Network on Nanotechnologies in Food and Feed Minutes of the 6th meeting

Held on 30 June and 1 July 2016, Madrid

(Agreed on 30 September 2016)

Participants

- **Network Representatives of Member States (including EFTA Countries):**

Country	Name
Austria	Helmut Hinterwirth
Belgium	Pieter-Jan De Temmerman
Bulgaria	Angel Angelov
Croatia	Darko Mikec
Czech Republic	Vladimir Ostry
Denmark	Katrin Loeschner
Finland	Pertti Koivisto
France	Gilles Rivière
Germany	Alfonso Lampen
Greece	Aristotelis Xenakis
Hungary	Andrea Zentai
Ireland	Patrick O'Mahony
Italy	Francesco Cubadda
Netherlands	Agnes Oomen
Portugal	Maria de Lourdes Bastos
Slovakia	Peter Simon
Slovenia	Viviana Golja
Spain	José Manuel Barat Baviera
Sweden	Lena Hellmer
United Kingdom	Sabrina Roberts
Norway	Ragna Bogen Hetland

- **External experts invited as speaker**

Claus Svendsen (Centre for Ecology & Hydrology, UK) (for item 6.4)

- **European Commission and EU Agencies:**

Nicolas Segebarth (DG RESEARCH, RTD.D.3)

Rafael Perez Berbejal (DG SANTE, DDG2.E.2.001)

Hubert Rauscher and Kirsten Rasmussen (DG JRC, F.2)

Celia Tanarro (ECHA, in videoconference on the second day)

- **EFSA:**

SCER Unit: Reinhilde Schoonjans (Scientific Officer and meeting Chair), Francesca Piombini (Assistant)

NUTRITION Unit: Reinhard Ackerl (Scientific Officer)

Scientific Committee member invited as speaker: Alicja Mortensen (ANS Panel Chair)

1. Welcome and apologies for absence

The Chair, Reinhilde Schoonjans (EFSA), welcomed the participants and everybody introduced him/herself during a tour de table.

Apologies were received from Popi Kanari (Cyprus), Angela Ivask (Estonia), Vaclovas Jurgelevicius (Lithuania), Wojciech Wasowicz (Poland), Andreia Alvarez Porto (DG SANTE, DDG2.E.2.001) and Siret Surva (DG SANTE, DDG2.E.2).

2. Adoption of agenda

The agenda was adopted without changes.

3. Agreement of the minutes of the 5th meeting of the Network on Nanotechnologies in Food and Feed held on 7-8 July 2015, Parma.

The minutes were agreed by written procedure on 10 December 2015 and published on the EFSA website on 11 January 2016.

4. Topics for discussion

4.1. Declarations of interest and confidentiality statements

Network members duly addressed declarations of interest and confidentiality statement according to the EFSA policy.

4.2. Presentation and discussion of EFSA

- **Update on the ongoing re-assessment of food additives by the EFSA ANS Panel**

The Chair of the EFSA ANS Panel, Alicja Mortensen, informed the participants that the Commission requested EFSA to start a programme for the re-evaluation of food additives. With this aim, Regulation (EU) No 257/2010 lays down rules for the re-assessment of food additives that were already permitted in the European Union before 20 January 2009.

For the re-evaluation of food additives, there are no applicants and no technical dossiers submitted, but interested parties who submit information following public calls for data.

During the ongoing re-evaluation, the ANS Panel noted that the manufacturing process for powdered or particulate food additives resulted in material with a range of sizes. Overall, these food additives are not designed as nanomaterial but the bulk materials may comprise a small fraction of the nanoscale material, which can be considered as unintentionally present or formed. However, none of the re-evaluated food additives were considered as nanomaterial according to the definition in Commission Recommendation of 18 October 2011 (2011/696/EU). This was concluded on the basis of data on particle size distribution and data on characterization for the food additives as submitted to EFSA by interested parties and/or gathered from the public literature. The Panel noted that no limits for particle size of any food additive are set in Commission Regulation (EU) No 231/2012 laying down specifications for food additives. Therefore, the ANS Panel has suggested the particle size and particle size distribution may be included in the EU specifications of the re-evaluated food additives.

The Network acknowledged the recommendations made by the ANS Panel, as they enhance the understanding of state of play for food additives and encouraged the recommendations be taken up in future data generation by interested parties.

- **Guidance on the human and animal risk assessment of the application of nanoscience and nanotechnologies in agri/food/feed: update and role of the NanoNetwork**

EFSA has started a new working group under the Scientific Committee to update its 2011 guidance on risk assessment of nanotechnologies in food and feed. Reinhilde Schoonjans (EFSA) discussed the required expertise with the network and the main issues to be addressed which will be considered in the fine tuning of the Terms of Reference of the mandate. The progress of this work will be presented on the yearly meetings and a public consultation on the draft guidance is planned in 2018. Appropriate liaison with ongoing work e.g. at JRC and ECHA is foreseen.

- **Tender specifications**

The network was informed about the intention to support the above mentioned working group with outsourcing under an existing EFSA framework contract. The subject of such outsourcing will be better defined considering the issues that emerged during the present and past network meetings.

4.3. Presentation and discussion of MSs

- **Risk communication of results of food additives evaluation that are partially as nano size in food materials**

Pertti Koivisto (FI) acknowledged that nanostructures in food/feed and food contact materials are well understood by the national safety officials. It is essential to make a difference between naturally occurring nanostructures and engineered nanomaterials. From the start of the discussion, safety has been considered as an important part of the legislation.

The network discussed that risk communication on engineered nanomaterials would require a case-by-case approach, but that in general, as for any new technology in the food/feed sector, the implementation of the new technology follows a cautious approach through legislation and regulatory science

development. National workshops including all involved stakeholders (i.e. producers, regulators, academics, consumer groups, media, and politicians), have been organised in a few a Member States and can be an effective platform for dialogue about the current state of the art and future directions.

- **Consequences of the implementation of the Novel Food Regulation with regard to nanomaterials and methods for their safety assessment**

Francesco Cubadda (IT) explained the new situation wherein a food consisting of engineered nanomaterial is a novel food under the new European Regulation on Novel Food, (EC) No 2015/2283. Vitamins, minerals or other substances that contain or consist of engineered nanomaterial are also considered novel foods: to be re-assessed first in accordance with this Regulation and subsequently in accordance with the relevant specific legislation. The engineered nanomaterial definition for food use is incorporated in this Regulation and deleted from Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers (FIC Regulation). Engineered nanomaterial thus requires a novel food authorization, with EFSA assessing potential risks. EFSA will have to verify that "the most up-to-date test methods are used to assess their safety". Furthermore, "When test methods are applied to nanomaterials, an explanation should be provided by the applicant of their scientific appropriateness for nanomaterials and, where applicable, of the technical adaptations and adjustments that have been made in order to respond to the specific characteristics of those materials".

- **New approach on hazard assessment for nanoforms (read-across) and recent publications from NL**

For read-across, Agnes Oomen (NL) explained a step-wise approach for read-across between nanoforms of the same substance. This step-wise approach is described in a working document by ECHA/RIVM/JRC[1], which is used by ECHA for guidance development. Data on physico-chemical properties of each nanoform are a crucial starting point. A read-across hypothesis between nanoforms can be substantiated by a kinetic argument (related to properties under 'where they go') and a hazard argument (related to properties under 'what they do').

Regarding intake and risk assessment of titanium dioxide nanoparticles through oral exposure, including toxicokinetic considerations, the Dutch representative explained that the oral intake of titanium dioxide (TiO2) and its nanofraction from food product, food supplements and toothpaste by the Dutch population has been estimated by Rompelberg et al. (2016)[2] based on measured concentrations of Ti and TiO2 nanoparticles in food products and food

[1] See https://echa.europa.eu/documents/10162/13630/eco_toxicological_for_bridging_grouping_nanoforms_en.pdf

[2] Rompelberg C, Heringa MB, van Donkersgoed, Drijvers J, Roos A, Westenbrink S, Peters R, van Bemmel G, Brand W and Oomen A 2016. Oral intake of added titanium dioxide and its nanofraction from food product, food supplements and toothpaste by the Dutch population. Nanotoxicology, Early Online: 1-11.

consumption data. In another recent study by RIVM[3], a risk assessment on oral intake of nano-TiO2 was performed, based on the information available and including toxicokinetic considerations. In toxicokinetic considerations it was considered important to include long-term tissue accumulation as well as very low oral absorption. Even though there is a margin between estimated organ levels in animal studies and estimated human organ levels, the Dutch research concludes that a health risk cannot be excluded as greater margins are desired to allow for factors such as inter- and intraspecies differences and study duration. The data presented by the speaker during the Nanonetwork meeting had been submitted to EFSA for consideration during the EFSA ANS Panel re-evaluation of E 171.

4.4. Presentation and discussion from EC and EU research

- **Safety research ongoing at DG JRC**

The OECD Test Guidelines Programme include Test Guidelines suitable for NMs. Work is ongoing in the areas of Read-across, Risk Assessment and Hazard assessment. Kirsten Rasmussen (DG JRC) gave an overview of the scientific support provided for the regulation of NMs (particularly on the nanodefinition), for research projects (such as NANoREG) feeding into the regulatory processes, and for filling the knowledge gaps (e.g. methods to detect NMs in products and the environment). Reference nanomaterials for size and also for other characteristics, as well as representative test materials are available or under development at DG JRC. The DG JRC is considering the whole life cycle in nanomaterial safety assessments. As a result of NANoREG, the terminology for nanomaterials is being harmonised and better accessibility to quality data is under development via agreed templates. The European Nanomedicine Characterisation Laboratory (EU-NCL) funded by the European Union's Horizon 2020 research and innovation programme has been established. The laboratory is a cooperative arrangement between Europe and the United States and the first European transnational infrastructure in nanomedicine. The laboratory will provide a trans-disciplinary testing infrastructure for Europe, fostering the deployment of standard operating procedures, benchmarking materials and quality management of medicinal nanoproducts. It will also promote inter-sectorial and interdisciplinary communication among key drivers of innovation, especially between developers and regulatory agencies.

- **Indication of the state of play on the implementation of the Novel Food Regulation with regard to NMs**

Rafael Perez Berbejal (DG SANTE), informed the participants that according to the new novel food regulation (EU) No 2015/2283, the Commission shall, by means of delegated acts, adjust and adapt the definition of engineered nanomaterials to technical and scientific progress or to definitions agreed at international level. The Commission is working on it. The legal procedure for a novel food application was discussed. According to the EU legislation, food is considered as novel when it has not been used for human consumption to a significant degree within the EU before 15 May 1997 and fall under the

[3] Heringa M, Geraets L, van Eijkeren JCH, Vandebriel RJ, Jong WH, and Oomen A, 2016. Risk assessment of titanium dioxide nanoparticles through oral exposure, including toxicokinetic considerations. Nanotoxicology, Online 29 Sept 2016.

categories established in the novel food regulation. The safety aspects of the novel food is one of the 3 conditions to be authorised.

- **Overview safety research in EU**

Nicolas Segebarth (DG Research&Innovation) informed about the substantial amount of nano safety research that is taking place in the EU under Horizon 2020. The aim is to remove obstacles to NanoTech innovation and trade through a science-based and responsible governance of nanotechnologies. The network remarked that there are no calls for research proposals relating specifically to nano in food (e.g. measuring the physicochemical properties in food matrices, in vitro digestion and bioavailability/toxicity of (engineered) nanomaterials in the food matrix) and that, as such, the field is at present underrepresented in the spectrum of ongoing and scheduled EU research activities. Nicolas Segebarth noted that Horizon 2020 does not allow for such specific calls but that food related nano-safety research is being tackled in the large projects (e.g. detection of nano in food matrices, ingestion toxicity endpoints, etc.).

- **The H2020 project consortium HISENTS: development of an array sensor for the determination of nanoparticles toxicity in mammals**

Peter Simon (SK) introduced the HISENTS project, having the vision to address the problem of the shortage of high-quality tools for nano-safety assessment by introducing an innovative multi-modular high throughput screening (HTP) platform including a set of individual modules, each of them representing a critical physiological function. These functions are connected and integrated in a hierarchical vectorial manner by a microfluidic network. The increase of the capacity to perform nano-safety assessment will be realised by innovative instrumentation developments for HTP. The project entails a comprehensive performance evaluation with respect to each individual device, a calibration of results with corresponding in vivo data and toxicity pathway analysis to model the toxicokinetics of a toxicant/nanomaterial in a simulated organism representing the multimodular device using a systems biology approach incorporating the physiologically-based pharmacokinetic (PBPK) model. The Network will be provided with regular updates of this project.

- **Development and validation of TEM methods in the context of the EC definition linked to the NANoREG project**

The network was informed by Pieter-Jan De Temmerman (BE) that methods (can) be implemented, uncertainties (can) be estimated and electron microchip based (and other) methods (can) be validated. The challenges to implementation are due to the following factors: 1A Automation (cheap, fast, many); 2T True (certified reference materials), Traceable (SI vs method-defined); 3S Size, Shape, Surface; 4M Multi-layered, Multi-component, Mixtures, Matrix; 5X sample preparation, sample preparation, sample preparation. There are issues with the tested material NM-300K (nano-silver) that interfere, but those interferences are not fully understood. Only with certain techniques (that pick up coating) different results are obtained. The role of the corona on nanomaterials requires further discussion. Distinguishing individual particles as primary particles in aggregated material is automated in the NanoDefine project, but under this project addressed manually. This method is however integrated in the imaging software under the NanoDefine project, which will have a fully

implementable manual (18 months from now, i.e. by the end of 2017). The method will also be applicable to body samples. Standard operating procedures for some sample preparation are however not developed under this project. As it remains crucial to see what is really in the matrix, one of the remaining challenges for detection is the availability of matrix/particle/method combination.

- **Exposure issues in environmental risk assessment for nanomaterials, focus on inputs to agriculture (e.g. nano pesticides, fertilizers, sludge and manure) - Perspectives from the NanoFASE (H2020) and NanoFARM (ERANETSIINN) projects**

The research results provided by Claus Svendsen, provide further insights in how environmental risk assessments for nanomaterial might develop further. The following general ideas were tabled for discussion: fate rules would help to identify if and where there may be possible nano exposure issues and inform what nanoform this might take. This would include product form, release form, pre-uptake form, internalised form and form at target. This information should be used to inform what constitutes the correct/most informative hazard data for each endpoint/organism of concern. Claus Svendsen also gave a prospect on various sources of information that can be expected to be useful for environmental risk assessment.

4.5. Presentation and discussion from risk assessment bodies

- **Guidance development at ECHA**

In 2012, ECHA prepared updates to the guidance on Information Requirements and Chemical safety Assessment (IR&CSA) in the form of Appendices to the guidance on "Recommendations for nanomaterials". These Appendices explained the issues that are different for nanomaterials (compared to non-nanomaterials). For instance: Appendix to R7a includes specific consideration regarding the information requirement (IR) on granulometry and Appendix to R14 includes specific consideration regarding exposure assessment for nanomaterials (available devices, measurement strategy etc.). As explained by Celia Tannaro (ECHA), ECHA is currently developing a new project for guidance on NMs, covering the topics of:

- Registration issues and nanoforms - New appendix to the guidance on Registration;
- Information requirements for human health - Update of the current guidance Appendix to Chapter R7.a Chapter R7.c;
- Information requirements for the environment - Update of the current guidance documents Appendix to Chapter R7.a, to R.7b and R7.c;
- Read-across between nanoforms - New Appendix to the Chapter R.6 of the guidance on IR&CSA on QSARs and grouping of chemicals.

This process includes transparent and multiple-step stakeholder consultations.

5. AOB

Food-grade material (i.e. authorised food ingredients with an E classification) to be used for research purposes are typically purchased from different sources online.

The network discussed the potential to launch a COST action on nanomaterials in food. This will be further explored by individual network members.

6. Date for next meeting

The next NanoNetwork meeting is currently scheduled for 29-30 June 2017 in the UK (London).

7. Conclusions

The Chair thanked the participants for all the information shared and for the relevant input given to the risk assessment work of EFSA.

8. Closure of the meeting