# Network & Working Group on Nanotechnologies in Food and Feed

# Minutes of the 7th Network meeting and 10th Working Group meeting

**Held on 28th November – 29th November 2017, Parma**

**(Agreed on 20 March 2018)**

## Participants

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

| Country | Name |
|---|---|
| Austria | APOLOGIES |
| Belgium | Jan Mast |
| Bulgaria | APOLOGIES |
| Croatia | Darko Mikec |
| Cyprus | APOLOGIES |
| Czech Republic | Vladimir Ostry |
| Denmark | Katrin Loschner |
| Estonia | Angela Ivask |
| Finland | Pertti Koivisto |
| France | Bruno Teste |
| Germany | Alfonso Lampen |
| Greece | Aristotelis Xenakis |
| Hungary | Andrea Zentai |
| Ireland | Karl McDonald |
| Italy | Francesco Cubadda |
| Lithuania | APOLOGIES |
| Luxembourg | Micheline Rosch |
| Netherlands | Jacqueline Castenmiller |
| Norway | Ragna Bogen Hetland |
| Poland | APOLOGIES |
| Portugal | APOLOGIES |
| Romania | Gina Popovici |
| Slovak Republic | Peter Simon |
| Slovenia | APOLOGIES |
| Spain | José Manuel Barat |
| Sweden | Lena Hellmer |
| United Kingdom | David Gott |

- **Nano working group:**

Alicja Mortensen (NANO WG Chair), Qasim Chaudhry (NANO WG vice Chair), Agnes Oomen (NANO WG member)

- **European Commission:**

Takis Daskaleros (DG SANCO), Hubert Rauscher (DG JRC)

- **EFSA:**

SCER Unit: Reinhilde Schoonjans (Scientific Officer and meeting Chair), Melpo Karamitrou (Trainee)

FIP Unit: Federica Lodi and Ana Maria Rincon (teleconference)

NDA Unit: Reinhard Ackerl (teleconference)

## 1. Welcome and apologies for absence

The Chair, Reinhilde Schoonjans, welcomed the participants.

Apologies were received from Daniela Hofstaedter (Austria), Angel Angelov (Bulgaria), Popi Kanari (Cyprus), Vaclovas Jurgelevicius (Lithuania), Wojciech Wąsowicz (Poland), Viviana Golja (Slovenia), Helena Carmo (Portugal)

## 2. Adoption of agenda

The agenda was adopted without changes.

## 3. Agreement of the minutes

### a. The minutes of the 6th meeting of the Network on Nanotechnologies in Food and Feed held on 30 June and 1 July 2016, Madrid.

The minutes were agreed by written procedure on 30 September 2016 and published on the EFSA website[1].

### b. The minutes of the 9th meeting of the Working Group on Nanotechnology in agri/food/feed

The minutes were agreed without changes and published on the EFSA website[2].

[1] https://www.efsa.europa.eu/en/events/event/160630

[2] https://www.efsa.europa.eu/sites/default/files/wgs/cross-cutting-science/wgNanotechnologies.pdf

## 4. Declarations of interest and confidentiality statements

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

Declarations of Interest of Working Groups members: In accordance with EFSA's Policy on Independence and Scientific Decision Making Processes and the Decision of the Executive Director on Declarations of Interest, EFSA screened the Annual Declaration of Interest and the Specific Declaration of Interest filled in by the working group members invited for the present meeting. No Conflicts of Interest related to the issues discussed in this meeting were identified during the screening process or at the Oral Declaration of Interest at the beginning of this meeting.

## 5. Topic for discussion: Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health.

The Chair, Reinhilde Schoonjans, introduced the goals of this meeting:

(1) Comments received from the Member States on the draft update of the guidance, are to be addressed immediately in the text. Comments which need further consideration will be addressed at the next working group meeting in March 2018. The major topics that needed clarification in each section are presented below.

(2) Outstanding tasks for the working group were addressed while going through each section of the guidance.

The Chair, Reinhilde Schoonjans (EFSA), welcomed the active contributions received by all participants beforehand. During a tour the table, all participants expressed their general views on this guidance.

### General comments and principles

In response to the general comments received from Member States, the following principles were clarified as underlying this draft guidance:

- This draft guidance appears as a summarising guidance to be followed by applicants as well as a (lengthy) scientific opinion explaining rationales. This is because this draft document can only give generic guidance and cannot anticipate every possible case with its specific requirements for risk assessment. Because of the latter, it was deemed beneficial that the draft guidance describes also to a large extent, the issues with materials that are known and that are relevant for safety.
- Nano specific data must come from the applicants, even if there is still some uncertainty on the legal framework for some materials. The guidance should stimulate safety testing.

- Where testing approaches and protocols are not yet established, this draft guidance cannot be more specific for risk assessment. Whilst highlighting the issues that require attention, it is expected that a degree of expert judgement will be applied to address them in risk assessment.

## Chapter 1: Introduction

1.2. Terms of Reference as provided by EFSA

It was asked how the draft guidance deals with risk assessment of nanomaterials in food supplements. Since food supplements contain nutrients, they will be assessed under the nutrient source legislation. In addition, a food supplement may be a novel food. In this section a few examples are presented for the products that are covered by the guidance. There is no need for an exhaustive list of examples.

1.2.2. Definition of nanomaterial

It was questioned whether the definition of nanomaterial is always followed in the guidance or to be determined on a case by case basis. Several situations have been outlined in the guidance to address this, based on current experiences with materials under assessment that do not fall clearly in the definition of nanomaterial as per the EU recommendation. In these situations, the general food law and the principles of this guidance apply.

For example, "*potential risks arising from specific properties related to the nanoscale have to be assessed focusing on such properties and potentially related hazards, which may be independent of the proportion of particles constituting the material with a size below 100 nm*". There is no scientific basis for establishing a threshold for such a proportion; moreover, there is a limit of detection of analytical techniques/uncertainties.

Regarding the "*particles above 100 nm which retain properties that are characteristic of the nanoscale*", a maximum size for a nanoparticle in that sense can also not be established. Such an upper limit is not specified in the guidance due to weak evidence. The upper sizes are associated with the capability for uptake by certain mechanisms by the gut (i.e. likely 250nm).

It was clarified that this guidance will be valid from its date of publication. EFSA guidance is not legally binding, but will be implemented by EFSA panels. Nano food or food supplement producers can already start following the guidance.

1.3. Scope of the guidance and when to apply

A concern was expressed that the minimum information that needs to be provided by the applicant is not clearly enough delineated from the extensive list of properties mentioned in the guidance. The concern is that

it will be very difficult for the applicants to investigate all these properties. The decision was taken not to make any changes and wait for the results from public consultation. Moreover, whilst the list of parameters to be provided is comprehensive, it is acknowledged that the entire set does not apply to each material. There is freedom for the applicants to not provide all the parameters upon justification.

## Chapter 2: Data and methodologies

No major comments on this chapter.

## Chapter 3: Risk assessment of nanomaterials: general outline

No major comments on this chapter.

## Chapter 4: Physicochemical characterisation of nanomaterial

4.1. Framework for distinguishing nanomaterials and non-nanomaterials

Changes were made in the text to enhance clarity as per suggestions by Member States. Figure 2 on the "*overview of NanoDefine global decision flow scheme material evaluation according to the EC nanomaterial definition*" will be substituted by a later version (after being published) with more explanation given upon such publication.

4.2. Material characterisation

As requested by a Member State, a footnote was added to explain the difference between a coating and a shell. For the purpose of this guidance, a material is considered as a 'coating' where it is bound or adhered to the surface of a nanomaterial in the form a continuous outside layer, or a 'shell' where it is in the form of a nanosized covering/casing in which a (nano)material may be contained.

Table 1: Comments from MSs were discussed, clarifications were given and changes were made in the Table. It was suggested by many of the MS representatives and decided by the WG members to divide this Table in three different sections: Table 1A-Information on the overall material, Table 1B-Information on the chemical components, Table 1C-extrinsic properties.

To have a clear image of the uncertainty of a value measured, applicants should provide details for particle size measurement units and they should also specify if the value is measured directly in the unit provided or converted from another unit.

The question was raised if homo/hetero agglomeration/aggregation should be discussed in the guidance. At present the working group experts consider this too difficult to be measured. It is acknowledged,

however, that lessons can be learned from the field of ecotoxicology, but no guidance can be given because tools are not available and the field is still in development.

## Chapter 5: Exposure Assessment

Parts of the text were found confusing and will be considered for rephrasing. Figures 1 and 3 will be checked for alignment.

## Chapter 6: Hazard identification and hazard characterisation

6.3: Toxicokinetics (ADME)

It was noted that this topic is still under scientific development e.g. with respect to optimal sizes for uptake. The main issue is the relative density of nanomaterials and their possible sedimentation. A suggestion was made to check ISSD models, but to go into public consultation with the text as it stands.

6.4: In vitro dissolutions tests

What happens if aggregation occurs? The working group considers that aggregation is not expected to be formed in physiological conditions as it needs high energy conditions and occurs typically during production.

6.5: Genotoxicity testing

It was suggested to consider from this section onwards the possible need to test the safety of the coating (if applicable), especially in the cases when the stability studies indicate that under physiological conditions the coating is released from the nanomaterial. The group considers this aspect extremely challenging and EU research is ongoing.

6.6: In vitro toxicity testing

It was asked how one can decide which in vitro assay to use. Examples that can be relevant are mentioned in this draft guidance, but the working group so far cannot give more guidance for tests nor endpoints.

6.7: In vivo repeated-dose 90-day oral toxicity study

It was noted by the Netherlands that this guidance suggests a risk assessment that relies heavily on animal studies. Not only a 90-day oral study is requested /advised, but for kinetic studies extensions are requested. In addition, it is noted that additional studies might be needed depending on the outcomes of the 90-day studies. Briefly, integrated or intelligent testing strategies are mentioned (section 6.10.1). This is not in line with the most recent scientific insights and societal demands to reduce animal testing (nor is it in line with the Dutch ambitions to replace animal testing for regulatory toxicology in a few years' time). EFSA is recommended to define a strategy and roadmap to replace the need for animal testing in its guidance in a few years' time. Likely this can be

achieved by improving the current in vitro models and in combination with in silico modelling (IVIVE: in vitro in vivo extrapolations).

In response to this note, it was mentioned that the tiered approach, including in vitro tests and read across, can indeed minimize the in vivo animal testing. Also, it can be better clarified in the text that the working group is in favour of reducing animal testing. This information will be elaborated in a new section on how to use this guidance.

6.8: Tiered approach to toxicity testing

It was clarified that also for conventional materials such a tiered approach is followed. The triggers needed for such a tiered approach are explained in this nano-specific guidance, but the approach is the same as for conventional materials.

- **Chapter 7: Risk characterisation**

No major comments received from the MSs.

- **Chapter 8: Uncertainty analysis**

No major comments received from the MSs.

- **Chapter 9: Conclusions and Recommendations**

No major comments received from the MSs.

- **Appendix A: NanoDefine Decision flow scheme**

The figure will be replaced by a more recent one (once published).

- **Appendix B: Demonstration fact sheet**

Changes will be made to avoid repetitions.

## 6. Date for next meeting

The 2018 Nano Network meeting will be scheduled depending on the outcome of the public consultation.

## 7. Conclusions

The Chair thanked the participants for all the extensive and valuable comments received on the draft guidance and for the constructive cooperation during the meeting.

## 8. Closure of the meeting