# GRACIOUS: Grouping, Read-Across, CharacterIsation and classificatiOn framework for regUlatory risk assessment of manufactured nanomaterials and Safer design of nano-enabled products

## Rendicontazione

Informazioni relative al progetto

**GRACIOUS**

ID dell'accordo di sovvenzione: 760840

Sito web del progetto

**DOI**
10.3030/760840

Progetto chiuso

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## Periodic Reporting for period 3 - GRACIOUS (GRACIOUS: Grouping, Read-Across, CharacterIsation and classificatiOn framework for regUlatory risk assessment of

**manufactured nanomaterials and Safer design of nano-enabled products)**

**Periodo di rendicontazione:** 2021-01-01 al 2021-09-30

## Sintesi del contesto e degli obiettivi generali del progetto

Background: Manufacturing and functionalising materials at the nanoscale leads to a whole array of nanomaterials (NMs) varying in e.g. size, morphology and surface characteristics. Due to financial, time and ethical consideration, safety testing of every unique NM for their potential adverse effects is virtually impossible. For these reasons, more efficient ways to obtain safety information are needed.

Goal: The GRACIOUS consortium is building a Framework that will guide the grouping and read-across of NMs or nanoforms (NFs). This Framework will be useful both in a regulatory risk assessment context, as well as to inform the safe(r) by design of new nano-enabled products (NEPs).

To achieve this goal the GRACIOUS consortium will address the following objectives:

Objective 1: Integrate key stakeholder needs with state-of-the-art thinking on grouping and read-across of NMs/NFs (nanomaterials/nanoforms) in order to design, develop and refine a sustainable Framework.

Objective 2: Develop knowledge and generate data as the basis to derive hypotheses, criteria and guiding principles for grouping, leading to classification and read-across, as building blocks for the GRACIOUS Framework.

Objective 3: Refine and integrate tools to build the GRACIOUS Framework, Guidance Document and software module.

## Lavoro eseguito dall'inizio del progetto fino alla fine del periodo coperto dalla relazione e principali risultati finora ottenuti

Through an iterative process, working with stakeholders, GRACIOUS has generated a Framework to support the grouping and read-across of nanoforms, in order to streamline risk assessment, safe(r) by design approaches, identification of precautionary measures and testing strategies. (Stone et al 2020, https://doi.org/10.1016/j.nantod.2020.100941).

The Framework has been constructed as and open access software blueprint, allowing it to be incorporated into different risk assessment software. The blueprint is incorporated into risk assessment software via the SUN decision support system, and the GUIDEnano tool.

The Framework has also being written as a Guidance Document including worked examples to

illustrate application of the Framework, Hints and Tips for each section to highlight important things for the user to consider and references to additional sources of information. A shorter 'Guidance in a nutshell' has also been generated as an induction to the GRACIOUS Framework. Both are published via Zenodo.

The project partners have used existing literature and databases to establish 40 pre-defined hypotheses incorporated in the Framework. These hypotheses cover different environmental compartments and different routes of exposure relevant to humans. Provision of limited basic information by the user allows identification of the most appropriate pre-defined hypothesis relevant to the nanoform(s) of interest and exposure route(s). The release of nanoforms (concentration and form) and exposure routes are determined via a series of decision trees that are supported by a release/ exposure library, providing data and information to support identification of relevant exposure scenarios and release pathways, and the consequent exposure concentrations.

For each hypothesis a tailored Integrated Approach to Testing and Assessment (IATA) has been developed. The IATAs are decision trees which guide the user through the most appropriate questions (decision nodes) to be addressed in order to identify the information and data needed to test the hypothesis. Each decision node is backed up by a tiered testing strategy of methods to allow acquisition of the most appropriate data where data gaps exist.

Completion of the IATA leads to population of a data matrix which collates all information for the proposed group members and benchmark materials for all decision nodes. This data matrix is required by ECHA for substance dossiers which utilise grouping and read-across.
A range of methods have been generated to quantitatively assess the similarity of nanoform using the data matrix. These methods have contributed to the generation of over 10 publications all submitted to generate a special issue of NanoImpact dedicated to the GRACIOUS similarity assessment work.

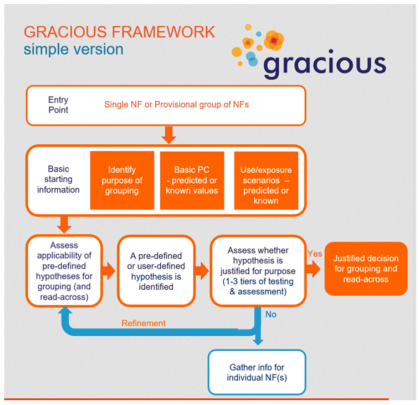
A range of internal and external case studies, including stakeholders from industry, regulators and academia were completed. These case studies assessed the whole Framework, IATAs and similarity assessment methods for both human and environmental applications of grouping and read-across. Feedback from these case studies was positive and allowed refinement of instructions included in the final Framework Guidance Document.

## Progressi oltre lo stato dell’arte e potenziale impatto previsto (incluso l’impatto socioeconomico e le implicazioni sociali più ampie del progetto fino ad ora)

The GRACIOUS Framework for grouping and read-across -
Progress beyond state of art is extensive. We have generated a detailed Framework description that is in line with the needs of regulators and industry. This Framework is ‘tunable’ to allow it to be used to inform safer(r) by design during innovation, as well as to support regulatory decision making.
ECHA has published a overview of the key steps required for grouping and read-across of nanoforms,

which GRACIOUS has now elaborated to allow application. The GRACIOUS Guidance Document is the first detailed step-by-step structured guide to allow users to conduct grouping and read-across of nanoforms. The GRACIOUS Framework is now being exploited by the OECD to update the OECD guidance on the grouping of chemicals, allowing the GRACIOUS project to have international impact. The Framework has now been tested by industry bodies and consultants who support industry to conduct risk assessment of nanomaterials and nanoenabled products. Through the case studies, these organisations have already utilised this tool to support their customers.
Potential impacts are diverse but include streamlining innovation and regulatory decision making for nanoforms, for both industry and regulators. This has the benefit of saving time and money as well as reducing animal use.

GRACIOUS FRAMEWORK COMPONENTS-
GRACIOUS generated:
(1) novel templates for hypothesis generation, physicochemical characterisation data, exposure and release data, and automated data input into the open access data repository (eNanoMapper), and criteria to determine data completeness and quality within these templates.
(2) Over 40 IATAs for human and environmental data/information generation to allow each hypothesis to be tested. These IATAs guide accumulation and integration of all of the information needed to conduct risk assessment of the source materials which can be used for read-across to target materials. The inhalation and oral IATAs have also been edited by the H2020 project BIORIMA to support the hazard assessment, risk assessment and benefit risk analysis of nanobiomaterials used in medical applications.
(3) A range of methods to assess similarity of nanoforms in a quantitative manner. These methods have been compared and critically analysed for their suitability and relevance. This is essential for regulatory applications of grouping.

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