

Prioritization of New Approach Methodologies towards stage-gate application

Diverse HRA tools are openly or commercially available for evaluating safety aspects of MNMs, yet it is clear that their application to that purpose often couples with notable degrees of uncertainty.

Current risk assessment practice for new industrial agents, such as manufactured nanomaterials (MNMs), including consideration of both exposure and hazard assessment, can be substantially aided by so called “New approach methodologies” (NAMs).

The term ‘NAM’, as applied by the European Chemicals Agency (ECHA), represents “a broad context to include *in silico*, *in chemico*, and *in vitro* methodologies, plus inclusion of information from the chemical exposure in the context of risk assessment.

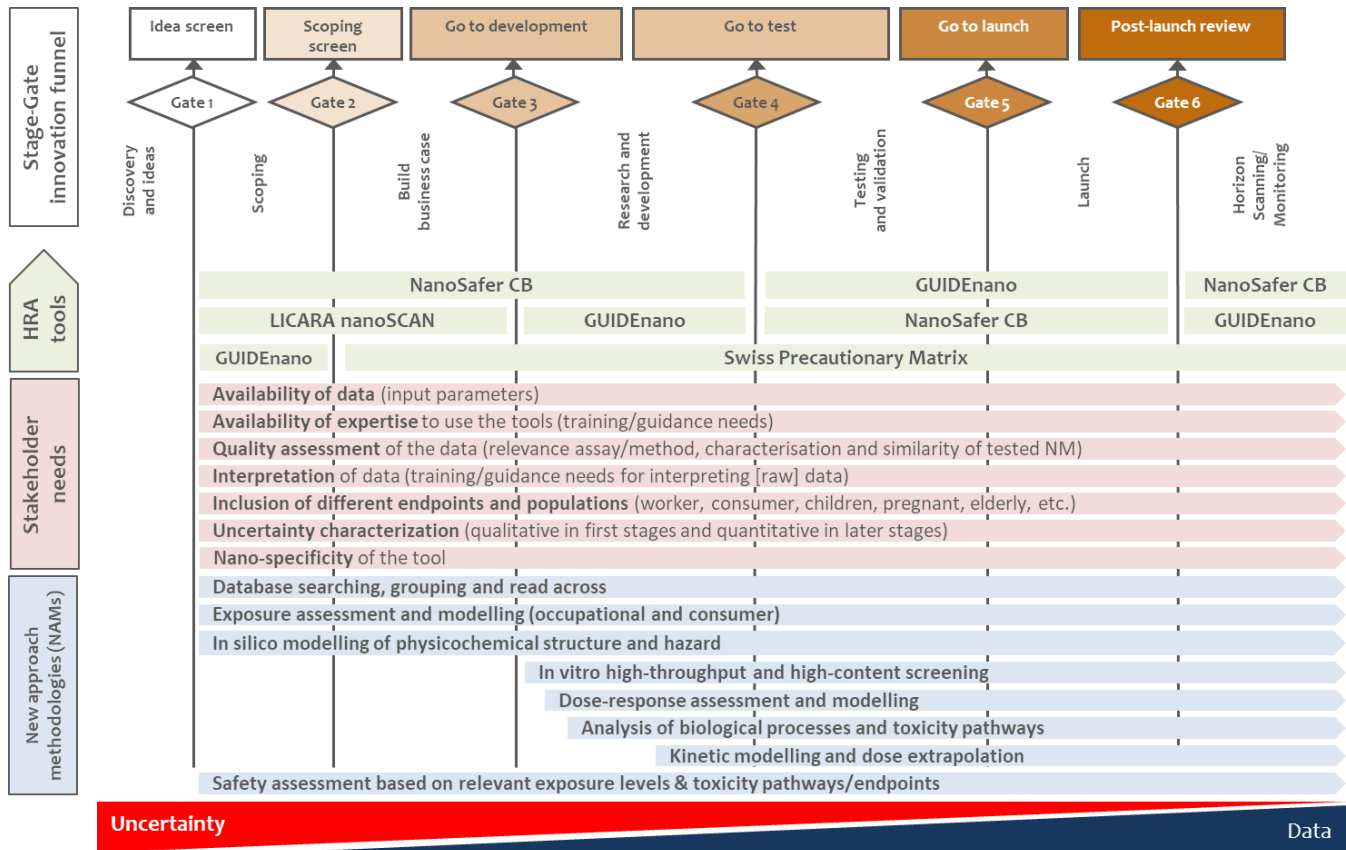
New cost-efficient alternative testing methods, such as high-throughput screening and ‘omics’ coupled to better exposure and toxicokinetic knowledge aim to improve understanding of toxic effects of substances.

Evaluation of NAMs based on stakeholder needs

Overall 50 NAMs were evaluated by considering input from other tasks within the project, such as articulated “stakeholder needs”, a set of caLIBRAte-selected human risk assessment (HRA) tools, official test method validation criteria, and finally, the innovation process as it progresses from idea stage to product launch in the Cooper Stage-Gate model.

Stakeholder needs	Definition
Availability of data	Need for data in all areas (i.e. characterization, hazard and exposure), esp at early innovation
Availability of expertise to use the tools	Need for training/guidance to use the current HRA tools
Quality assessment of the data	QA on data from non-traditional studies
Interpretation of data	Need for expertise for interpreting (raw) data from assays that are not directly indicative of human toxicity
Inclusion of different endpoints and populations	Need for additional endpoints (biocompatibility, cytotoxicity, oxidative stress, genotoxicity and immunotoxicity)
Characterisation of uncertainty	Need for characterized/quantified uncertainty e.g. through assessment of the predictive value
Nano-specificity of the tools	Need for nano-specific strategies

The Cooper Stage-Gate innovation funnel with aligned NAMs and HRA tools



The value of NAMs for nanomaterials innovation

caLIBRAte reviewed 50 NAM-related methods and concepts with varying specificity and conceptual broadness.

Each was summarized and reviewed for their applicability in HRA tools and the Stage-Gate funnel.

The composite result indicates extensive opportunity for added value of NAMs to currently available HRA tools, and moreover that several NAMs are generally able to provide support in diverse manners to MNM innovations/applications driven using the Cooper Stage-Gate innovation funnel.

This fact sheet is based on caLIBRAte Deliverables 2.4 and 2.5.: D2.4 *Review article with completed evaluation and guidance on prioritization of innovative hazard exposure and risk assessment models towards applications in the stage-gate model.* D2.5: *Integrated HRA tools, in the format of a suite of models and written guidance documentation* as the result of a collaboration between Karolinska Institute (SE), National Research Centre for the Working Environment (DK), TNO (NL), MISVIK (FI), GAIKER (ES), RIVM (NL), University of Helsinki (FI), Health Canada (CA), National Institute of Occupational Health (ZA) and Tampere University of Technology (FI).

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