

# NETWORK ON NANOTECHNOLOGIES IN FOOD AND FEED (NANONETWORK)

## 13<sup>th</sup> meeting



26 September 2023

09:00-13:00

Minutes agreed on 14 November 2023

**Location:** EFSA - Parma (Board Room) and web-conference

**Attendees:**

o **Network Participants:**

Country	Name
Austria	Veronika Plichta
Bulgaria	Angel Angelov
Croatia	Ivana Vinkovic Vrcek
Cyprus	Eleni Anastasi Demetris Kafouris
Czech Republic	Simona Lencová
Denmark	Katrin Loeschner
Estonia	Kaja Kasemets
Finland	Pertti Koivisto
France	Fernando Aguilar
Germany	Holger Sieg
Greece	Aristotelis Xenakis Nikolaos Katerelos
Hungary	Zsófia Keresztes
Ireland	Pat O' Mahony
Italy	Olimpia Vincentini
Lithuania	Zygimantas Janeliunas
Luxembourg	Micheline Rosch
Netherlands	Eric Bleeker
Norway	Gro Mathisen
Portugal	Helena Carmo
Romania	Georgeta Popovici
Slovakia	Peter Šimon
Spain	José Manuel Barat Baviera
Sweden	Sara Gunnare

o **Observers:**

Mar Gonzalez (OECD)

- o **Members of the cross-cutting Working Group on Nanotechnologies participating as Hearing Experts:** Mohammad Chaudhry; Francesco Cubadda (also Nano Network representative of Italy); David Gott; Jan Mast (also Nano Network representative of Belgium); Alicja Mortensen; Agnes Oomen (also Nano Network representative of The Netherlands);



- Franz Roland; Eveline Verleysen (also NanoNetwork representative of Belgium);
- **European Commission/Other EU Agencies representatives:** Hubert Rauscher (EC Joint Research Centre); Andrej Kobe (DG Environment); Laurence Deydier (ECHA); Marianne Matzke (ECHA); Panagiotis Daskaleros (DG SANTE); Susanne Bremer-Hoffmann (EC Joint Research Centre)
  - **Methodology & Scientific Support (MESE) Unit:** Maria Chiara Astuto; Djien Liem; Claudia Roncancio Pena; Irene Cattaneo; Ketty Antonelli; Claudia Cascio;
  - **Food Ingredients & Packaging (FIP) Unit:** Ana Maria Rincon; Agnieszka Mech
  - **Front-Desk & Workforce Planning (FDP) Unit:** Federico Morreale

## 1. Welcome and apologies for absence

The Chair, Djien Liem, welcomed the participants, and particularly the new members and one-time participants.

Apologies were received from Maria de Lurdes Bastos, Henriqueta Louro, Jacqueline Castenmiller, Anil Patri, Catherine Simoneau, Bruno Teste, Jana Tulinska, Viviana Golja, Andrea Haase.

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## 2. Adoption of agenda

The agenda was adopted without changes.

## 3. Agreement of the minutes of the 12<sup>th</sup> Network meeting held on 24-25 October 2022, in Parma.

The minutes of the 12<sup>th</sup> meeting of the Nano Network held on 24-25 October 2022, web-conference had been previously agreed by written procedure on 17 November 2022 and published on the EFSA website on 17 November 2022<sup>1</sup>.

## 4. Terms of Reference (ToR) of the NanoNetwork: specific objectives and deliverables.

The Chair presented to the Network members the Terms of Reference (ToR) of the EFSA Scientific Network for Risk Assessment of the use of Nanotechnologies in Food and Feed (Nano Network) renewed in 2021<sup>2</sup>. As formulated in the ToR, the main objectives of the Nano Network are to facilitate harmonisation of methodologies by sharing guidance, best practices and experience, promoting information exchange between EFSA and EU Member States. Furthermore, the Network ensures international coordination, mutual cooperation, surveillance on national applications, and flags priority research needs. EFSA may entrust certain tasks to

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<sup>1</sup> <https://www.efsa.europa.eu/sites/default/files/2022-11/12th-meeting-efsa-scientific-network-risk-assessment-nanotechnologies-food-and-feed-minutes.pdf>



the Network, such as collection of data and identification of emerging risks, as well as organisation of national conferences/trainings/workshops on the EFSA relevant guidance documents with interested and relevant stakeholders. The Terms of Reference for the Nano Network were recently approved by the EFSA Advisory Forum and are confirmed until 2024.

## **5. Update on EFSA Nano Guidances<sup>2,3</sup> implementation**

Maria Chiara Astuto (EFSA) presented an update of the activities of the EFSA cross-cutting Working Group (ccWG) on Nanotechnologies, which supports EFSA's Panels and Units in the implementation of EFSA's Nano Guidances, namely the Guidance on Particle – Technical Requirements<sup>2</sup> and the Guidance on Nano – Risk Assessment<sup>4</sup>. The NanoNetwork was presented with an overview of recent requests for assistance received by the WG from EFSA's Panels and Units and with the outcome of their evaluations<sup>4</sup>. Furthermore, the Network was informed about an analysis ongoing at ccWG level with the aim to collect ideas and input from the users of the EFSA Nano Guidances and to reflect on possible refinements after this first implementation phase. In this regard, the NanoNetwork will soon be requested to respond to a Survey to report any practical problem encountered in the implementation of the Nano Guidances, and to highlight any related scientific or regulatory issues.

### **5.1 Development of a reporting template for Electron Microscopy results**

Jan Mast (Expert of the EFSA ccWG Nanotechnologies and NanoNetwork representative of Belgium) presented a proposal for the development of a checklist of information requirements and a reporting template for Electron Microscopy (EM) results. This work, aimed at providing further guidance in the execution of EM analysis and in the reporting of results in line with the provisions in the EFSA Nano Guidances, is one of the follow up activities undertaken by the WG after the publication of the Nano Guidances. The document will be structured with a checklist format to ensure completeness of regulatory dossiers and standardised reporting. The NanoNetwork was requested to provide input on the approach proposed by the ccWG. The input collected will be used by the ccWG to finalise a first draft of the document which will be shared with the NanoNetwork for a consultation.

## **6. New scientific developments, ongoing activities and/or emerging issues of concern, input from NanoNetwork members:**

The NanoNetwork members were requested to provide input on ongoing activities.

### **6.1 Results of the EU HISENTS Project**

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<sup>2</sup> <https://www.efsa.europa.eu/sites/default/files/Nanonetwork.pdf>

<sup>3</sup> EFSA Scientific Committee, 2021. Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health. EFSA Journal 2021;19(8):6768, 111 pp. <https://doi.org/10.2903/j.efsa.2021.6768>

<sup>4</sup> <https://www.efsa.europa.eu/sites/default/files/wgs/cross-cutting-science/wg-nanotechnologies.pdf>



Peter Šimon (Slovakia) presented an overview and results of the EU Horizon 2020 HISENTS (High level Integrated SENSor for NanoToxicity Screening) project<sup>5</sup>. This EU Project is aimed at introducing an innovative multimodular high throughput screening (HTP) platform for nano-safety assessment including a set of individual modules each representing a critical physiological function connected and integrated in a hierarchical vectorial manner by a microfluidic network. The HISENTS body-on-a-chip platform is accompanied by a PBK model which enables predicting biodistribution of (nano)toxicants in mammals. The individual sensors are tailored to monitor interaction of (nano)toxicants with specific cells, and the sensor response is related to a cellular damage. The structure and specific Work Packages of the project were presented, with a specific focus on WP5: Modelling mechanisms, pathways and effects<sup>6,7,8,9</sup>.

## **6.2 Endocrine disruptive effect of complex mixtures: case study on nanoplastics and pharmaceuticals**

Ivana Vinkovic Vrcek (Croatia) provided an overview and presented the results of a project dealing with the evaluation of exposure of the human body to complex mixtures of different chemicals having endocrine disruptive effects, including micro and nanoplastic particles and pharmaceuticals. After the presentation of background information and the experimental design of the project, the NanoNetwork was presented with the conclusions and the expected challenges related to the implementation of the project to complex mixtures such as nanoplastics. A discussion followed on the physicochemical characterisation and particle size distribution of tested materials and on their possible correlation with the observed effects. The complete set of results of the project will be published soon in peer-reviewed journals.

## **6.3 OECD steering group on advanced materials - Early4AdMa as a tool in Regulatory Preparedness**

Agnes Oomen (Expert of the EFSA ccWG Nanotechnologies, NanoNetwork representative of The Netherlands, and co-Chair of the OECD Steering Group on Advanced Materials) presented the early awareness and action system for advanced materials (Early4AdMa) as a tool in Regulatory Preparedness on behalf of the OECD Steering Group on Advanced Materials (AdMa). AdMa are innovative materials considered to be key in response to global challenges. The nature of the innovation is related to advancement from 'simple' nanomaterials to complex 'advanced' nanomaterials and this additional complexity should be properly addressed in terms

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<sup>5</sup> <https://cordis.europa.eu/project/id/685817>

<sup>6</sup> Kohl Y, Biehl M, Spring S, Hesler M, Ogourtsov V, Todorovic M, Owen J, Elje E, Kopecka K, Moriones OH, Bastús NG, Simon P, Dubaj T, Rundén-Pran E, Puentes V, William N, von Briesen H, Wagner S, Kapur N, Mariussen E, Nelson A, Gabelova A, Dusinska M, Velten T and Knoll T, 2021. Microfluidic In Vitro Platform for (Nano)Safety and (Nano)Drug Efficiency Screening. *Small*, 17:2006012. doi: <https://doi.org/10.1002/sml.202006012>

<sup>7</sup> Dubaj T, Kozics K, Sramkova M, Manova A, Bastús NG, Moriones OH, Kohl Y, Dusinska M, Runden-Pran E, Puentes V, Nelson A, Gabelova A and Simon P, 2022. Pharmacokinetics of PEGylated Gold Nanoparticles: In Vitro-In Vivo Correlation. *Nanomaterials (Basel)*, 12. <https://doi.org/10.3390/nano12030511>

<sup>8</sup> Breza M and Šimon P, 2019. Quantum-chemical studies of rutile nanoparticles toxicity I. Defect-free rod-like model clusters. *Acta Chimica Slovaca*, 12:168-174. <https://doi.org/10.2478/acs-2019-0023>

<sup>9</sup> Breza M and Šimon P, 2020. On shape dependence of the toxicity of rutile nanoparticles. *Journal of Nanoparticle Research*, 22:58. <https://doi.org/10.1007/s11051-020-4773-1>



of safety, considerations on the suitability of existing regulations and guidelines and current policy ambitions to increase sustainability. To respond to these questions, a screening tool was developed to identify and anticipate on safety and sustainability issues of advanced materials<sup>10,11</sup>. Finally, ongoing case studies and preliminary results were presented.

#### **6.4 NANOPERSIST: *In chemico* testing of GIT and lysosomal fate of particulate materials and nanomaterials used in food-related applications**

Francesco Cubadda (Expert of the EFSA ccWG Nanotechnologies, NanoNetwork representative of Italy) presented the results of the NANOPERSIST project. This project is the outcome of a collaboration between Istituto Superiore di Sanità of Italy and the European Commission Joint Research Center (EC JRC) under the framework for access to the Joint Research Centre physical Research Infrastructures of the European Commission (Research Infra-structure Access Agreement N° 35050/5). The aim of the project was to study transformations and fate of food-relevant nanoparticles during human digestion and in lysosomal conditions. In this project, *in vitro* simulated gastrointestinal digestion and lysosomal degradation were studied in line with the conditions described in the EFSA Guidance on Nano – Risk Assessment<sup>4</sup> (e.g. half-lives, time points, test concentrations). After the presentation of the materials studied and the analytical techniques used, the NanoNetwork was presented with the results of the case study on food-grade titania (E 171)<sup>12</sup>.

#### **7. EC JRC Guidance on the implementation of the Commission Recommendation 2022/C 229/01 on the definition of nanomaterial**

Hubert Rauscher (European Commission Joint Research Center (EC JRC) representative for the EFSA ccWG on Nanotechnologies) presented the EC JRC Guidance on the implementation of the Commission Recommendation 2022/C 229/01 on the definition of nanomaterial<sup>13</sup>. This guidance supports the implementation of the nanomaterial definition adopted in the 2022 European Commission Recommendation (2022/C 229/01<sup>14</sup>) and gives an overview of the key terminology and concepts useful when addressing nanomaterials or issues concerning products of nanotechnologies. Also, this new guidance provides a

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<sup>10</sup>OECD 2022 Advanced Materials: Working Description - Series on the Safety of Manufactured Nanomaterials No. 104 NV/CBC/MONO(2022)29, Available at: <https://www.oecd.org/env/ehs/nanosafety/publications-series-safety-manufactured-nanomaterials.htm>

<sup>11</sup>OECD (2023), Early Awareness and Action System for Advanced Materials (Early4AdMa): Pre-regulatory and anticipatory risk governance tool to Advanced Materials, OECD Series on the Safety of Manufactured Nanomaterials, No. 108, Environment, Health and Safety, Environment Directorate, Available at: <https://www.oecd.org/chemicalsafety/safer-and-sustainable-innovation-approach/early-awareness-and-action-system-for-advanced-materials-pre-regulatory-anticipatory-risk-governance-tool.pdf>

<sup>12</sup> Ferraris F, Raggi A, Ponti J, Mehn D, Gilliland D, Savini S, Iacoponi F, Aureli F, Calzolari L and Cubadda F, 2023. Agglomeration Behavior and Fate of Food-Grade Titanium Dioxide in Human Gastrointestinal Digestion and in the Lysosomal Environment. *Nanomaterials*, <https://doi.org/10.3390/nano13131908>

<sup>13</sup> Rauscher, H., Kestens, V., Rasmussen, K., Linsinger, T. and Stefaniak, E., Guidance on the implementation of the Commission Recommendation 2022/C 229/01 on the definition of nanomaterial, EUR 31452 EN, Publications Office of the European Union, Luxembourg, 2023, ISBN 978-92-68-01243-7, JRC132102, <https://doi.org/10.2760/237496>

<sup>14</sup>[https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022H0614\(01\)](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022H0614(01))



decision tree to identify nanomaterials while addressing aspects related to their identification and characterisation.

## **8. SCCS Guidance on the safety assessment of nanomaterials in cosmetics - 2nd revision<sup>4</sup>**

Qasim Chaudhry (Chair of the EFSA ccWG on Nanotechnologies and Chair of the Scientific Committee on Consumer Safety (SCCS)) presented the recently published 2<sup>nd</sup> revision of the "SCCS Guidance on the safety assessment of nanomaterials in cosmetics"<sup>15</sup>. The NanoNetwork was provided with an overview of the state of the art of the assessment of nanomaterials in the cosmetics' regulatory framework, which completely relies on the use of New Approach Methodologies (NAMs) due to the ban of animal testing applicable to cosmetic ingredients/products, and to the marketing of cosmetic ingredients/products tested on animals in Europe since March 2013 (Regulation (EC) No 1223/2009 on cosmetic products)<sup>16</sup>. In this regard, the new SCCS Guidance on Nanomaterials provides a detailed overview of the available non-animal methods considered scientifically valid to address the potential toxicity of nanomaterials for specific endpoints. A list of nanomaterials assessed for safety by the SCCS was provided.

## **9. Start of the art of OECD Test Guidelines and Guidance Documents for nanomaterials**

Mar Gonzalez (OECD) and Eric Bleeker (The Netherlands) provided an overview of the state of the art of OECD Test Guidelines (TG) and Guidance Documents (GD) for nanomaterials, which are developed by the Working Party on Manufactured Nanomaterials (WPMN) and the Working Group of the National Coordinators of the Test Guidelines Programme (WNT). A list of published and ongoing projects on Nanomaterials in the field of physicochemical characterisation, human health, effects on biotic systems, environmental fate and behaviour were presented<sup>17,18,19</sup>. The NanoNetwork was also presented with a recent research activity aimed to identify and to prioritise further work on the development and adaptation of OECD TGs/GDs for nanomaterials<sup>20</sup>. Needs for further action and priorities for developing TGs/GD to address nanospecific issues were identified. Efforts in place to address these issues will result in better fit-for-purpose test methods for EU regulatory compliance.

## **10. AOB and conclusion**

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<sup>15</sup> [https://health.ec.europa.eu/publications/sccs-guidance-safety-assessment-nanomaterials-cosmetics-2nd-revision\\_en](https://health.ec.europa.eu/publications/sccs-guidance-safety-assessment-nanomaterials-cosmetics-2nd-revision_en)

<sup>16</sup> <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:02009R1223-20190813>

<sup>17</sup> <https://www.oecd.org/chemicalsafety/testing/oecd-guidelines-testing-chemicals-related-documents.htm>

<sup>18</sup> <https://www.oecd.org/chemicalsafety/nanosafety/>

<sup>19</sup> <https://www.oecd.org/chemicalsafety/nanomet/>

<sup>20</sup> Bleeker EAJ, Swart E, Braakhuis H, Fernández Cruz ML, Friedrichs S, Gosens I, Herzberg F, Jensen KA, von der Kammer F, Kettelarij JAB, Navas JM, Rasmussen K, Schwirn K and Visser M, 2023. Towards harmonisation of testing of nanomaterials for EU regulatory requirements on chemical safety - A proposal for further actions. Regul Toxicol Pharmacol, 139:105360. <https://doi.org/10.1016/j.yrtph.2023.105360>



The Chair thanked the members of the Nano Network for their continued contribution and scientific support to the work of EFSA. In the afternoon, a joint session of the EFSA NanoNetwork meeting and the Global Summit on Regulatory Science 2023 (GSRs23) was organised dedicated to qualification systems supporting the use of NAMs in food, and to challenges and ways forward to investigate nanoplastics<sup>21,22</sup>.

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<sup>21</sup> <https://www.efsa.europa.eu/en/events/13th-global-summit-regulatory-science-gsrs23>

<sup>22</sup> <https://gcsr.net/2023-gsrs/>