DISCUSSION FORUM ON LIFE CYCLE ASSESSMENT

Decision-making concept on medical nanoparticles

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Zurich, May 24th

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Bundesministerium für Bildung und Forschung

Nano BEL

NanoBEL-Project

- **B**iological **El**imination of complex diagnostic **Nano**particles
- Focus on degradation and long-term effects of core-shell iron oxide nanoparticles

Project-Team

Industrial partners

chemicell

micromod Partikeltechnologie GmbH
modular designed particles

DYOMICS
Colours for Life

Hospitals

JG|U UNIVERSITÄTSmedizin. MAINZ

UNIVERSITÄTS KLINIKUM jena

Scientific partners

Fraunhofer IKTS

LEIBNIZ-INSTITUT für PHOTONISCHE TECHNOLOGIEN ipht jena

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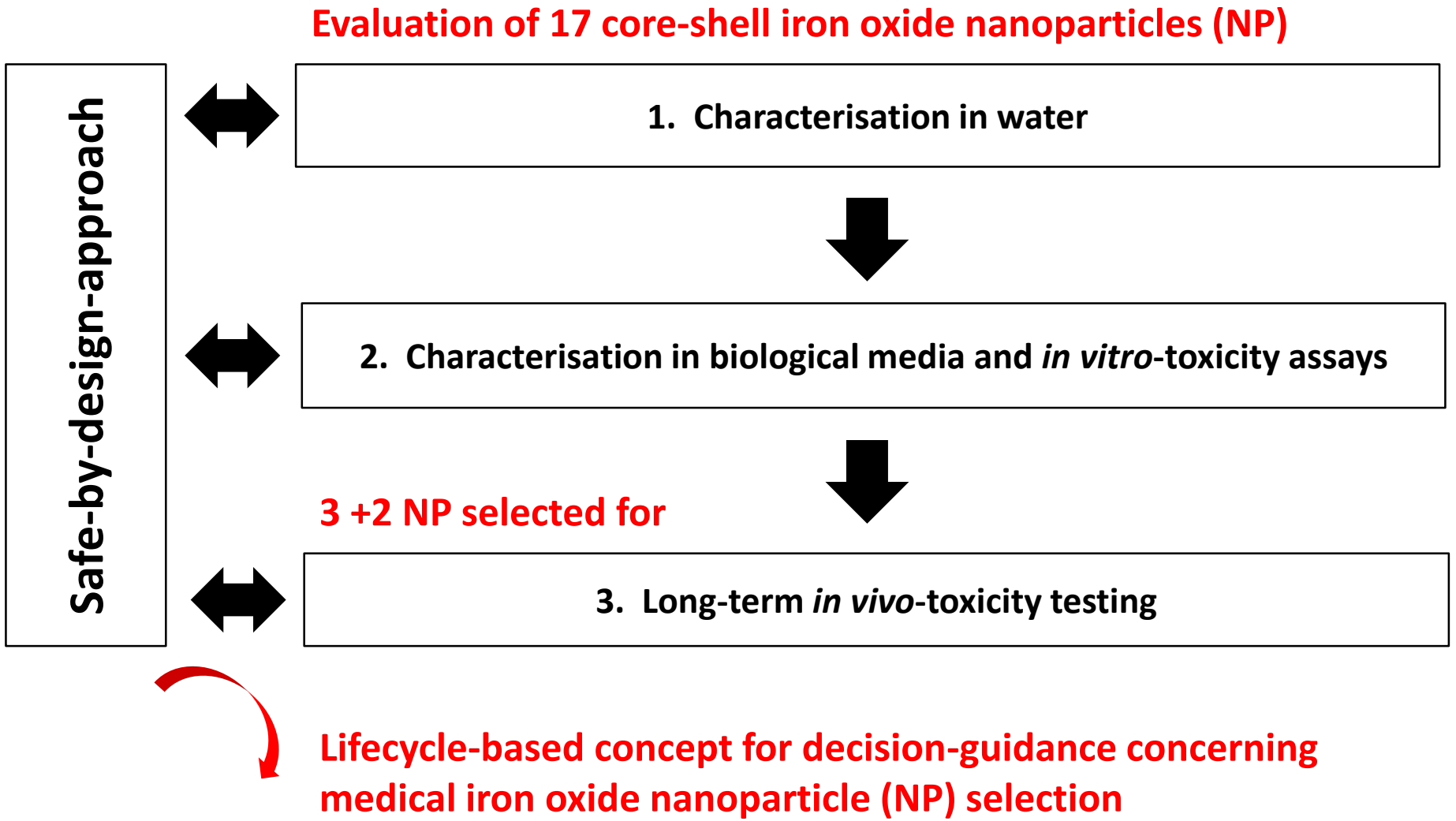
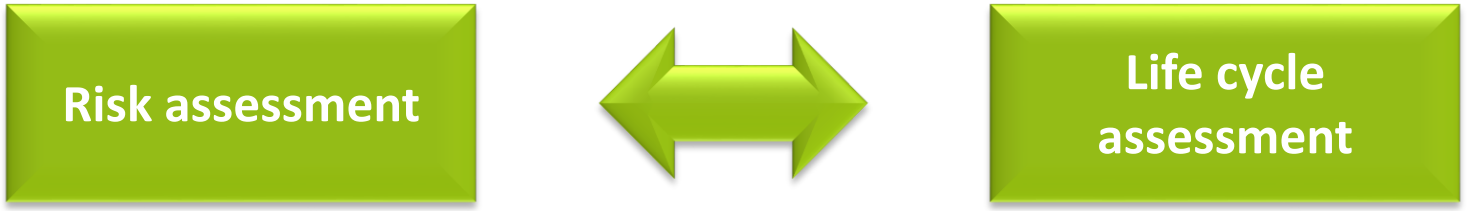
Safe-by-Design – Particle Selection



Combination of Risk Assessment (RA) & Life Cycle Assessment (LCA)



- Analyse effect of a single substance
- Characterise hazard effects of the substance
- Estimate potential emission along a product life cycle
- Perspective on risk for limited group of persons (e.g. employee)

- Identification of all relevant environmental emissions along products life cycle
- Quantification of emissions
- Estimation of potential environmental impact along product life cycle
- Perspective on risk for overall environment and human population

- **RA and LCA differ in perspective**
- **Combination is basis for safe-by-design approach in NanoBEL**

ENV/JM/MONO(2015)30

Risk Screening Approach

Safe by Design – Stage 1
Physicochemical characterisation
(nanopowder or suspension in water)

Criteria	Applied methods
Chemical constitution	RFA, EDX, ICP-OES
Particle size	FESEM, TEM
Crystal size	XRD
Crystal phase	XRD, Raman-spectroscopy
Specific surface area (only nanopowder)	BET
Magnetic properties	Vibrating sample magnetometer
Stability in water over 6 month	PCS, MRI, Raman-, IR- spectroscopy

Safe by Design – Stage 2
Biological-toxicological characterisation

Criteria	Applied methods
Stability in biological media (e.g. simulated body fluid)	PCS, MRI
Degradability in Simulated body fluid	BPS- assay, MRI, IR- spectroscopy
in vitro- cytotoxicity in 3 human cell lines	PrestoBlue®- assay
Effects in blood	ex- ovo- hens egg model, hemolysis, aggregation of erythrocytes

Nanoparticle selection

***in vivo*-study (6 month)**
long-term effects in mouse-model

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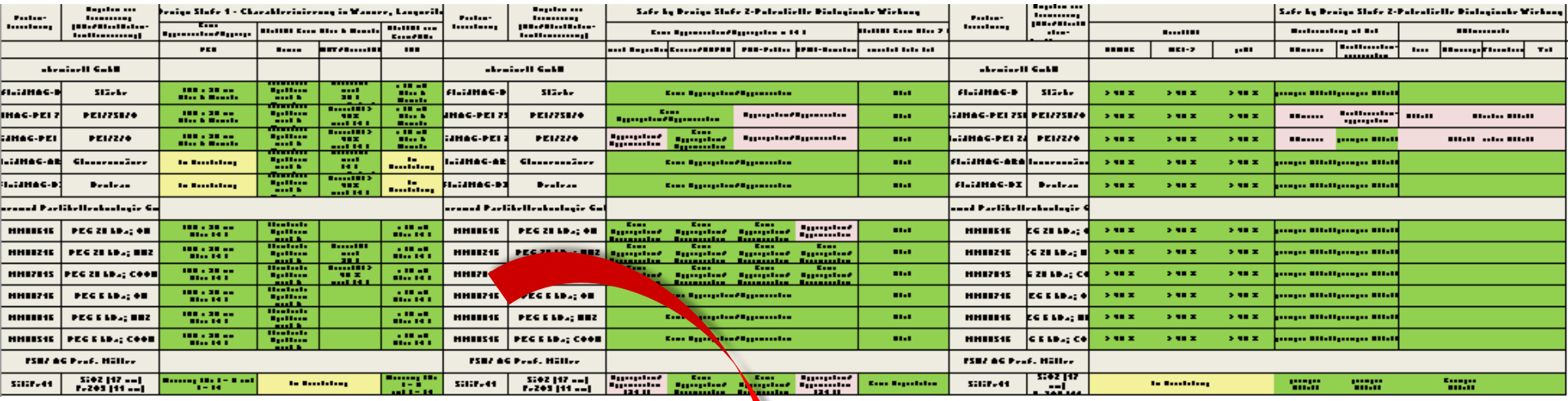
Risk-Screening



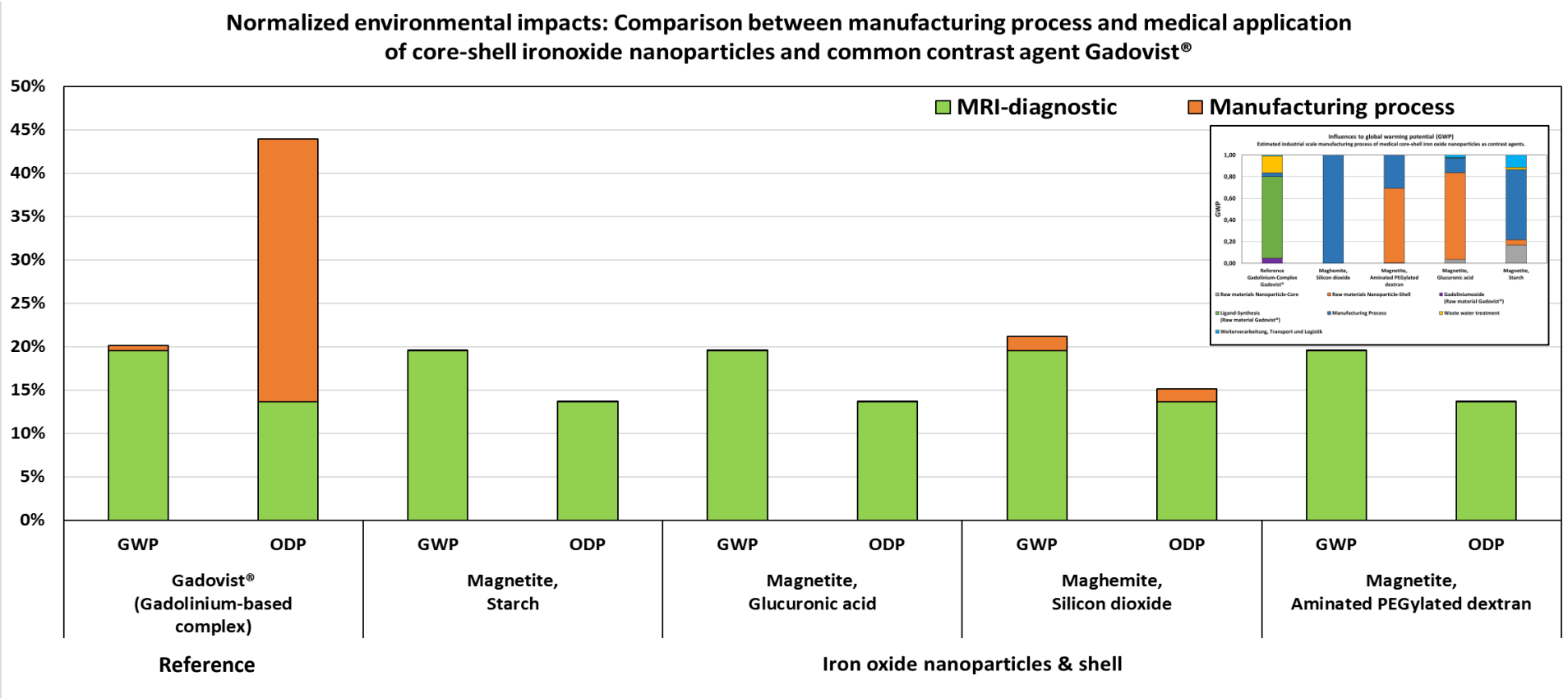
Results from physicochemical characterisation

Results from biological and toxicological characterisation

- All NP formulations investigated are applicable for medical applications
- Selection based on different degradation behaviour in physiological media
- Holistic assessment / LCA of selected nanoparticles (Part of Safe by Design Step 3)

Life Cycle Assessment

- LCIA-Method: CML2001, functional unit = 1 dosis contrast agent for MRI-diagnostic



- **Comparative LCA – production of NP vs. common chemical contrast agent (reference)**
- **Environmental impacts significantly differentiate between manufacturing processes, but energy consumption in MRI-diagnostic dominates LCA results (exception: ODP of reference)**

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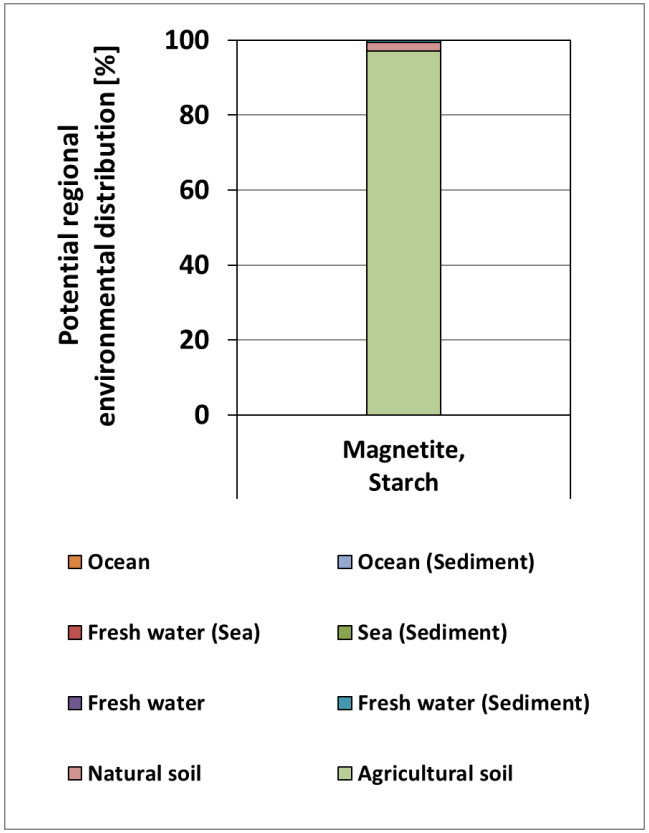
Limitations of LCA

- **Currently no characterisation factor for direct NP emissions**
- **Experimental characterisation of NP-stability in environmental media**
- **Estimation of environmental distribution → Simple Box 4.0 nano**
  (Meesters et al., Environ. Sci. Technol. 2014, 48, 5726−5736)



- Characterisation of nanospecific parameters, e.g.:

  → Homo- and hetero aggregation
  → Particle size
  → Particle degradation and solubility

- Implementation in LCIA would be a step forward in development of nanospecific characterisation factors

Summary

- **German NanoBEL project focus on long-term effects of medical iron oxide nanoparticles**
- **Development of an integrated Safe by Design-approach for the selection of medical nanoparticles**
  → Combination of risk assessment and LCA
- **LCA is appliciable for nanoproducts, but limitations exist in consideration of direct nanoparticle emissions within impact assessment**

Thank you for your attention!