Concept paper on the revision of the 'Guidance on submissions for safety evaluation of sources of nutrients or of other ingredients proposed for use in the manufacture of foods'

1. Problem statement

Upon request from the European Commission, the EFSA Panel on Food Additives and Nutrient Sources (ANS Panel) often performs scientific assessments on nutrient sources or other ingredients added to foods because of their nutritional or physiological function.

Nutrient sources are typically used either as ingredients of food supplements or added to normal food for fortification purposes or in foods for specific groups (e.g. infant formula, food for special medical purposes).

The assessment performed by the ANS Panel is based on the information contained in a dossier submitted by an applicant to the European Commission in agreement with the currently applicable 'Guidance on submissions for safety evaluation of sources of nutrients or of other ingredients proposed for use in the manufacture of foods' issued by the former Scientific Committee on Food (SCF) in 2001.

This concept paper refers to the above guidance and discusses the need for its revision in light of the experience accrued by the ANS Panel over recent years and the evolving principles of risk assessment in the area of food ingredients.

The assessment of the nutritional and safety aspects of the nutrients will not be covered in this revised guidance

2. Discussion

The aim of the assessment of nutrient sources carried out by the ANS Panel is two-fold:

- Evaluation of the safety of the intact source; and
- Evaluation of the bioavailability of the nutrient from the source

With respect to the **safety of the intact source**, the principle of the assessment is not different from the safety assessment of food additives, for which updated guidance was adopted by the ANS Panel in 2012. This introduced the principles of a tiered approach to toxicological testing to reflect 3Rs principles (replacement, reduction, refinement). The current Guidance on Nutrient Sources makes reference to the earlier Guidance on Submissions for Food Additive Evaluations issued by the SCF in 2001, which uses an older paradigm which needs to be replaced.

Recently, the ANS Panel has been requested by the European Commission to assess the safety of nutrient sources that would also fall under the definition of 'novel food ingredients'. Also in this case, the guidance needs to be updated to make reference to the latest available guidance which is being issued by the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA Panel).

Similarly, in the event of nutrient sources consisting of, containing, or produced from genetically modified microorganisms or that would be classified as nanomaterial, the guidance should be updated in order to refer to the latest currently applicable guidance.

With respect to the **bioavailability of the nutrient from the source**, the current guidance neither provides a definition for this nor indicates which parameters should be measured for demonstrating bioavailability of the nutrient (or other ingredient) from its source following oral absorption. In its past assessments, the ANS Panel interpreted bioavailability implicitly as the amount of the nutrient which is systematically available (e.g. as measured in plasma or in urine following oral administration of the nutrient sources) however an explicit definition should be given in the revised guidance.

In addition for comparison of different nutrient sources it would be desirable to provide a definition of equivalent bioavailability.

In the majority of cases, nutrient sources are inorganic or organic salts, which have been assumed to dissociate prior to absorption following oral intake into its components.

The current guidance indicates that data on the bioavailability should be submitted, resulting from:

- Human studies
- *In vitro* studies
- Animal studies
- Information from analogous sources

In the revised guidance the relative merits and weaknesses of these approaches should be described. This will include consideration of their associated uncertainties and adequacy for risk assessment

Other points for consideration in the revised guidance would include:

- Revision of the technical data requirements, such as physicochemical characterisation of the source;
- The fate of the non-nutrient part of the source and, when relevant, its bioavailability;
- Data requirements on interaction between the source and different matrixes in which it is intended to be used and effects on bioavailability;
- Effect of particle size on bioavailability;
- Comparative data on bioavailability of the source and a 'reference' nutrient source

The Panel intends to base the new guidance on relevant existing approaches already incorporated into other regulatory frameworks.

3. Recommendation

A new guidance of the ANS Panel will be drafted, elaborating the items described above amongst others and taking into account issues raised and proposals submitted by stakeholders based on this concept paper.

4. Proposed timetable

This concept paper has been released on 8 June 2016 for 6 weeks for public consultation with all relevant stakeholders.

The comments received will be presented at a forthcoming Plenary meeting of the ANS Panel and then considered during the elaboration of the draft guidance.

It is expected the new guidance will be endorsed for public consultation by the ANS Panel in the first quarter of 2017, for final adoption by June 2017.

5. Interested parties

European Commission, EU Member States, National Competent Authorities, relevant food sector industry associations, academia, consumers group.

1. References.

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2012; Guidance for submission for food additive evaluations. EFSA Journal 2012;10(7):2760. 60 pp. doi:10.2903/j.efsa.2012.2760.

SCF (Scientific Committee on Food), 2001. Guidance on submissions for safety evaluation of nutrients or of other ingredients proposed for use in the manufacture of foods. Opinion expressed on 11 July 2001. Available at: http://ec.europa.eu/food/fs/sc/scf/out100_en.pdf