Network on Risk Assessment of Nanotechnologies in Food and Feed

Minutes of the 4th meeting

Held on 21-22 October 2014, Parma
(Agreed on 26 January 2014)

Participants

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

Country	Name
Austria	apologies
Belgium	Jan Mast
Bulgaria	Angel Angelov
Cyprus	apologies
Croatia	Darko Mikec
Czech Republic	Vladimir Ostrý
Denmark	apologies
Estonia	no nominations received
Finland	Liv Kukkonen
France	Gilles Rivière
Germany	Alfonso Lampen
Greece	Aristotelis Xenakis
Hungary	apologies
Ireland	Patrick O'Mahony
Italy	Francesco Cubadda
Latvia	no nominations received
Lithuania	no nominations received
Luxembourg	no nominations received
Malta	no nominations received
Netherlands	Agnes Oomen
Poland	Wojciech Wąsowicz
Portugal	Maria de Lourdes Bastos
Romania	No nominations received
Slovakia	Peter Simon
Slovenia	Viviana Golja
Spain	José Manuel Barat Baviera
Sweden	no nominations received
United Kingdom	apologies
Iceland	No nominations received
Liechtenstein	No nominations received
Norway	Ragna Bogen Hetland
Switzerland	no nominations received

- Hearing Experts

Qasim Chaudhry and Peter Hoet (for all items).

- European Commission:

Andreia Alvarez Porto, Sirkku Heinimaa (DG SANTE); Karin Aschberger, Hubert Rauscher (JRC).

- EFSA:

SCER Unit: Reinhilde Schoonjans (Chair), Tilemachos Goumperis

FIP Unit: Paolo Colombo

FEED Unit: Maria Vittoria Vettori

PRAS Unit: Andrea Terron, Maria Arena

AFSCO Unit: Jeff Moon, Julia Finger

- Others (if applicable such as WGs/other country representatives)

None

1. Welcome and apologies for absence

The Chair welcomed the participants. Apologies were received from Daniela Hofstaedter (Austria), Andrea Zentai (Hungary), David Gott (UK), Alicja Mortensen (Denmark), Popi Kanari (Cyprus), Hermann Stamm (JRC).

2. Adoption of agenda

The agenda was adopted without changes.

3. Agreement of the minutes of the 3th meeting of the Network on 6-7 June 2013, Parma.

The minutes were agreed by written procedure on 15 September 2013 and published on the EFSA website.

4. Topics for discussion

4.1 National cooperation and network coordination

Jeff Moon (EFSA AFSCO Unit) discussed with the Nano Network the procedures for the renewal of the EFSA Scientific Networks mandate, the nominations of representatives and the Terms of References of the Networks. He also presented the recommendations of a review carried out in 2013 and issued in 2013. A new provision, incorporated in the updated mandates, specifies that Member States representatives in this Network shall commit to liaise as appropriate at national level before and after each Network meeting. For the coordination of the networks at the national level, Focal Points are appointed to assist Network representatives in preparation for meetings and should receive a copy of Agenda of the nominated representative. Focal Points have the possibility to organise events at the MS level to 'network' between representatives.

4.2 EFSA Procurement Nanomaterial inventory

Karin Aschberger (JRC) presented on behalf of the contractors (RIKILT and JRC) the outcomes of the project "Inventory of nanotechnology applications in the agricultural, feed and food sector". The purpose of this inventory was to predict upcoming applications for EFSA. The members of the network welcomed the work delivered by the external contractors for EFSA and acknowledged the challenge to distinguish what is confirmed on the market and what is claimed or envisaged to be marketed. It was reminded that this is of great importance for consumers who should be able to distinguish what is now already in food and what is under development. France and Belgium are also working on national registries of Nanoparticles.

4.3 Nano Definition and issues around measurement

Hubert Rauscher (JRC) presented to the Nano Network the technical aspects for considering a material as a nanomaterial (NM) for the regulatory purpose of food labelling. Technical challenges exist particularly for particles with external dimensions in the lower nanometer range (below approximately 30nm), for nanoparticles embedded in complex matrices (such as food and feed), and for representative sampling. The formation of aggregates and the measurement of constituent particles in such aggregates deserves particular attention. The conversion of mass-based particle size distributions to number-based particle size distributions in the nanometre-scale is very problematic, and hence particle size measurements need to take into account the required number-based metrics. These challenges are being addressed in continued method development, with the goal of validating methods, including sample preparation, for specific purposes. One step forward would be to agree if the definition should be applied to the pristine state of the ingredient (rather than the final product) and whether it covers solid particles only (soluble or non-soluble). Exclusion from the definition is envisaged under food-law for natural, soft, and degradable nanomaterials. The NanoDefine project (FP7) is expected to deliver by 2017 an implementable test-scheme for regulatory purposes.

4.4 Update from Member states: DE - What mode of action do Nanomaterials have in Liver and Intestine?

Alfonso Lampen (DE) presented research results showing that the accumulation in enterocytes is lower for Ag-Pure NP than for Ag-PVP corona. The molecular effects were monitored and showed a Ag NP dose response with upregulation of 2134 genes and downregulation of 2918 genes. These nano-effects were confirmed with RT-PCR. The involved pathways are oxidative stress, loss of cell-cell contacts and cell-matrix contacts, and remodelling of cytoskeleton. Silver nanoparticles may indeed overcome the gastrointestinal juices in their particulate form without forming large aggregates. Silver particles can reach the intestinal epithelial cells after ingestion with only a slight reduction in their cytotoxic potential. Further research results are to be presented in 2015: an on-going NL-DE project is expected to unravel the influence/protection of food matrix components and digestion on the cytotoxicity of NP; an on-going DE-FR research is expected to unravel the influence on uptake and toxicity of solubility (Al -NP) versus non-solubility (TiO2).

4.5 Update from EU Member States: IT - 90 day oral toxicity study on SAS within the NanoReg project

Francesco Cubadda (IT) discussed with the network members the progress report of the only sub-chronic oral study in the large EU NanoReg project: a Repeated-Dose 90-day Oral Toxicity Study on Synthetic Amorphous Silica (E551). The global market volume of SAS is 1.5 million tons a year (i.e. not limited to food applications) and dietary exposure of the general population to nanosized SiO2 occurs and could increase in the near future. The results of SAS toxicokinetics of two different nanoforms showed that they had different kinetics, whereas common features were low oral bioavailability and relatively

slow tissue elimination. The goals of the 90-day study are to identify hazards and obtain dose-response data. The pyrogentic SAS nanoform is used with a soluble counterpart (silicic acid) as comparator. The endpoints of this ongoing study include tissue deposition, general toxicity, histopathology, genotoxicity, reproductive toxicity and immunotoxicity. The results will be available in 2015.

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5. Welcome and apologies for absence

The Chair welcomed the participants for the second half day of the meeting and extra apologies were received from Maria De Lourdes Bastos (Portugal).

6. Topics for discussion

6.1 Update from EU Member States: NL - research on SAS TK and SAS RA

Agnes Oomen (NL) presented novel insights into the risk assessment of the nanomaterial SAS in food. There are a lot of uncertainties and assumptions that make it difficult to draw firm conclusions on (1) Intake estimation (based on measurement in 27 products and worst case but on other hand not all product groups included) (2) Absorption (Worst case based on NanoGenotox data, not RIKILT data, Dose dependent, and SAS-type dependent) (3) Relevance of high dose oral toxicity studies for risk assessment (4) Extrapolation of kinetic data from rat to man (Allometric scaling and absorption) (5) Silica in tissues determined by measuring Si and assumed to be present as particles (control corrected), and (6) Differences between types/forms of silica (kinetics and toxicity). Initial concerns about nanomaterials are their potential slow elimination and accumulation and the potential variation and lack of information in behaviour between various forms/types. Therefore, assessment of combination of potential for accumulation and low oral absorption for realistic exposure by kinetic model should be explored. Some differences in behaviour of different nanoforms have been indeed observed, but there is no clear overview. A new issues of concern is that absorption is not linear with dose: high dose studies often used for tox testing for estimation safe dose and the high dose may result in aggregation, agglomeration, gelation and as a consequence dose-dependent absorption. Absorption may therefore decrease with increasing oral dose, leading to a potential underestimation of risk. High dose oral studies must only be applied with caution for nanomaterials. Focusing risk assessment on internal exposure in the target organ is a way forward to accommodate these issues.

6.2 Update from EU Member States: FR: Évaluation des risques liés aux nanomatériaux Enjeux et mise à jour des connaissances

Gilles Rivière (FR) presented the outcome of a review on the state of the art on nanomaterial risk assessment (i.e. not limited to food applications).The focus was to determine what are the substances already on the market that should be risk assessed. This was a challenging task due to limited information sources, high variability in collected information and variability in quality of the data. Gilles highlighted the methodological progresses needed in all domains relevant for risk assessment (higher quality in physico-chemical characterisations, set-up or adaptation of (eco-)toxicology testing realistic exposure; higher degree of harmonisation and standardisation of the methods. One of the major issues to be considered in risk assessment is the evolution of these materials all along their life cycle (oxidation state, dissolution or precipitation in a mineral form different than the initial, homo & hetero aggregation, adsorption, etc.) and the need for a multidisciplinary approach (e.g. discussion between experts of atmospheric pollution & nanomaterial). Many recommendations were made to help advance the scientific knowledge and address the needs for risk assessment, to steer risk management evolutions and legislation.

6.3 SCENIHR opinion on Nanosilver

Peter Hoet (KUL, SCHENIHR) presented the SCENIHR risk assessment opinion on Nanosilver, detailing the different nanoforms, the role of solubility on their toxicity and the different exposure routes and levels. During the discussion, special attention was given to the main risks due to toxic potential for nano-Ag and the selection for Ag resistant micro-organisms. The main conclusion is that over the already widespread and increasing use of silver containing products, additional effects caused by widespread and long term use of Ag-NPs cannot be ruled out. More data and more long term-exposure studies are needed.

6.4 Food additives re-evaluation programme

Paulo Colombo (EFSA FIP Unit) presented the food additives re-evaluation programme to be finalized by 2020 and a picture of the current situation. With respect to nanomaterials used as food additives, the Regulation (EC) No 1333/2008 Art 12 clearly mentions that if there is a change in particle size, for example through nanotechnology, the food additive shall be considered as a different additive. The ANS Panel evaluated nanomaterials (characterisation and identification, toxicity testing) mainly with cross-reference to the Guidance of the EFSA Scientific Committee of April 2011 ("Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain", http://www.efsa.europa.eu/en/efsajournal/doc/2140.pdf). A definition of "engineered nanomaterial" is specified in Regulation (EU) 1169/2011 and more clarity on the definition of "nanomaterial" and its characteristics is expected from the revision of the Recommendation of 18 October 2011 (EC OJ L 275/38). In the applications received by EFSA, there has been a clear distinction between adventitious particles and declared nanomaterial; and in the near future other food additives that could be in a nanoform will be assessed. Particular attention on this aspect will be paid.

7. Any Other Business

7.1 Date for next meeting: 7-8 July, Parma

7.2 Nanoplastics

The nanonetwork was asked to provide information on (1) MS activities to develop detection methods for micro/nano plastic particles in food (2) possible occurrence data from sampling food for micro/nanoplastics and (3) ongoing national or European research projects that address micro/nano plastics particles in food. Feedback will be transmitted to the EFSA CONTAM Unit.

7.3 Possible topics for next year

Food law is being implemented by the EFSA Panels. Nanomaterials are covered and addressed by cross-referring to the Nanomaterial Guidance from the Scientific Committee published in 2011. Food and feed additives currently comprise nano-fractions, but nano-specific data are not always provided. The EFSA Nano Network advises EFSA to assess the nano-fraction, no matter how small in % of the bulk material (particle size% or mass%).

The EFSA Nano Network also made the suggestion that EFSA could help in giving steer to research activities, especially on how to generate data useful for RA: e.g. low doses should be used in toxicity studies, and exposure assessment should be based on internal dose (not only external dose).

The EFSA Nano Network reminded about the useful work delivered by the former EFSA WG on nano and underlined new developments that could trigger new activities. There is a growing body of evidence showing that NP act very differently from the non-NP (both as hazard, fate in the environment and life cycle) and can cause harm. EFSA could clarify

the role of solubility and dissolution in toxicity and also take a position on soft nanomaterials.

Document history	
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