Workshop on risk assessment of nanomaterials and materials containing small/nanoparticles in the food and feed chain, 11-12 June 2025, Brussels

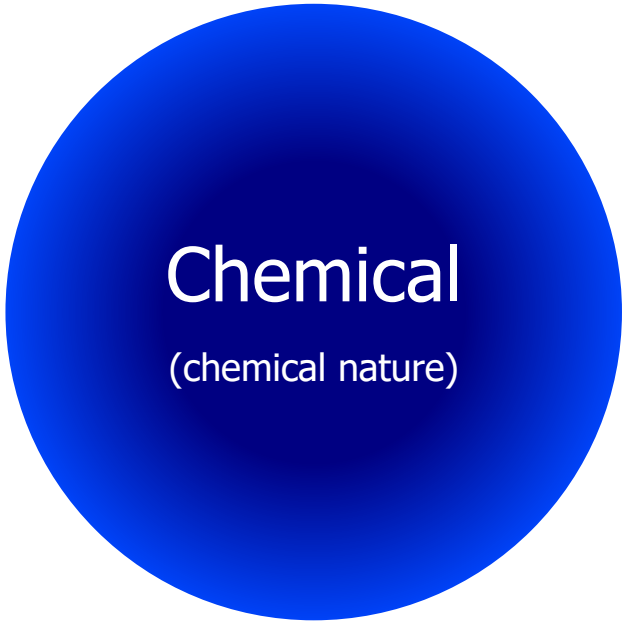
UPDATE OF EFSA GUIDANCE AND ACTIVITIES RELATING TO RISK ASSESSMENT OF SMALL/NANO PARTICLES IN THE FOOD AND FEED CHAIN

Qasim Chaudhry
Chair of EFSA's WG on Particle Risk Assessment

Maria Chiara Astuto on behalf of
EFSA Methodology and Scientific Support Unit

EUROPEAN FOOD SAFETY AUTHORITY

WHAT DRIVES THE HEALTH CONCERNS FROM EXPOSURE TO SMALL/ NANO PARTICLES?



PARTICLE-SIZE DRIVEN PROPERTIES & EFFECTS

Normal physicochemical rules do not apply well to particles at the nano-scale:

- Properties and behaviour of particles can change at the nano-scale compared to larger sizes;
- Extremely small size = very large surface area = increased reactivity per equivalent weight;
- Nano-sizing of particles may generate new properties/functionalities.

By the same token

Particle-size driven alterations in the properties and behaviour of materials may also lead to a departure from (expected) toxicological properties:

- Changes in surface properties; reactivity; TK/TD profile;
- Ability to cross biological barriers (GI Tract, Cellular membrane);
- Potential interaction with biological moieties close to molecular level.

PARTICULATE FORMS

CONVENTIONAL CHEMICAL

Chemical toxicity

Chemical toxicity
Plus
Physical effects at the point of contact
(friction, abrasion, inflammation, physical injury)

LARGE PARTICLES

250 nm

Chemical toxicity
Plus
Physical effects at the point of contact
Plus
Systemic effects at cellular/subcellular level

Potential translocation from GI Tract to other organs and cellular uptake

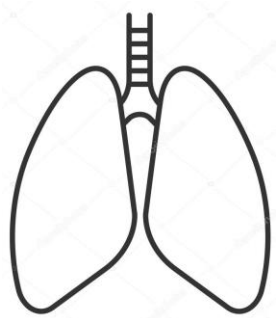
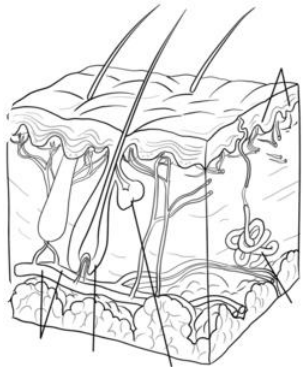
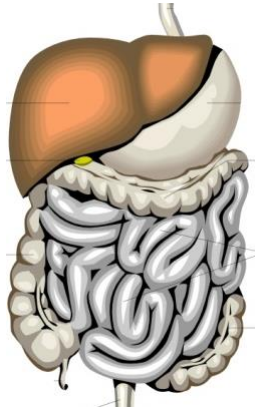
SMALL PARTICLES

100 nm

NANO PARTICLES

1 nm

Small/Nano particles

	Inhalation	Dermal	Oral
Routes of exposure			
Systemic uptake?	Systemic uptake and translocation to other organs is possible if small/nano particles are not cleared through phagocytosis/ lung clearance.	Limited studies so far. Healthy intact skin appears to be a good barrier to particulate materials, including small/nano particles.	Limited studies so far. Translocation to other organs and systemic availability is possible if small/nano particles can persist in food and the gastrointestinal tract

NOT EVERY SMALL/NANO PARTICULATE MATERIAL IS HARMFUL

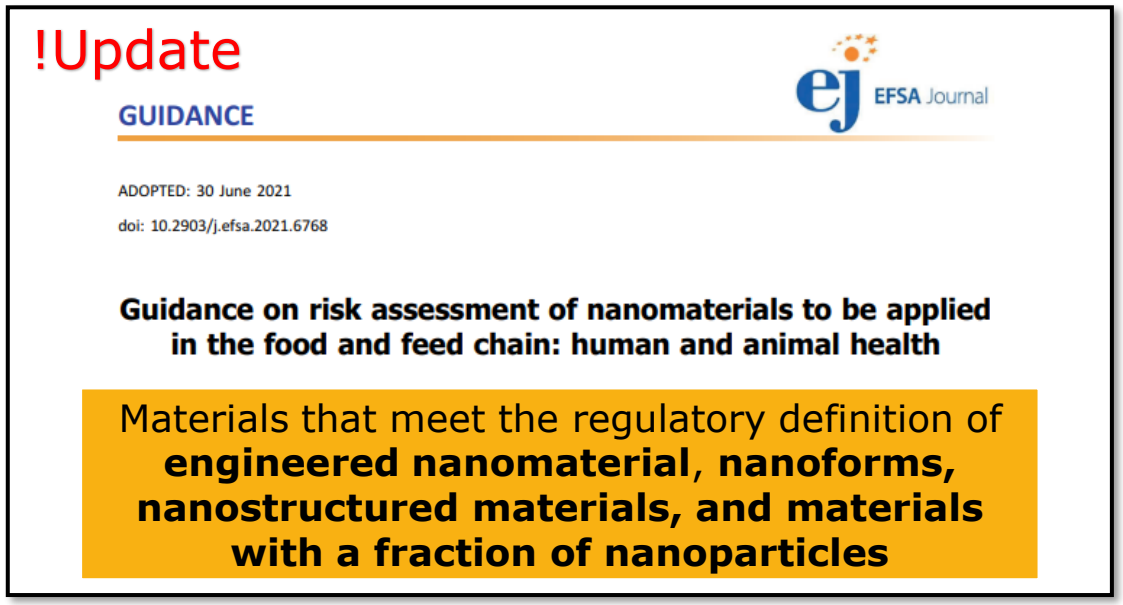
- Toxicological hazards of a small/nano particulate material are determined by a combination of **chemical and physical (particle-related) aspects**.
- No hard and fast rules, but health concerns increase with a **decrease in particle size**, and/or when the particles:
  - are insoluble or slowly-dissolving, persistent/ accumulative in the body,
  - are able to cross biological membrane barriers and translocate from the GI tract to other organs,
  - are composed of chemicals that are harmful as such, or can deliver harmful moieties inside cells/ tissues,
  - have reactive surfaces - as such, or due to surface modifications,
  - have certain morphological features of concern (e.g. needle shape, rigid long fibres),
  - show a different biokinetic behaviour than the conventional equivalent,
  - have been used as vehicle for nano-scale delivery of other substances,
  - have been designed for a new/specific function (e.g. a smart/functional material).

EFSA 2021 NANO GUIDANCE DOCUMENTS

Aim: assess and/or exclude possible risk from the presence of small/nano particles in food and feed

Guidance on Nano – Risk Assessment:
How to conduct a 'nanoscale' risk assessment?

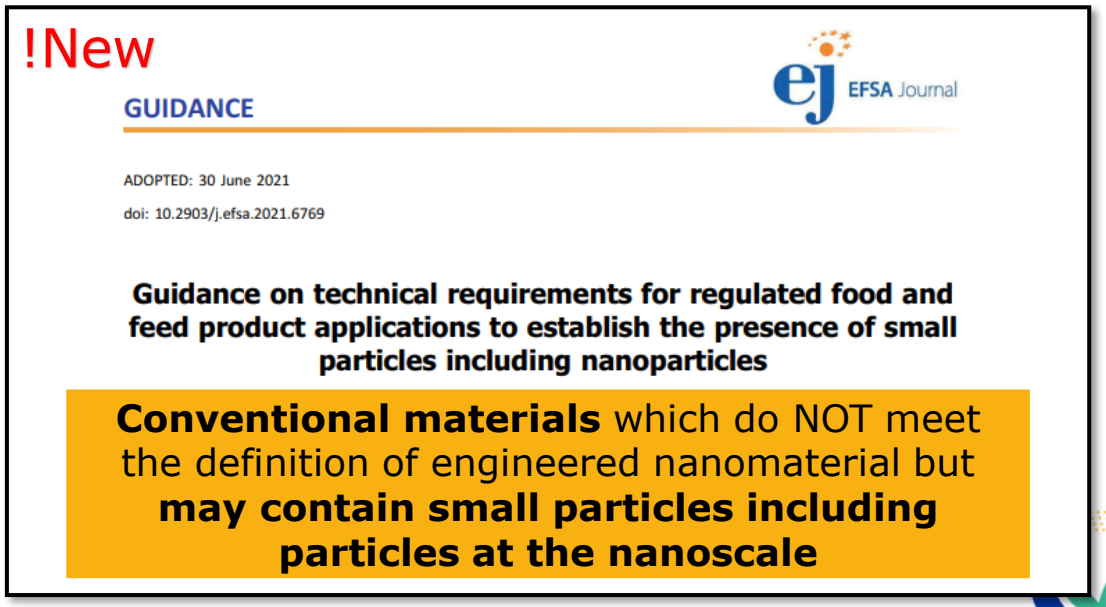
!Update



Materials that meet the regulatory definition of **engineered nanomaterial**, **nanoforms, nanostructured materials, and materials with a fraction of nanoparticles**

Guidance on Particle - Technical Requirements:
Are 'nanoscale considerations' needed for the risk assessment?

!New



Conventional materials which do NOT meet the definition of engineered nanomaterial but **may contain small particles including particles at the nanoscale**

RECENT ACTIVITIES: 2021→ 2024

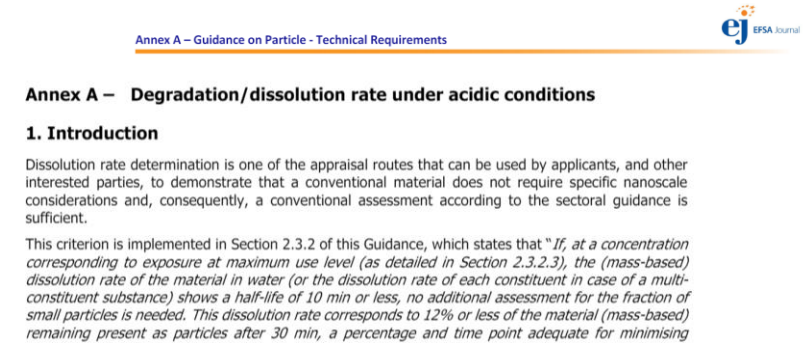
Based on the experience gained from the implementation phase, **some updates were published on the EFSA website** to provide further guidance to applicants and risk assessors →

New Annex A on Dissolution added in Nov 2022, as per request from the CEP Panel

Clarification on DLS published in Feb 2024, as per request from the FIP Unit

New Annex B on 'Clarification on the use of a Kow-based threshold for lipid-soluble substances as a possible appraisal route' in July 2024 produced as per request from the NIF Unit/NDA Panel

New Annexes C-D to support the reporting of electron microscopy analysis results in December 2024

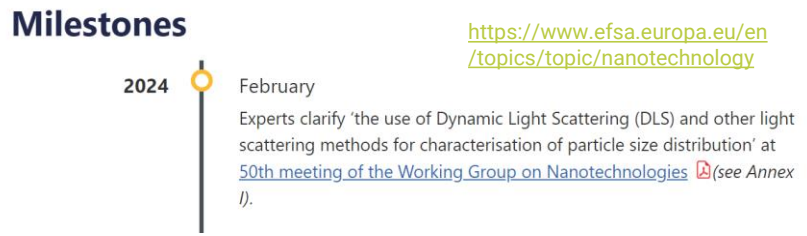

Annex A – Guidance on Particle - Technical Requirements

Annex A – Degradation/dissolution rate under acidic conditions

1. Introduction

Dissolution rate determination is one of the appraisal routes that can be used by applicants, and other interested parties, to demonstrate that a conventional material does not require specific nanoscale considerations and, consequently, a conventional assessment according to the sectoral guidance is sufficient.

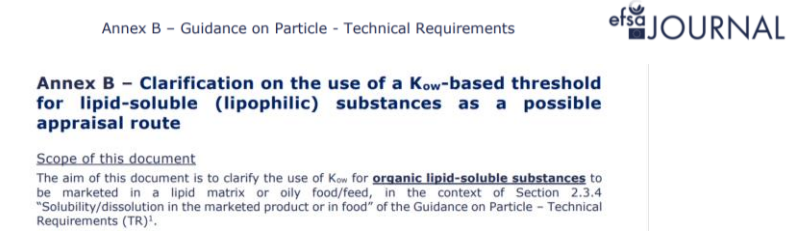
This criterion is implemented in Section 2.3.2 of this Guidance, which states that "*If, at a concentration corresponding to exposure at maximum use level (as detailed in Section 2.3.2.3), the (mass-based) dissolution rate of the material in water (or the dissolution rate of each constituent in case of a multi-constituent substance) shows a half-life of 10 min or less, no additional assessment for the fraction of small particles is needed. This dissolution rate corresponds to 12% or less of the material (mass-based) remaining present as particles after 30 min, a percentage and time point adequate for minimising*


Milestones

https://www.efsa.europa.eu/en/topics/topic/nanotechnology

2024 February

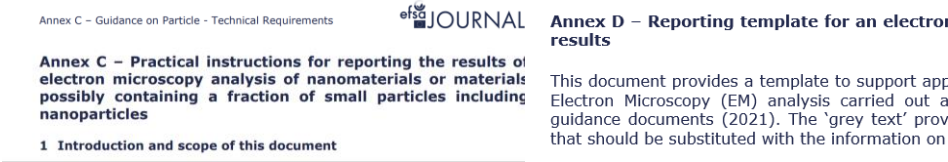
Experts clarify 'the use of Dynamic Light Scattering (DLS) and other light scattering methods for characterisation of particle size distribution' at 50th meeting of the Working Group on Nanotechnologies *(see Annex I).*


Annex B – Guidance on Particle - Technical Requirements

Annex B – Clarification on the use of a K_{ow}-based threshold for lipid-soluble (lipophilic) substances as a possible appraisal route

Scope of this document

The aim of this document is to clarify the use of K_{ow} for **organic lipid-soluble substances** to be marketed in a lipid matrix or oily food/feed, in the context of Section 2.3.4 "Solubility/dissolution in the marketed product or in food" of the Guidance on Particle – Technical Requirements (TR)[1].


Annex C – Guidance on Particle - Technical Requirements

Annex C – Practical instructions for reporting the results of electron microscopy analysis of nanomaterials or materials possibly containing a fraction of small particles including nanoparticles

1 Introduction and scope of this document

Annex D – Reporting template for an electron results

This document provides a template to support app Electron Microscopy (EM) analysis carried out a guidance documents (2021). The 'grey text' prov that should be substituted with the information on

NEXT STEPS: 2024 → 2029 | SELF TASK MANDATE


GUIDANCE

EFSA Journal

Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles


GUIDANCE

EFSA Journal

Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health

New self-task mandate from EFSA SC to work on the update of 2021 EFSA's Nano Guidances for development of a '***Guidance document for risk assessment of nanomaterials and materials containing nanoparticles in the food chain***' (M-2024-00062)

Phase 1 (by Q3 2026)

- Focus to merge the existing GDs and clarify structure and requirements. Start integrating further guidance on the use of NAMs

Phase 2 (by Q4 2027)

- Focus on major scientific updates (e.g. indications for ERA, nanocarriers, advanced materials, SSbD, detailed provisions for feed additives*)

Phase 3 (by Q4 2029)

- Focus to incorporate results from the NAMs4NANO Project (Lot 1-2-3)

Engagement activities

*M-2024-00163

NEXT STEPS: 2024 → 2029 | ENGAGEMENT PLAN

1st phase Guidance update: Q4 2024 (kick off) → Q3 2026 (adoption & publication)

Q1 2025:
Call for views on mandate objectives and Terms of Reference

Open for feedback from **regulators & stakeholders**

Q2 2025:
Scoping document outlining proposed structure and key elements of the updated Guidance

Open for feedback from **regulators & stakeholders** and for discussion during **ad hoc meetings/workshop**

Q3-4 2025:
Finalisation draft Guidance (phase 1 update)

Open for feedback from **regulators & stakeholders**, **ad hoc meetings** can follow up as needed

Q1 2026:
Public consultation on the final draft EFSA Guidance (phase 1 update)

Open for feedback from **regulators & stakeholders** on new scientific developments for phase 2

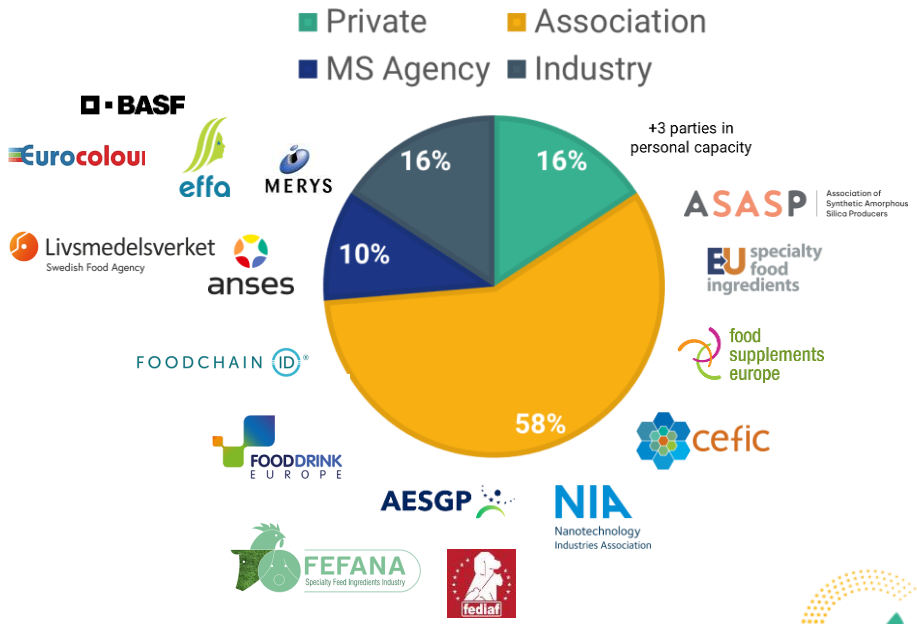
CALL FOR VIEWS: INPUT RECEIVED

- Support effort to **merge** guidance documents for more **clarity and ease of use**
- Provide **more precise provisions on methodologies proposed in the guidance** (e.g. relating to solubility, dissolution rate, physicochemical characterization methods) to facilitate implementation
- Provide **more guidance on the characterisation/assessment of complex materials** e.g. plate-like structures, gellable materials, organic or natural origin materials and in complex/food matrices
- Support the considerations of **realistic exposure** in **sample preparation dispersion protocols**
- Support the inclusion of **new provisions on the use of NAMs**, in line with the EC Roadmap commitment to phase out animal testing

Dec 2024
(Start of comment period)

Feb 14th, 2025
(End of comment period)

19 RESPONDENTS

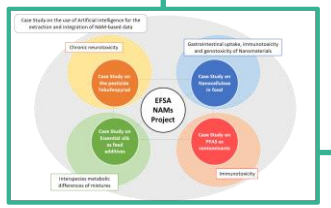


EFSA'S PROJECTS ON NAMS & NANO

☑ Q1 2021 - Q2 2023

EFSA Pilot Project on NAMs for the hazard assessment of nanofibers

(GP/EFSA/SCER/2020/04)



- **Lot 1**: '**NANOCELL**ulose oral exposure: gastrointestinal digestion, nanofibers **UP**take and local effects'
- **Lot 2**: 'Exploring the use of gut-on-a-chip models for risk assessments of nanofibers'

Vincentini et al., 2013

Italiani et al., 2013

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Consiglio Nazionale delle Ricerche · Istituto di Biochimica e Biologia Cellulare / Institute of Biochemistry and Cell Biology · IRGB

Final goal: Develop further recommendations on the use of NAMs for addressing nanoscale considerations and in parallel foster the general implementation of NAMs

⏳ Q1 2023 - Q2 2027

EFSA NAMS4NANO Project

(GP/EFSA/MESE/2022/01)

Integration of New Approach Methodologies results in chemical risk assessments: case studies addressing nanoscale considerations

Usmani et al., 2024

Haase et al., 2024

- **Lot 1**: Review of NAM-based tools for nano -specific risk assessment and developing a 'Qualification System for NAMs' using the experience from EMA & US FDA
- **Lot 2**: Designing and conducting a set of risk assessment case studies
- **Lot 3**: Designing and conducting a set of methodological case studies

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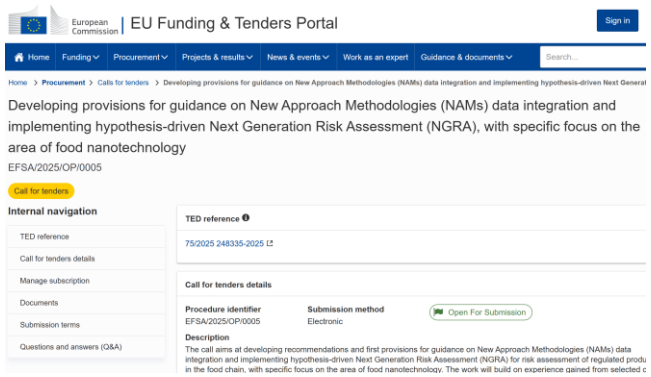
EFSA'S PROJECTS ON NAMS & NANO

Q4 2025 – Q4 2027

EFSA NAMs Data Integration Project (EFSA/2025/OP/0005)

Developing provisions for NAMs data integration and implementing hypothesis-driven NGRA, with specific focus on the area of food nanotechnology

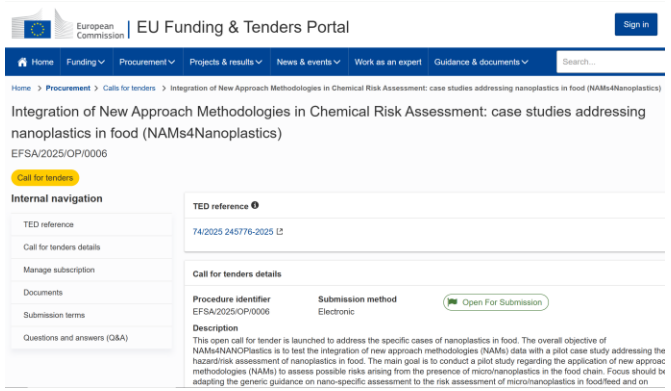


- Duration of the contract: 24 months
- Call for tenders open until **26/06/2025** 14:30 CEST

Q4 2025 – Q4 2027

EFSA NAMs4NANOplastics Project (EFSA/2025/OP/0006)

Integration of NAMs in chemical risk assessment: Case Studies Addressing Nanoplastics in Food



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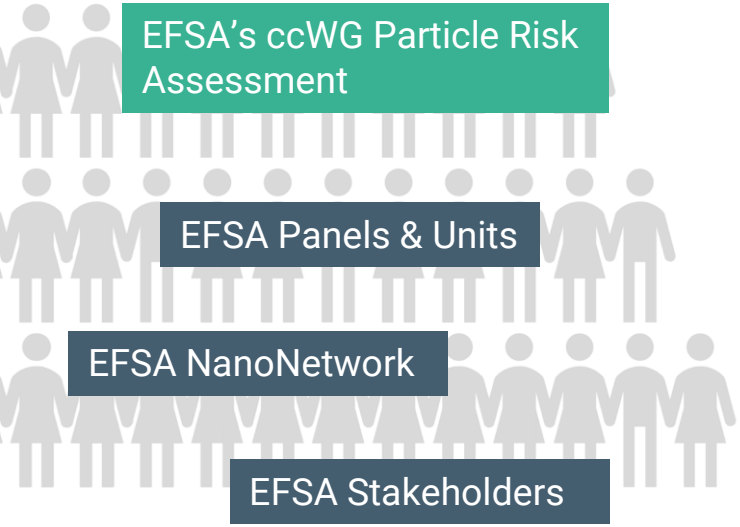
Final goal: Develop further recommendations on the use of NAMs for addressing nanoscale considerations and in parallel foster the general implementation of NAMs

ACKNOWLEDGMENTS



WG Members

- **WG Chair**: Qasim Chaudhry
- **Subgroup Guidance**: Anthony Cadène, Jacqueline Castenmiller, Laurence Castle, Francesco Cellesi, Wim de Jong, Francesca Maranghi, Jan Mast, Agnes Oomen, Olimpia Vincentini, Ivana Vinković
- **Subgroup Risk Assessment**: Maria Bastos, Ulrike Bernauer, Francesco Cubadda, Roland Franz, Henriqueta Louro, Eveline Verleysen

EC Representatives

- Susanne Bremer Hoffman and Hubert Rauscher (**EC JRC**), Ivona Babic, Aurélien Perez, Martinus Nagtzaam, Jiri Sochor, Rafael Luis Perez Berbejal (**DG SANTE**), Camelia Constantin, Virginia Rodriguez Unamuno (**ECHA**), Noemi Garcia del Blanco, Susana Casado, Francisca van Doesum-Wolters (**EMA**)

EFSA Taskforce

- **MESE Unit**: Maria Chiara Astuto, Irene Cattaneo, Claudia Cascio, Ana Diges
- **FIP Unit**: Eric Barthélémy, Daniele Comandella, Agnieszka Mech, Ana Rincon
- **FEEDCO Unit**: Orsolya Holczknecht, Vittoria Vettori
- **NIF Unit**: Reinhard Ackerl, Marcello Laganaro

Thank you for your attention!

Any questions? Input?

MESE@efsa.europa.eu

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