MACRAMÉ

Advanced Characterisation Methodologies to assess and predict the Health and Environmental Risks of Advanced Materials

Regulatory Research for Safety & Sustainability in the EU – Advancements of international Harmonisation & Standardisation Approaches and NAMs

SOT – 64th Annual Meeting and ToxExpo
16. – 20. March 2025, Orlando (USA)

The MACRAMÉ project has received funding from the European Union's Horizon Europe Research and Innovation programme under grant agreement No. 101092686.

Associated Partners (i.e. (a) Swiss Partners and (b) UK Partners) have received national funding from (a) the Swiss State Secretariat for Education, Research and Innovation (SERI), and (b) Innovate UK.

Overview of the Presentation – The Projects

- MACRAMÉ – Advanced Characterisation Methodologies to assess and predict the Health and Environmental Risks of Advanced Materials,
- CHIASMA - Accessible Innovative Methods for the Safety & Sustainability Assessment of Chemicals & Materials,
- INSIGHT - Integrated Models for the Development and Assessment of High Impact Chemicals and Materials
- PINK - Provision of Integrated Computational Approaches for Addressing New Market Goals for the Introduction of Safe-and-Sustainable-by-Design Chemicals and Materials

Overview of the Presentation – The Projects

- Initial provision of proofs-of-concept for advanced characterisation, life-cycle (impact) assessments (LC(I)As), test methods (i.e. Organisation for Economic Cooperation and Development Test Guidelines and Guidance Documents) and standards of advanced materials,
- Development of New Approach Methodologies (NAMs),
- Integration of mechanistic impact assessment frameworks and computational safe and sustainable by design (SSbD) models and workflows, and
- Deployment of an advanced interoperability framework that enables both the design and modelling of a new material's or chemical's functionality and safety, based on tiered *in-silico* approaches that combine existing and novel data.

The MACRAMÉ R&I Approach:
… handing Outcomes to policy-informing Bodies

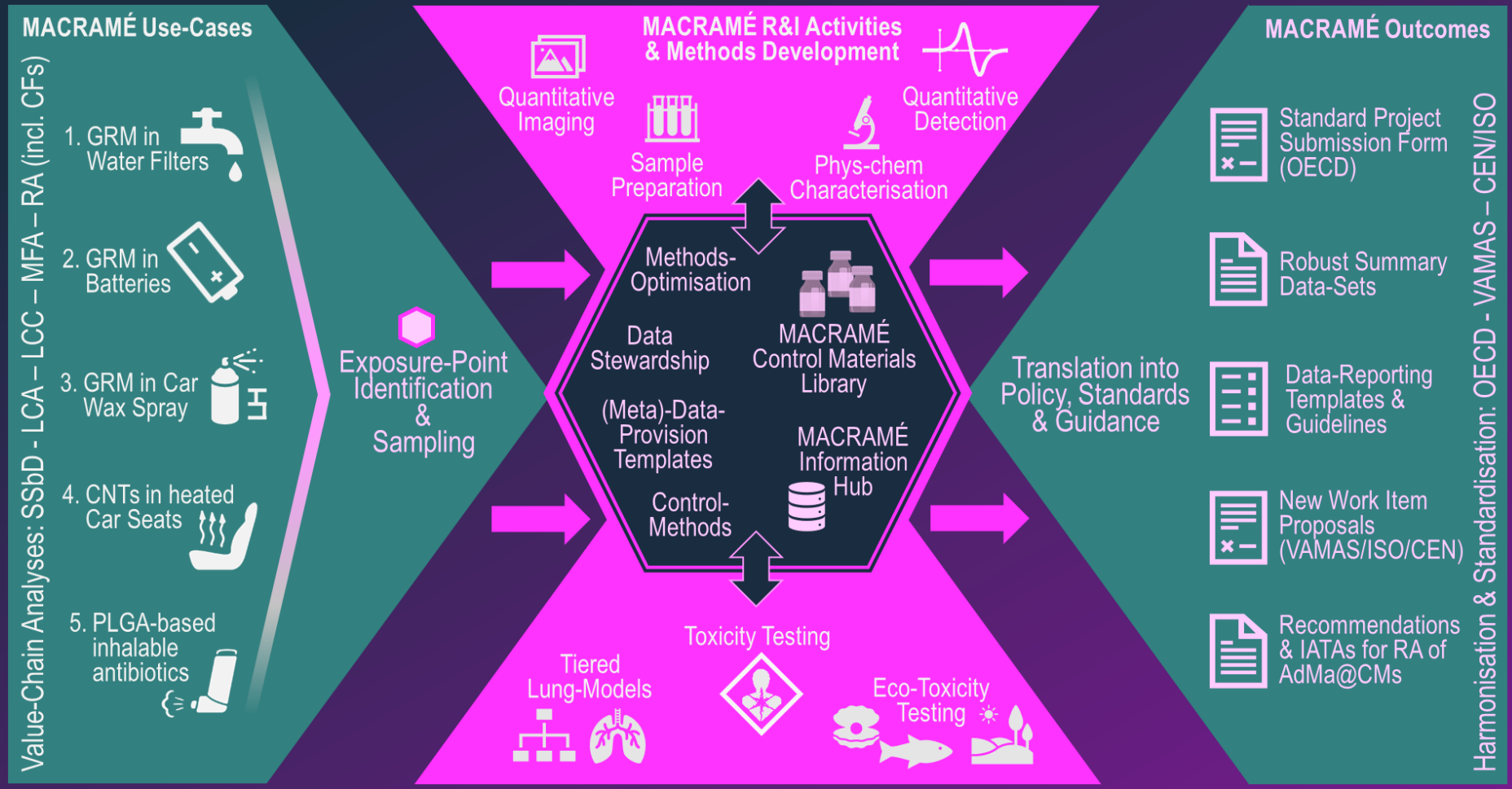


Illustration of the MACRAMÉ R&I Approach (AdMa@CMs: Advanced Materials in complex matrices; CF: Characterisation Factor; GRM: graphene-related material; IATA: integrated approaches to testing and assessment; LCA: Life-Cycle Assessment; LCC: Life-Cycle-Costing; MFA: Material-Flow Analysis; RA: Risk-Assessment; SSbD: Safe-&-Sustainable-by-Design).

The Context of the MACRAMÉ R&I Strategy

Harmonisation & Standardisation of (Nano)Materials – A brief History

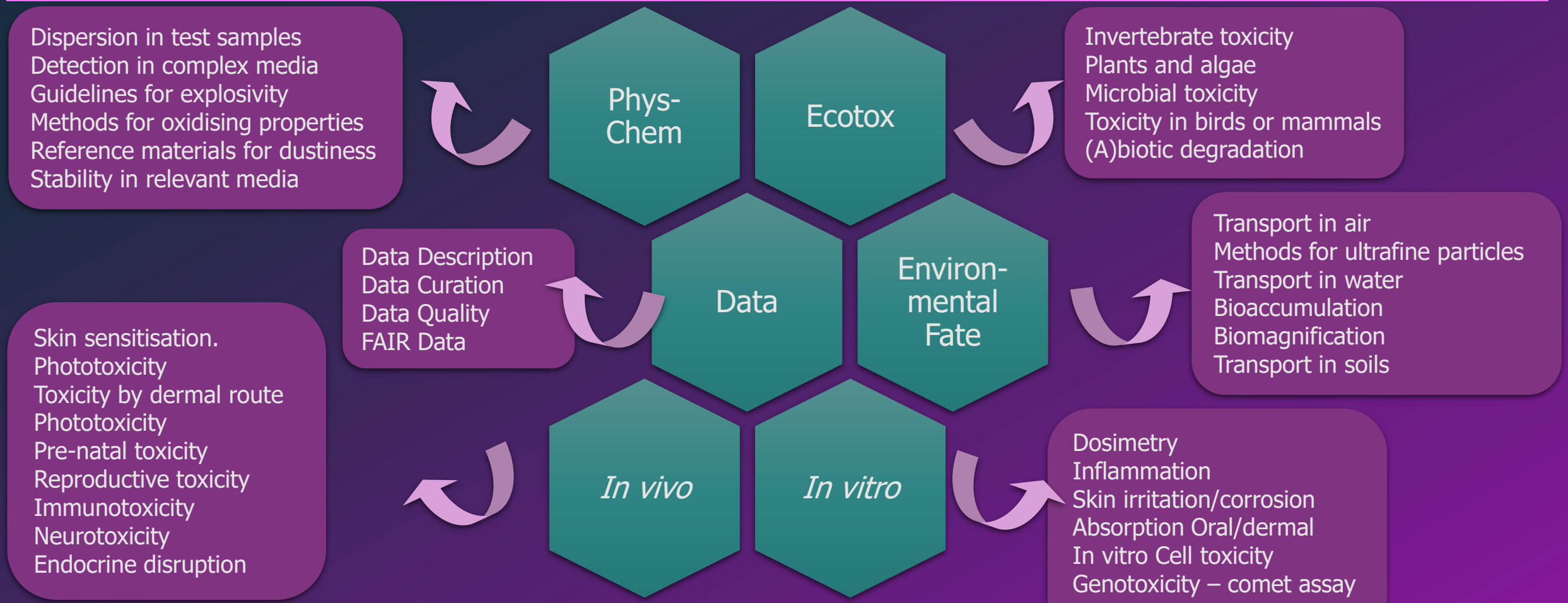
Harmonisation & Standardisation of Nanomaterials

ISO	Terminology Achieved 18 On-going 7	Measurement Achieved 8 On-going 6	Characterisation Graphene Achieved 13 On-going 8	Characterisation (Other) Achieved 27 On-going 2	Exposure and Risk Achieved 23 On-going 11	Performance Evaluation Achieved 3 Ongoing 3
CEN	Terminology Achieved 7 On-going 5	Measurement Achieved 5 On-going -	Characterisation (Other) Achieved 1 On-going 3	Exposure and Risk Achieved 19 On-going 11	Other Achieved 4	
OECD	Physico-chemical Characterisation Achieved 5 On-going 5	Human Toxicology Achieved 5 On-going 5	Environmetal Toxicology Achieved 1 On-going 4	Environmental Fate Achieved 1 On-going 3	End of Life Achieved 1 Ongoing 1	

215 Standards! → *But we still have gaps*

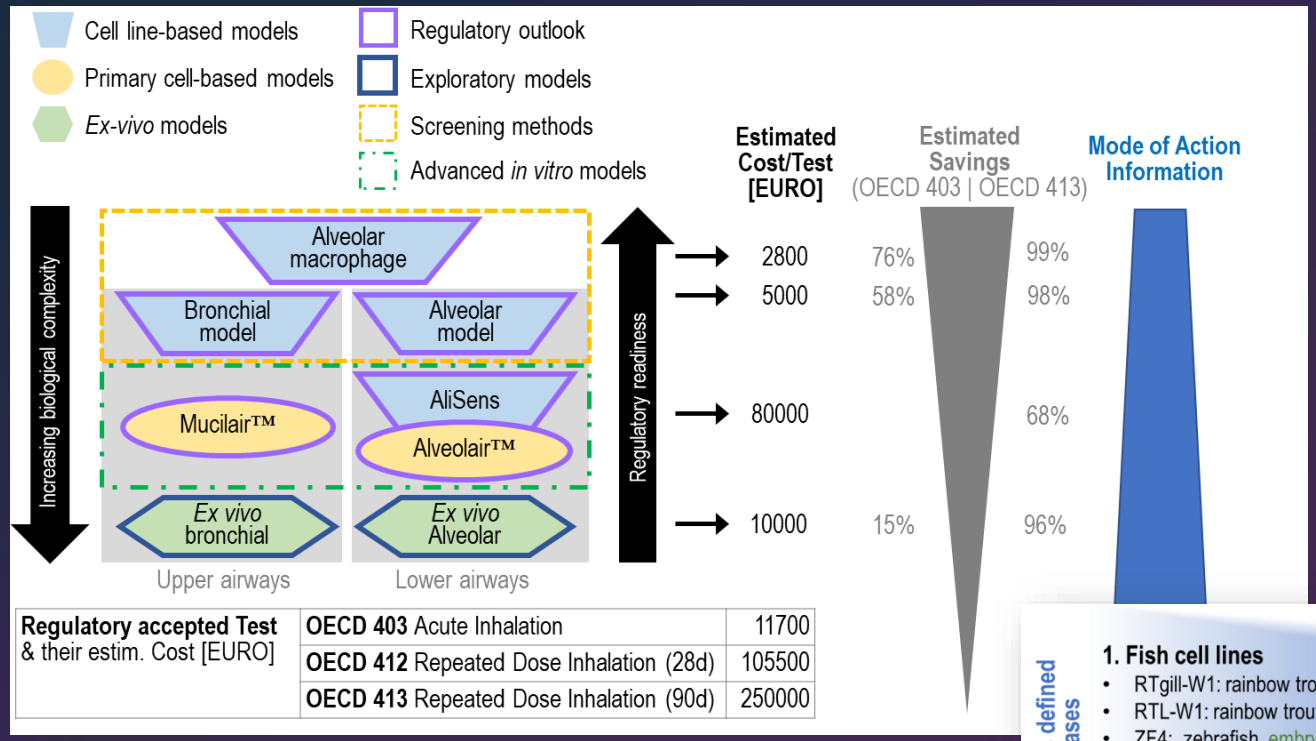
[snapshot as of September 2023; courtesy: MACRAMÉ Partner TEMAS Solutions]

(Nano)Materials Standardisation Gaps (September 2023)



[snapshot as of September 2023; courtesy: MACRAMÉ Partner TEMAS Solutions]

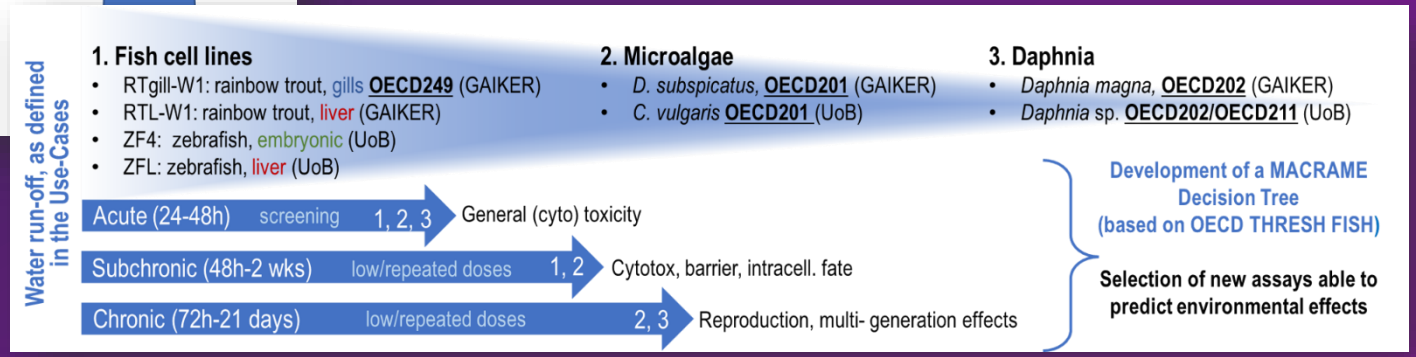
Regulatory relevant R&I in MACRAMÉ: Characterisation & Testing of AdMas in complex Matrices



Regulatory accepted Test & their estim. Cost [EURO]		
	OECD 403 Acute Inhalation	11700
	OECD 412 Repeated Dose Inhalation (28d)	105500
	OECD 413 Repeated Dose Inhalation (90d)	250000

In vitro and *ex vivo* Models that will be assessed within the Project, indicating the estimated cost that can be saved and MoA-Information that can be obtained at the different tiers.

Contact: Tommaso Serchi (LIST)



Schematic illustration of the MACRAMÉ ecotoxicity testing approach and outcomes.

Contact: Iseult Lynch (Uni Birmingham) & Alberto Katsumiti (GAIKER)

MACRAMÉ's three Sibling Projects

HORIZON-CL4-2023-RESILIENCE-01-**21**: Innovative methods for safety and sustainability assessments of chemicals and materials (RIA)

+

HORIZON-CL4-2023-RESILIENCE-01-**22**: Integrated approach for impact assessment of safe and sustainable chemicals and materials (RIA)

+

HORIZON-CL4-2023-RESILIENCE-01-**23**: Computational models for the development of safe and sustainable by design chemicals and materials (RIA)

>>> decreasing experimental (lab) work >>>

>>> increasing *in silico* work >>>

Sharing of Case-Studies of specific Chemicals & Materials

Integration of shared computational Methods

total budget: € 23.2 Mio. (ca. ¾ from EU, ¼ non-EU) ♦ 37 individual Research Institutions; ♦ Jan. 2024 – Dec. 2027

Accessible Innovative Methods for the Safety & Sustainability Assessment of Chemicals & Materials

The CHIASMA Project has received funding from:

The European Union's Horizon Europe Research and Innovation programme under grant agreement No. 101137613.

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Economic Affairs, Education and Research EAER
State Secretariat for Education, Research and Innovation SERI

National Research Foundation of Korea

UK Research and Innovation

The CHIASMA R&I Approach

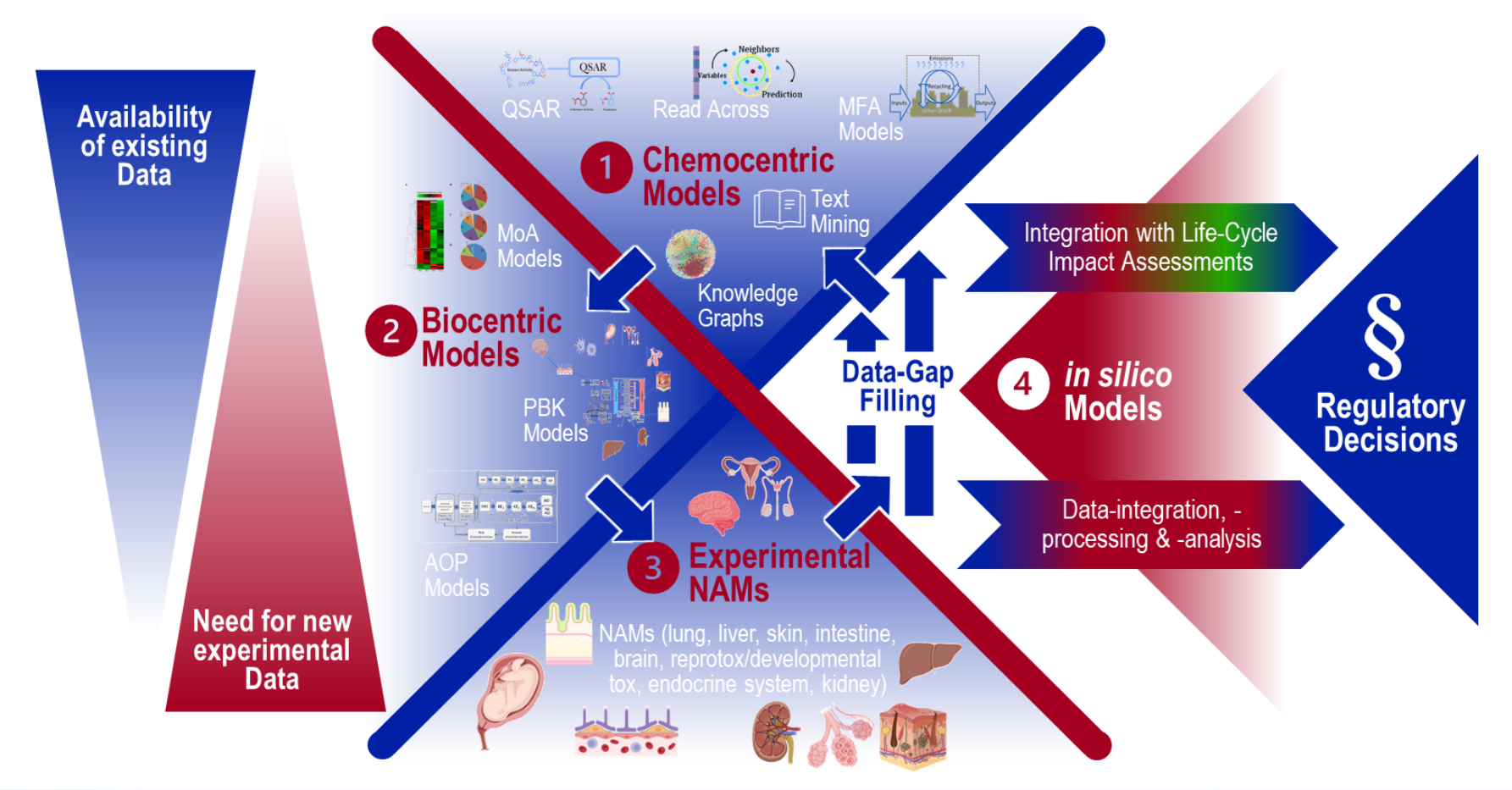


Illustration of the CHIASMA R&I approach to testing and assessment of materials.

Combining an iterative approach of:

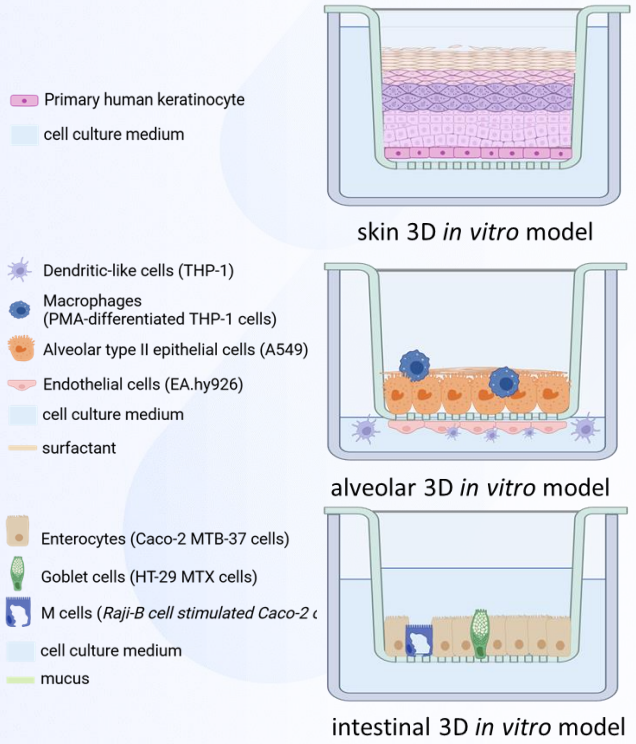
(1) chemocentric,

(2) biocentric, and

(3) new experimental models

into a conceptual framework for data-integration and -processing.

In vitro experimental NAMs



External Barrier

EMPA: RHE models

LIST: alveolar model

EMPA: small intestine model

Internal Barrier

AIT: Blood-Brain Barrier spheroid

EMPA: placental barrier model

Liver and Kidney

SU: liver spheroids

VU: proximal tubule cell and iPSC-derived models

Repro-/ Developmental Toxicity

UniTOV: placenta-embryo model

NMBU: gonadal model of fish sperm

Neuro-Toxicity/ (Neuro-) Endocrine System

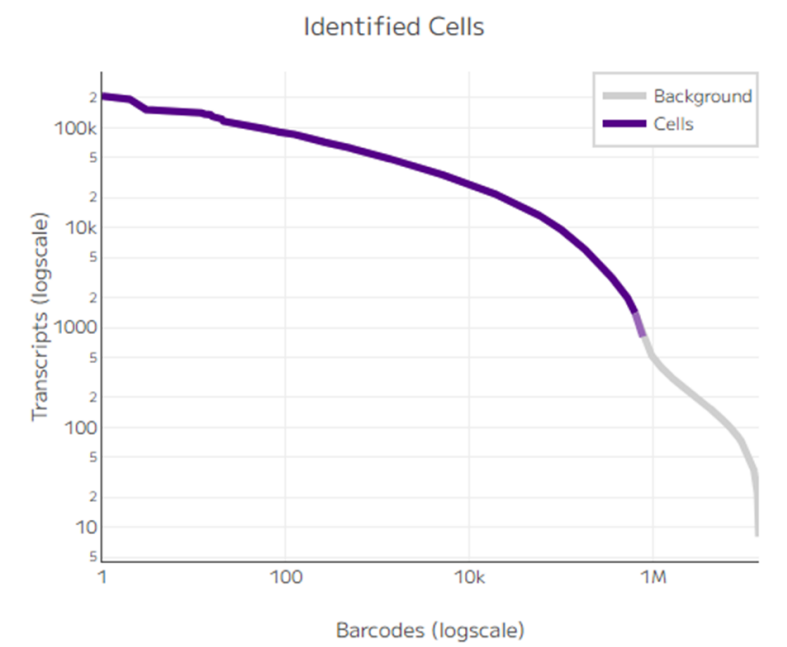
IUF: BrainSpheres DNT *in vitro* battery

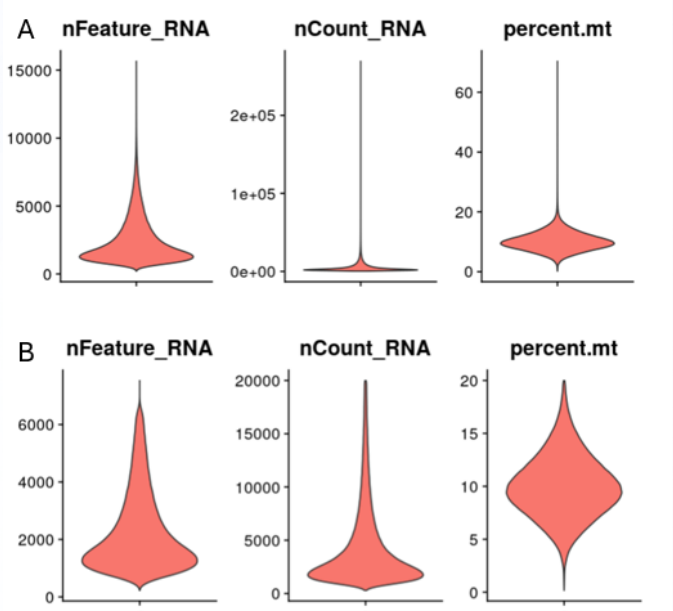
NMBU: neuro-endocrine *ex vivo* culture complexes

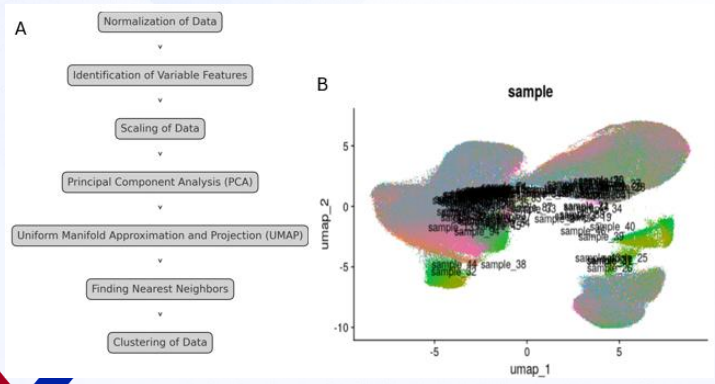
NAMs development workflow in CHIASMA

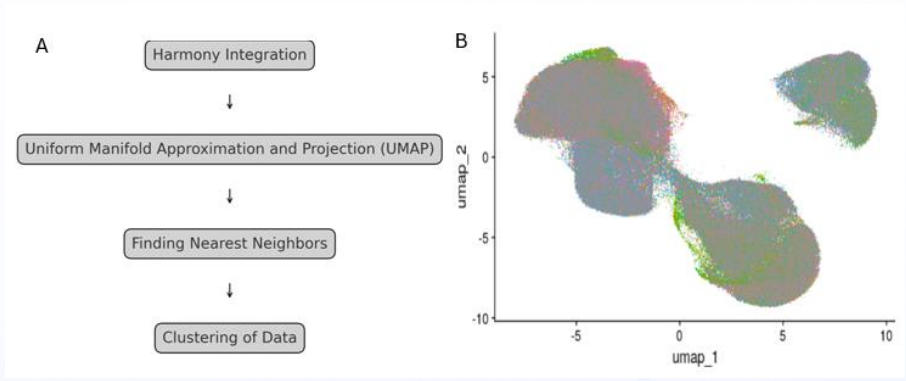
Laboratory progression of the NAMs → Benchmarking & verification of the NAMs using known reference chemicals → Inter-laboratory and transferability *in-project* validation → Applicability domain study on the 3 chemical/materials groups → Integration into the CHIASMA-framework

Bulk *vs* single cell transcriptomics and reproducibility of NAMs-derived OMICS data









Chemicals (PFAS and resp. sens)

Advanced materials / resp. sens.

PFAS

Integrated Models for the Development and Assessment of High Impact Chemicals and Materials

The INSIGHT Project has received funding from:

The European Union's Horizon Europe Research and Innovation programme under grant agreement No. 101137742.

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Economic Affairs, Education and Research EAER
State Secretariat for Education, Research and Innovation SERI

National Research Foundation of Korea
Funding Agency
Australia

UK Research and Innovation
Funding Agency
USA

FAPESP
FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE SÃO PAULO

INSIGHT's R&I Approach

1. Life Cycle thinking approach, identification of relevant data and models
2. Development of the model graph
3. Development of the data graph
4. FAIRification of models / research software & Data
5. Definition of integrated mechanistic models of impact
6. Development of the Decision Support System & INSIGHT framework GUI

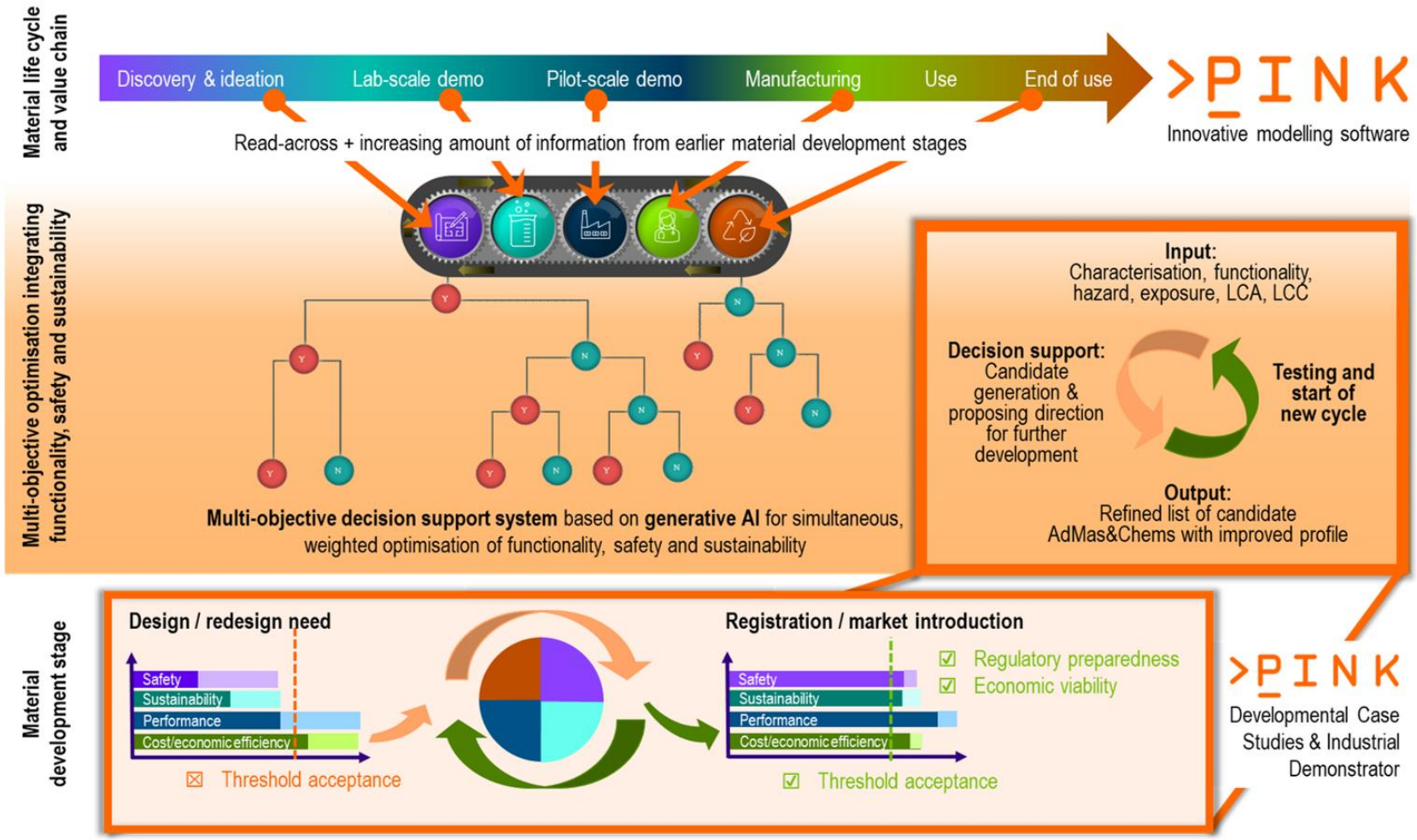
PROVISION OF INTEGRATED COMPUTATIONAL APPROACHES FOR ADDRESSING NEW MARKET GOALS FOR THE INTRODUCTION OF SAFE-AND-SUSTAINABLE-BY-DESIGN CHEMICALS AND MATERIALS

THE PINK PROJECT HAS RECEIVED FUNDING FROM THE EUROPEAN UNION'S HORIZON EUROPE RESEARCH AND INNOVATION PROGRAMME UNDER GRANT AGREEMENT NO. 101137809.

ASSOCIATED PARTNERS (I.E. (A) SWISS PARTNERS AND (B) UK PARTNERS) HAVE RECEIVED NATIONAL FUNDING FROM (A) THE SWISS STATE SECRETARIAT FOR EDUCATION, RESEARCH AND INNOVATION (SERI), AND (B) INNOVATE UK.

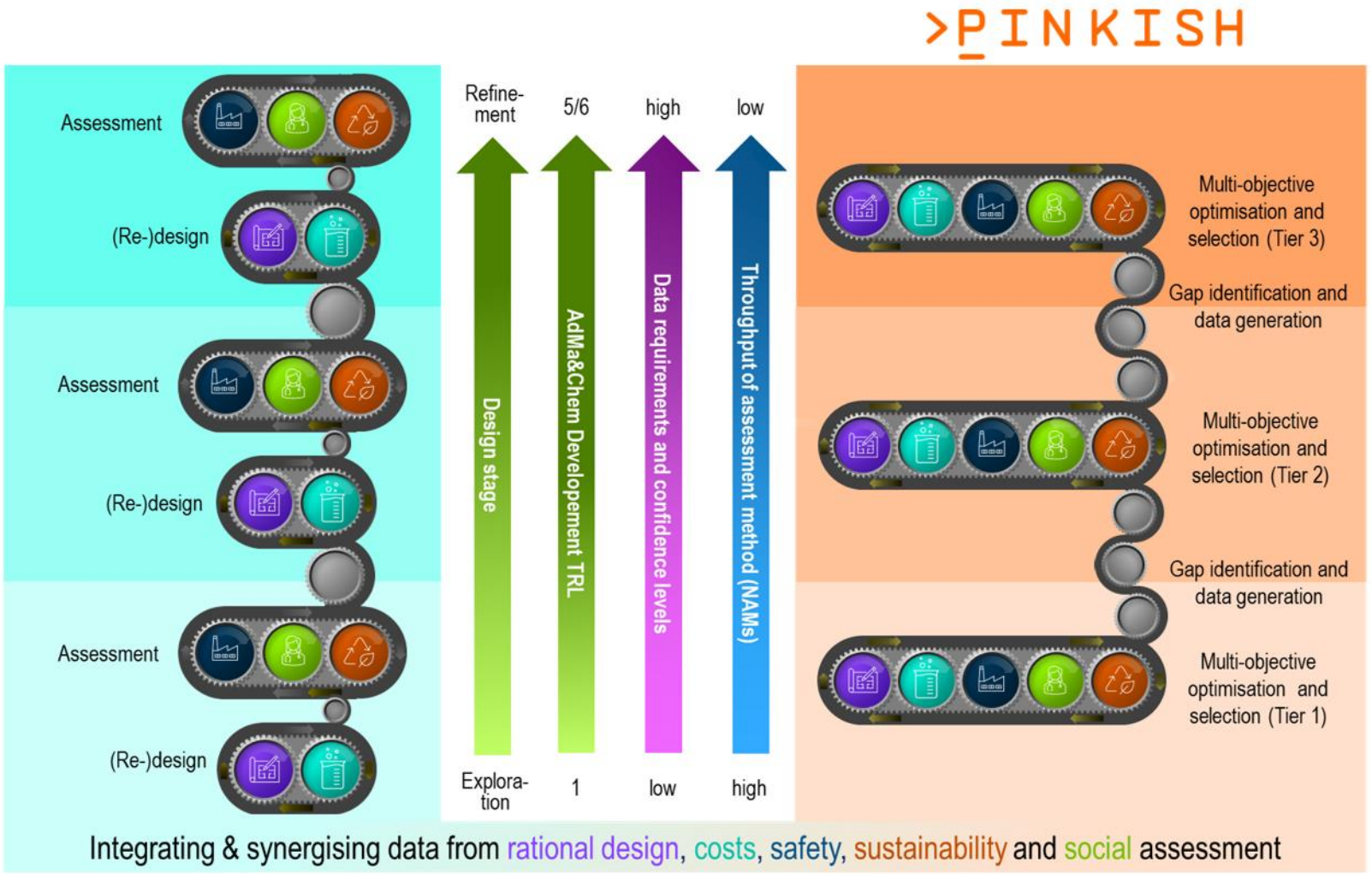
The PINK R&I Approach

… integrating the SSbD Framework into the development cycle of AdMas&Chems

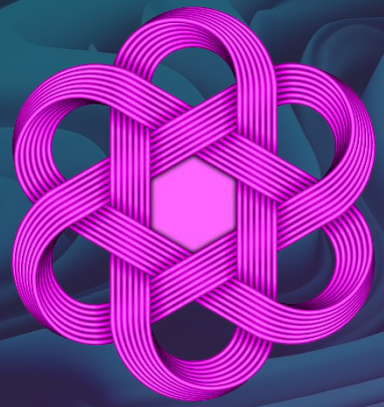


The PINK tiered Approach

… PINK Tiered Approach (i.e. **PINK *In Silico* Hub (PINKISH)**), (right) compared to the hierarchical approach described in the **EU SSbD Framework** (left).



Steffi Friedrichs
AcumenIST SRL
Steffi@AcumenIST.com



Thank you

www.macrame-project.eu

The MACRAMÉ Project has received funding from:

The European Union's Horizon Europe Research and Innovation programme under grant agreement No. 101092686.

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Economic Affairs, Education and Research EAER
State Secretariat for Education, Research and Innovation SERI

UKRI Innovate UK

Setting References:
The MACRAMÉ Control Materials Library

Launch of the MACRAMÉ Control Material Library

July 1, 2023

To support development, harmonisation, and benchmarking of testing methods applied within the HorizonEurope-funded Project, a MACRAMÉ Control Material Library (CML) has been established. The Library contains representative materials with largely known properties impacting the in vitro test development and of materials to be investigated in the MACRAMÉ Use Cases (UCs).

Read More »

Exemplary Excerpt: Table 2: Materials of the CML selected for the development and validation of controlled aerosol generation (Task 2.2).

	Name	Supplier	Link to Product	Criteria for the selection	Interesting Features	Also used in other projects
Nanotubes						
MWCNT test material	ARIGM001	BAuA Repository		Serves as default testing material for method development, available in large quantities	High dustiness, medium degree of entanglement, mean diameter ~35 nm, mean length ~1-2µm	CarboLifeCycle,
Graphitised MWCNT	NM401	OECD Repository		Positive control for fibre paradigm (rigid), test with µ-Dishes	Rigid and long fibres, easy to disperse, >20% WHO fraction	NanoGRAVUR, InnoMat.Life, HARMLESS, NanoHarmony
MWCNT	Baytubes C150P	BAuA Repository		Negative control for fibre paradigm (NM400 not a real one), test with µ-Dishes		older BAuA projects
Aligned flexible MWCNT	NG01AM0102	nanografi	Link	Thin commerical CNTs marketed as beeing produced in such way that they are aligned and bundled, test with µ-Dishes	Bundles are very long up to 95 µm.	not yet
MWCNT 30-50 nm	NG01MW0501	nanografi	Link	Presumed to be a mixture of more flexible and less rigid MWCNTs (proportions), test with µ-Dishes		not yet

→ https://macrame-project.eu/launch-of-the-macrame-control-material-library/

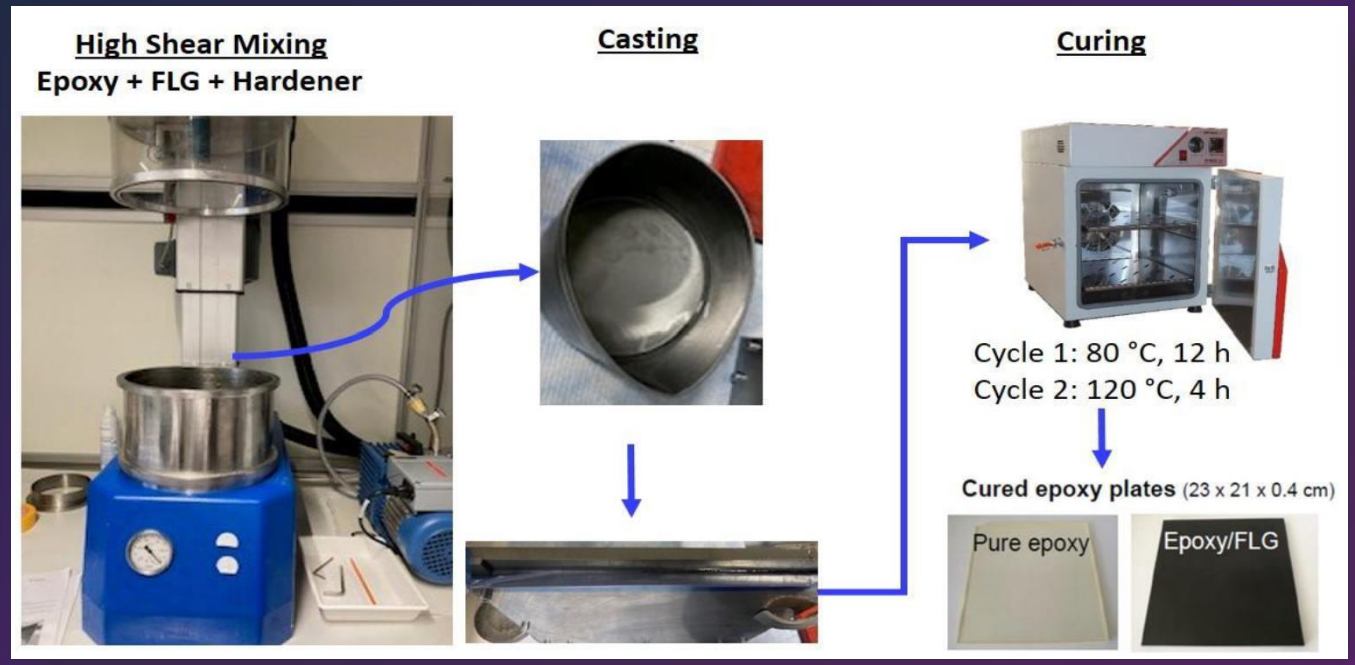
Developing SOPs:
The MACRAMÉ Sampling Approaches & Protocols

Sampling & Sample-Provision Protocols for AdMas in complex Matrices

March 1, 2024

The MACRAMÉ Project has published its first set of 'Sampling & Sample-Provision Protocols for AdMas in complex Matrices', in order to guide the sample collection that needs to be performed at the MACRAMÉ Use-Case (UCs) sites prior to sending the samples to MACRAMÉ laboratories for testing. Such sample collection is

Read More »



Exemplary Excerpt (Use-Case 2: BMS): Figure 3: Fabrication of Epoxy-FLG composite plates. Epoxy alone or epoxy-FLG composite are mixed with hardener (Baxxodur EC 301), moulded and then cured in the oven at indicated temperature cycles. The plates obtained after curing were used for abrasion.

Exemplary Excerpt (Use-Case 5: PGLA): Figure 12: PCL-samples.

→ https://macrame-project.eu/sampling-sample-provision-protocols-for-admas-in-complex-matrices/

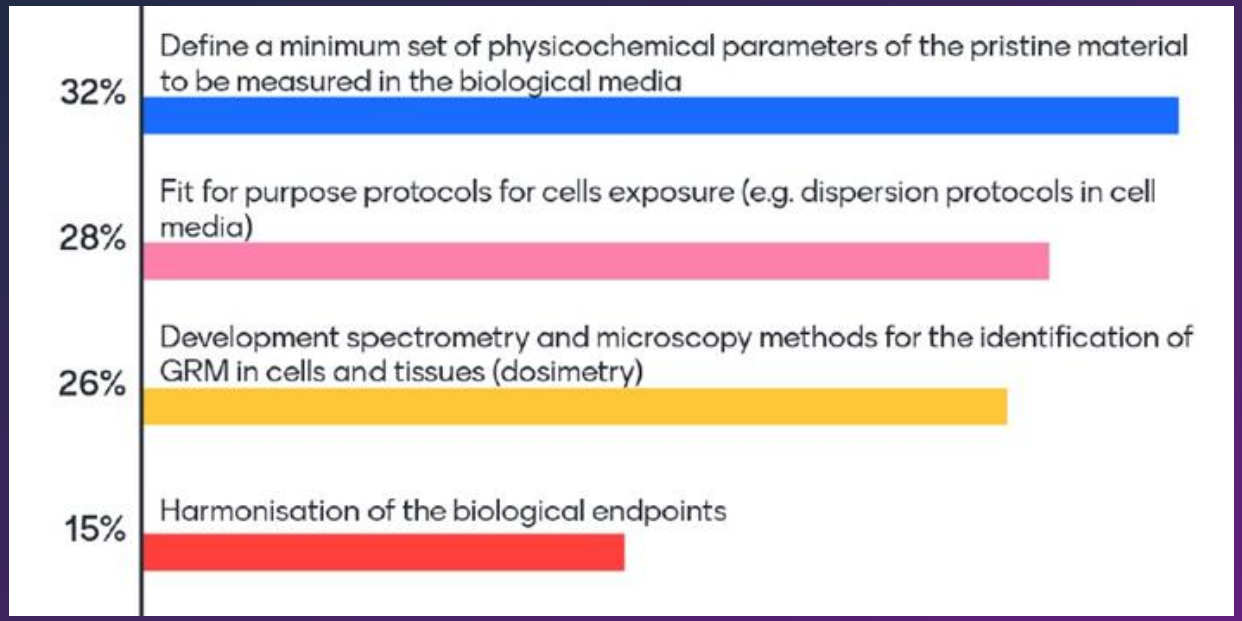
Recommending Pathways towards Impact: The MACRAMÉ Harmonisation & Standardisation Roadmap

MACRAMÉ Harmonisation & Standardisation Roadmap – a Summary Report of five important Destinations

June 3, 2024

The MACRAMÉ Project just published an important milestone report: the 'MACRAMÉ Harmonisation & Standardisation Roadmap Summary Report for MACRAMÉ Methods and Models'-report combines and summarises the Project's activities in the field of 'Development and Advancement of Characterisation- & Test-Methods &-Protocols' (Project work package 2) with the activities pertaining to the

Read More »



Exemplary Excerpt: Figure 4: Bar chart representation of the workshop participants' opinions regarding the identified priorities for robust toxicological and ecotoxicological assessment. Participants have been requested to rank the proposed options between 1 and 5. The average of 42 answers is reported.

→ https://macrame-project.eu/out-now-macrame-harmonisation-standardisation-roadmap/

Recommending Pathways towards Impact: The MACRAMÉ Harmonisation & Standardisation Roadmap

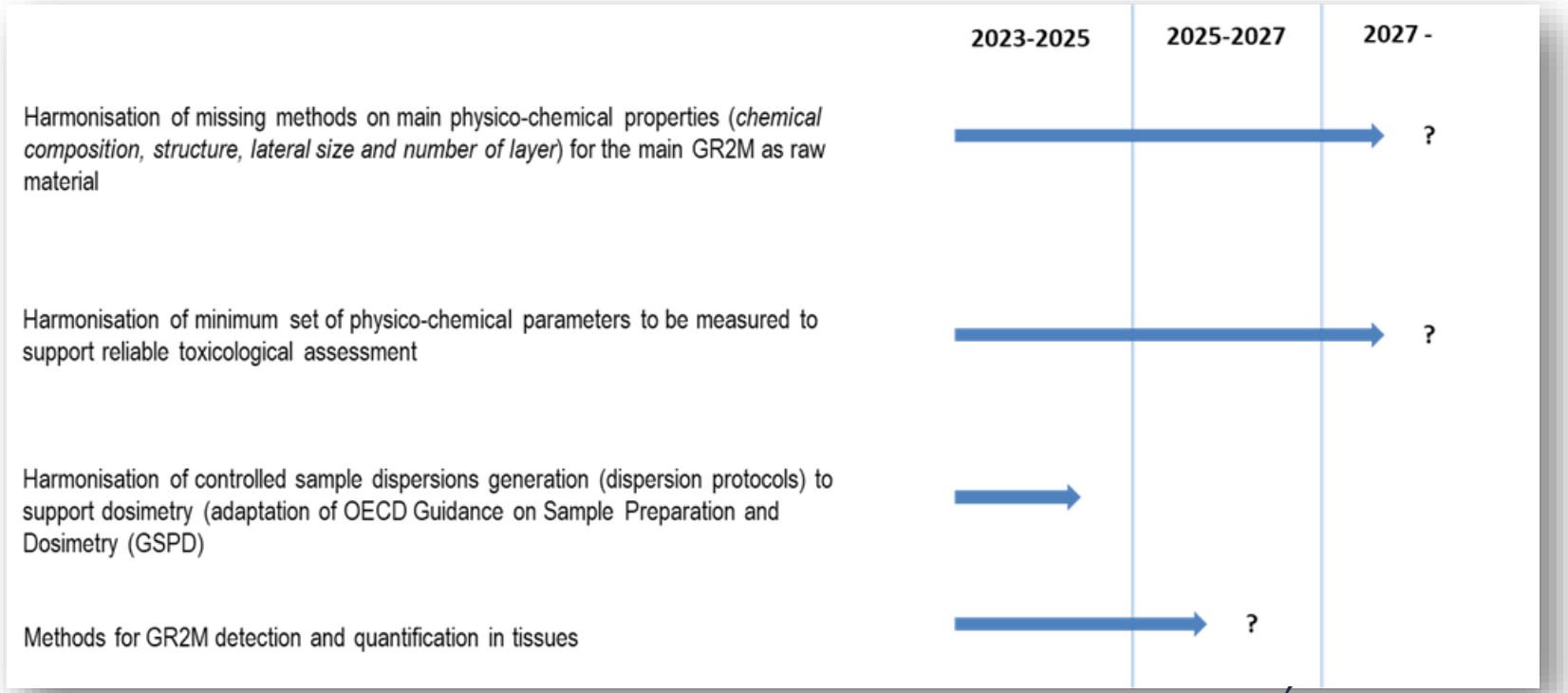
MACRAMÉ Harmonisation & Standardisation Roadmap – a Summary Report of five important Destinations

June 3, 2024

The MACRAMÉ Project just published an important milestone report: the 'MACRAMÉ Harmonisation & Standardisation Roadmap Summary Report for MACRAMÉ Methods and Models'-report combines and summarises the Project's activities in the field of 'Development and Advancement of Characterisation- & Test-Methods &-Protocols' (Project work package 2) with the activities pertaining to the

Read More »

… main results: A project is not an island



Exemplary Excerpt: Figure 5: Tentative overview of gaps identified in MACRAMÉ and tentative timeline to move them towards standardisation during and beyond the MACRAMÉ Project.

→ https://macrame-project.eu/out-now-macrame-harmonisation-standardisation-roadmap/