Ensuring regulatory Alignment in the R&I of Innovative Materials

Steffi Friedrichs[1], MACRAMÉ Consortium[2]

1. Introduction

The MACRAMÉ Project 'Advanced Characterisation Methodologies to assess and predict the Health and Environmental Risks of Advanced Materials' is fully aligned with the EU ambitions to secure the safety and sustainability of new chemicals, materials, products and processes in order to strive for zero pollution and toxic-free environments, as addressed in the EU's Chemical Strategy for Sustainability (2020), and in the European Green Deal (2019 & 2021); in doing so, the Project concentrates on methodologies that are applicable to nanomaterials, and widens them to '**Advanced Materials**' (AdMas) – a material category that includes but surpasses that of 'nanomaterials' (EU, 'Definition of a Nanomaterial') - in commercialised products and that are aligned with the future-oriented innovation, safety and sustainability considerations of the OECD (OECD (2020)), the EU (EU (2022)), and several of its Member States (e.g. Germany (2021)). This will be achieved through development and demonstration of novel methodologies, and by advancing their harmonisation & standardisation on **three MACRAMÉ Material Families** of **inhalable carbon-based AdMas** of various morphologies and dimensions (Tiwari *et al.* (2012)), beyond spherical particles: **(a) graphene-related material** (GRM), **(b) carbon nanofibres** (CNFs), e.g. carbon nanotubes (CNTs), and **(c) Poly Lactic-co-Glycolic Acid (nano)particles** (PLGA). The focus on carbon-based AdMas addresses unsolved detection and characterisation issues, especially in complex media. In doing so, MACRAMÉ builds on >15 years of research and innovation (R&I) and knowledge pooling in nanosafety, formed through numerous European and international collaborations. MACRAMÉ will add value to the results of collaborations, such as the Malta-Initiative, and the Graphene Flagship Validation Service and Standardisation Committee, to proactively support EU industries in becoming world-leaders in clean technologies and products and achieving the Green Deal's ambitious timeline.

2. Startegic R&I to support Harmonisation, Standardisation & Safe and Sustainable by Design

The **MACRAMÉ R&I Approach** (Figure 1) aims to widen the development of harmonised test guidelines (TGs) and guidance documents (GDs) (OECD) and standards (CEN, ISO) to **market-relevant AdMas in their complex product matrices**. This will be achieved by defining the R&I Strategy through life-cycle assessment for **five market-relevant industrial MACRAMÉ Use-Cases.** These **define the selection** of the **MACRAMÉ R&I Activities** and development of **MACRAMÉ Methods**, and the benchmarks chosen for monitoring the progress R&I. MACRAMÉ R&I Activities include a range of novel sample preparation techniques and ambitious quantitative detection and imaging

[1] AcumenIST SRL, Rue Fétis 19, 1040 Etterbeek, Belgium; email: Steffi@AcumenIST.com.
[2] cf.: https://macrame-project.eu/the-macrame-consortium/

methodologies that support reliable and reproducible determination of AdMas in different complex matrices (**AdMa@CMs**) and using **inhalation as their main exposure route**. By applying, combining and evaluating both established and novel inhalation toxicity tests a tiered approach to toxicity testing will be developed that will provide data on state-of-the-art characterised control materials for the **MACRAMÉ Control Material Library**. The library will serve future AdMa toxicological research. The ultimate **MACRAMÉ Outcomes** are proposals for harmonisation and (pre-)standardisation projects to be provided to and further elaborated with the relevant bodies, (i.e. OECD, VAMAS/CEN/ISO). The proposals will be founded on **robust summary datasets**, **scientific documents** and **recommendations for hazard- and risk-assessment methodologies for AdMas in complex product matrices** (AdMa@CMs). All data and information, obtained from external sources and generated during the Project, will be handled and stored in the **MACRAMÉ Information Hub** - the Project's central information processor, whose interoperability is based on a **Data Stewardship** concept, designed according to IndustryCommons principles.

The resulting efficiency and effectiveness of MACRAMÉ Methods will be demonstrated through their application in Use-Case evaluations, using LCA-, LCC- and 'Safe & Sustainable by Design' (SSbD)-based (EWARN (2022)), highlighting benefits like reduced costs of regulatory compliance, by following a **MACRAMÉ Safety & Sustainability Matrix**. This matrix will be a modular building block for MACRAMÉ's information-transferring interfaces for different scientific and regulatory communities, and thus provide a stepping-stone for Europe's route towards a ***'one substance – one assessment'*** approach (European Green Deal (2019)) and promote an open strategic autonomy (ETUI (2021)) through key enabling and emerging technologies, including digital ones.

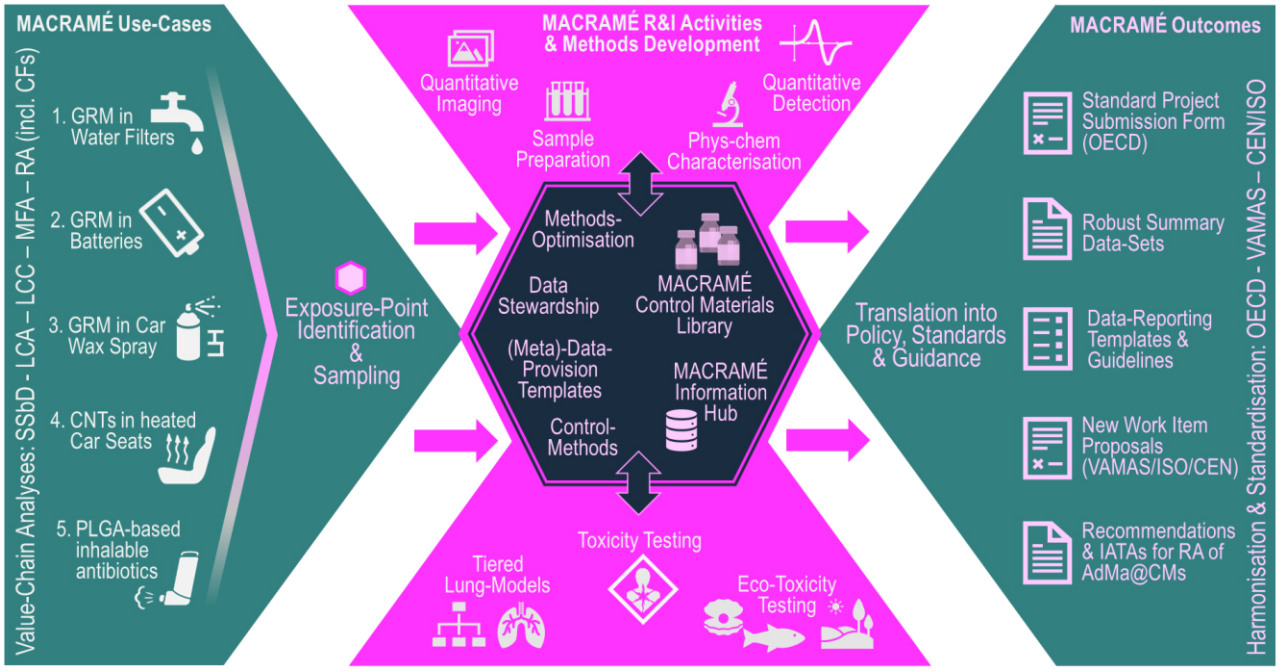

Figure 1: Illustration of the MACRAMÉ R&I Approach (AdMa@CMs: Advanced Materials in complex matrices; CF: Characterisation Factor; GRM: graphene-related material; IATA: integrated approaches to testing and assessment; LCA: Life-Cycle Assessment; LCC: Life-Cycle-Costing; MFA: Material-Flow Analysis; RA: Risk-Assessment; SSbD: Safe-&-Sustainable-by-Design).

3. Ensuring regulatory Relevance in the MACRAMÉ Project

To ensure the maximum impact and engagement with industrial actors, policy-informing and –making, as well as standardising bodies, two enhance the chances of acceptance and advancement of the developed methods toward standardisation and harmonisation.

The 1st MACRAMÉ Regulatory Risk Assessors Summit, held on the 27th – 28th November 2023 (as an in-person event), aimed to establish the concept of conducting environmental, health and safety assessments of AdMas along the entire life cycle of a product. In doing so, the Summit borrows from and applies elements from both **risk-** and **life cycle assessment** disciplines and introduces the concept of sustainability and its implementation in the **Safe and Sustainable by Design framework**, to elaborate needs, challenges and approaches for regulatory risk assessors. The first day of the Summit laid the foundation by providing insights into the policy frameworks of the European Green Deal, the SSbD framework, and LCA. Short talks and a panel discussion by scientists, regulators, large industry and SMEs, and consumers focussed on how the different stakeholder groups perceive and approach sustainability in challenges they face in risk assessment and how LCA-based approaches may help in addressing these challenges. The second day featured three breakout sessions led by experts for (a) occupational safety, (b) consumer safety, and (c) environmental safety, respectively, in order to further elaborate on needs and challenges. The outcomes of the breakout discussions form the basis for recommendations on future needs for AdMas in risk assessment within a Life Cycle context, including standards and test guidelines; they furthermore provide additional guidance to the mid-term review and (re-)confirmation of the Project's R&I Strategy.

4. Acknowledgements

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.