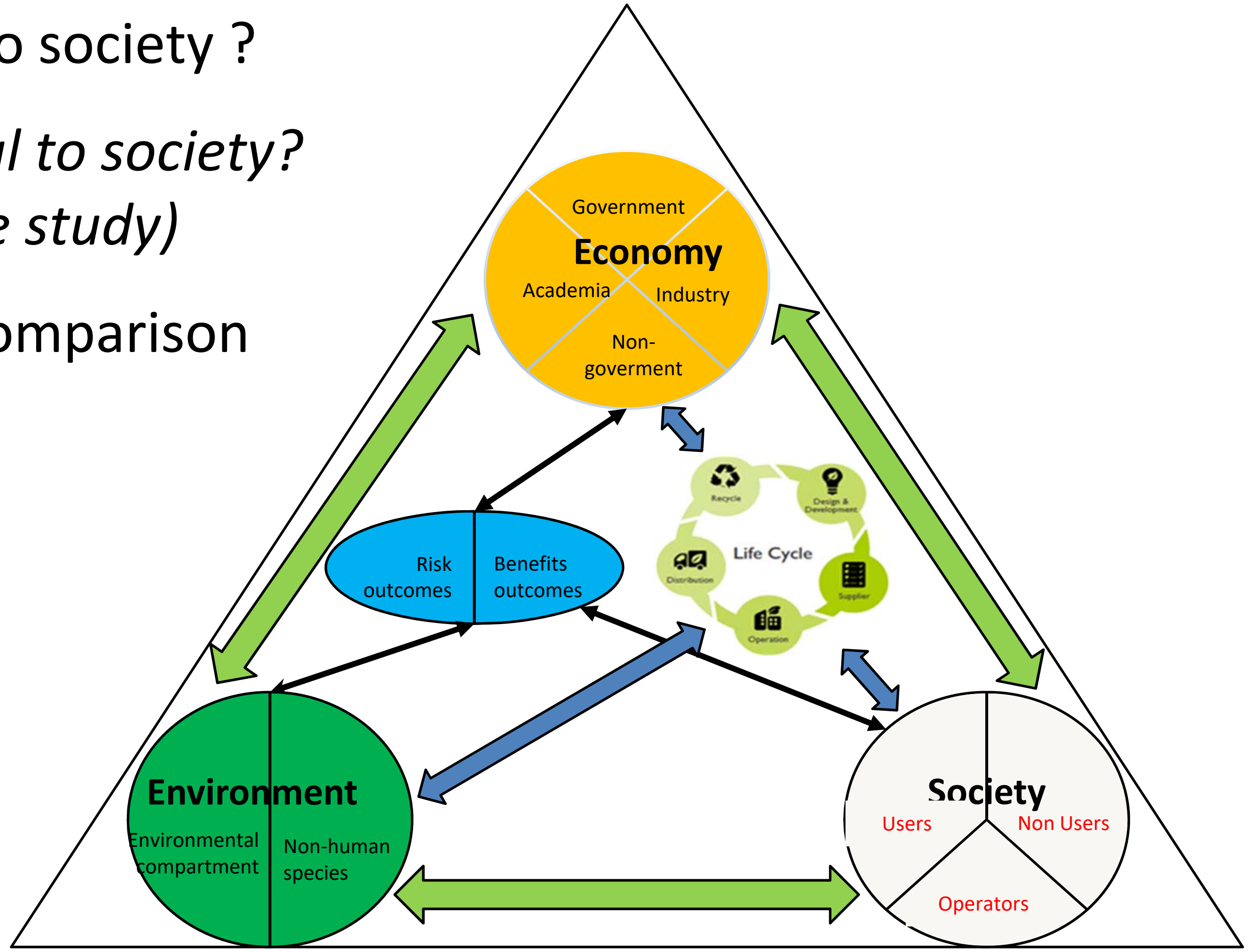
Use of **In-vitro toxicity data** for calculation of ED_{50} (in vivo) values via a **relative potency approach** ...



$$\frac{d_{reference}}{d_{test}} = \frac{D_{reference}}{D_{test}}$$

Safety and sustainability assessment. SEA

- Is SbD beneficial to society ?
- *Are NMs beneficial to society? (Nanomakers case study)*
- Methodological comparison of pros and cons



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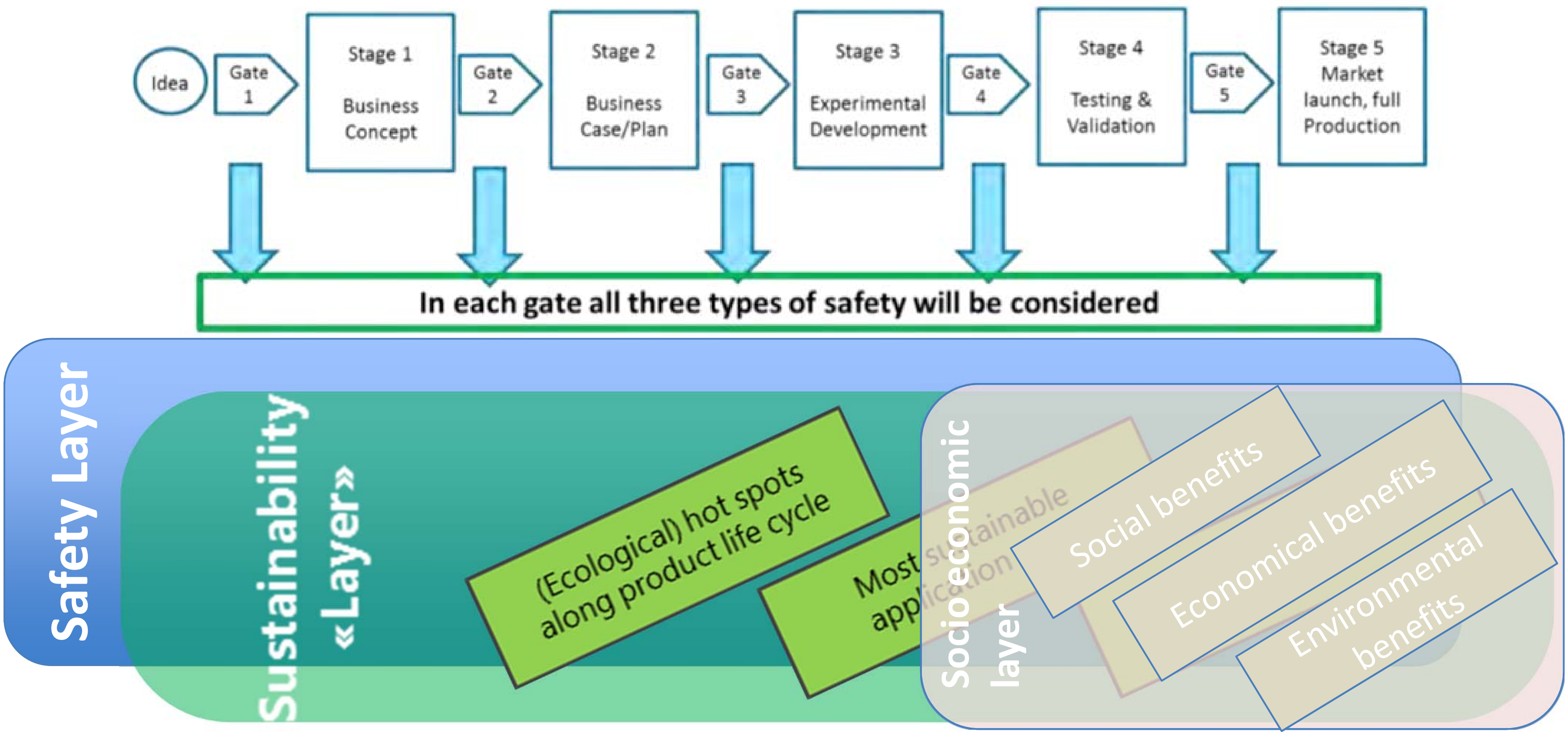
Data integration RA , LCA & SEA for SbD



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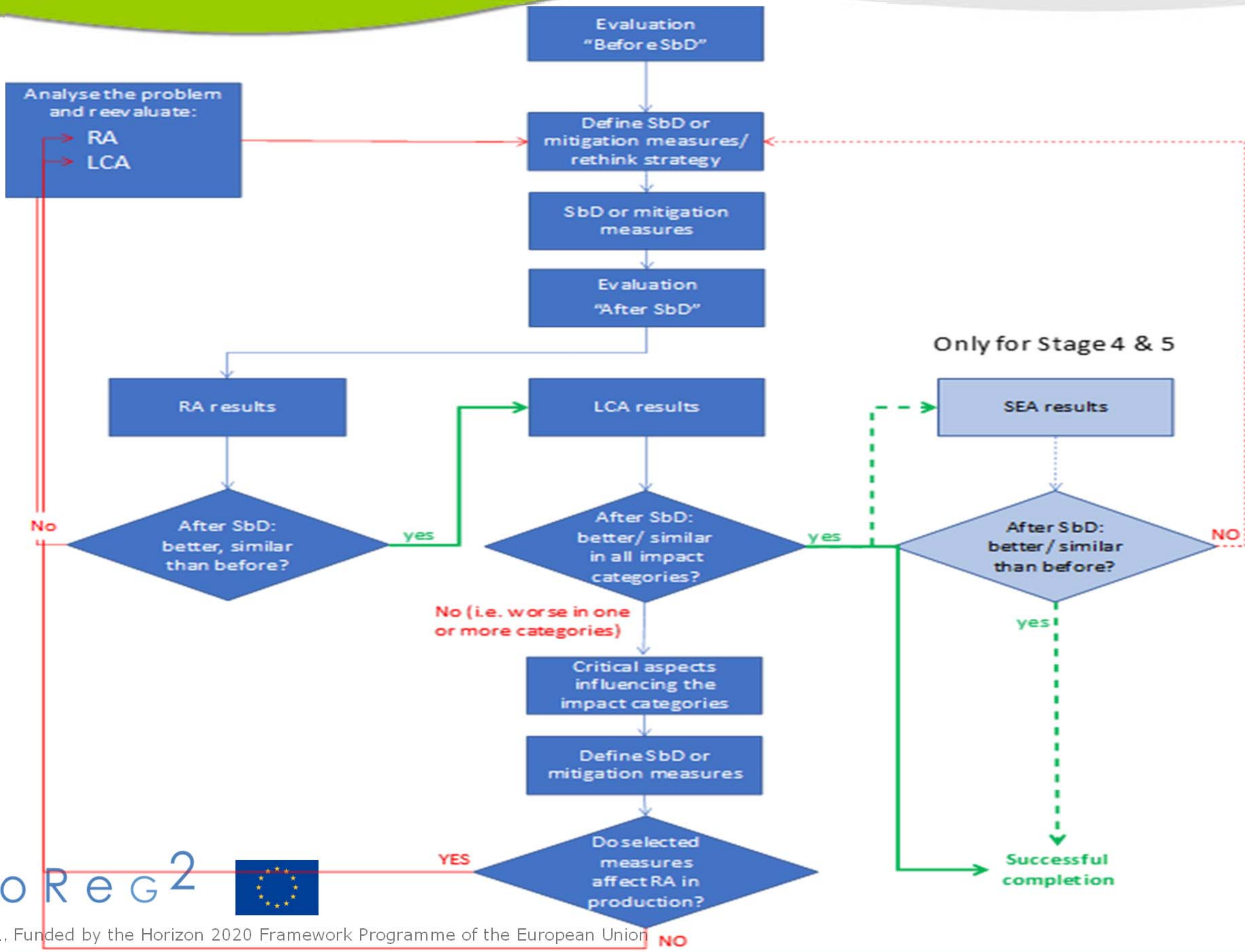
Data integration RA , LCA & SEA for SbD

	Stage 1 Buisness idea	Stage 2 Buisness Concept		Stage 3 Prototype (LabScale)		Stage 4 Pilot production (Upscaling)		Stage 5 Market entry
	GOAL AND SCOPE	GOAL AND SCOPE: Provide a screening assessment (RA &LCA)		GOAL AND SCOPE: Provide an RA and LCA at lab scale		GOAL and SCOPE: Provide an RA and LCA at lab scale-industrial setting		GOAL AND SCOPE: Legal compliance
General inormation	Provide the core business idea; Provide overview of the product : i) nanoparticle, ii) nanoapplication, iii) others; Provide info about futher application	ENM: YES/NO; Fiber based: YES/NO Nanoapplication: description	Data quality: qualitative	Description of the process -lab scale		Description of the process -industrial setting		
Detailed data	Provide a quantitative assessment of the potential impact and risk. The main legislative requirements are considered.	Characterization of the ENM: size, chemical composition; solubility (air, water); physical state (liquid, powder), toxcity & harzard (known/unknown)	Data quality: qualitative Data collection: Material Safety Data Sheet, Techncial Data Sheet, litterature	Characterization of the ENM: size, chemical composition; solubility (air, water); physical state (liquid, powder), toxcity & harzard; Exposure characterization (workers, consumer, environment)	Data quality: Quantitative data. Manufacturing/use/end of life characterization (i.e. energy , materials, emission), Toxcity &Harzard experimental data, case-specific data (EDC50, NOEC, LOEC, in vitro, litterature data); Characterization of the exposure :qualitative and quantitative	Characterization of the ENM: size, chemical composition; solubility (air, water); physical state (liquid, powder), toxcity & harzard; Exposure characterization (workers, consumer, environment)	Data quality: Quantitative data. Manufacturing/use/end of life characterization (i.e. energy , materials, emission), Toxcity &Harzard experimental data, case-specific data (EDC50, NOEC, LOEC, in vivo/vitro litterature data); Characterization of the exposure :quantitative	REACH, product-related regulations/requirements, Labelling requirements, … (regulatory compliance)
Tools	**NanoRiskCat, LICARA, SPM**			**Nanosafer, SPM, SUNDS, WoE; Revised use of LICARA; Lab -scale LCA &RA**		**(Nanosafer), SUNDS, WoE, real measurements, LCA&RA -industrial setting; revised use of LICARA**		
	SbD Implementation Plattform							
Overlapping data (LCA &RA)		Characterization of the ENM; characterization of the manufactuing process; toxcity characterization		Characterization of the ENM; characterization of the manufactuing process; toxicity &exposure value;collecting info from to provide a first assessemnt of CF		Characterization of the ENM; characterization of the manufactuing process; toxcity characterization		
OUTCOMES		Hazard risk; LCA : life cycle thiking introduction		LCIA characterization factor; Hazard risk; LCA and RA (simplified)		LCA and RA		

Decision tree RA , LCA & SEA for SbD



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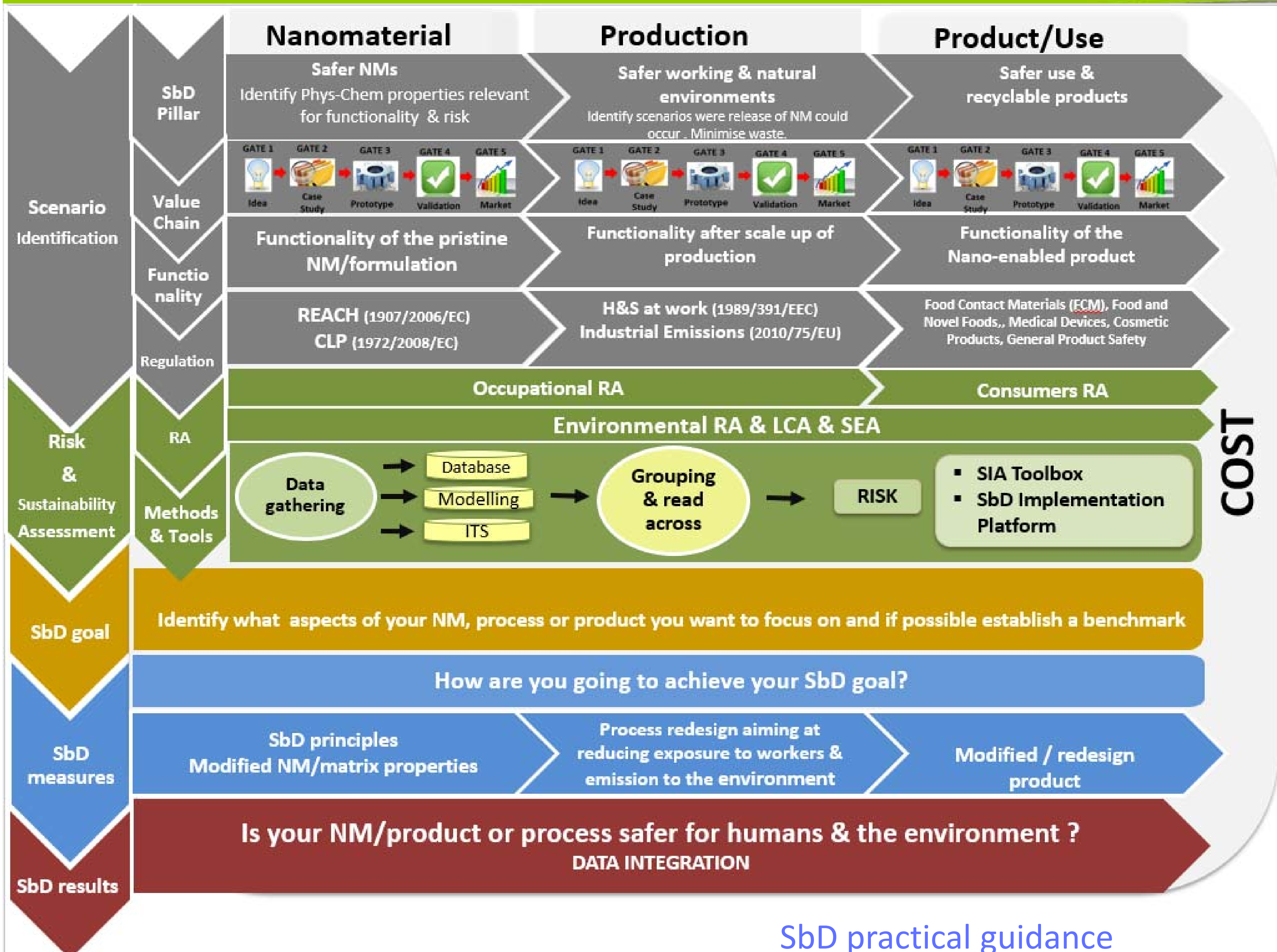

SbD practical guidance

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thank you

dankeschön

cám òn qúi vi rhât

谢谢

eskerrik asko

grazie

eskerrik asko

شكرا

go raibh maith agaibh

evgaristó

Shokrán

gracias

arigato

matu suksama

gracias

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moltes gràcies

merci

ありがとうございます

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thank you

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