STATEMENT

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Approach followed for the refined exposure assessment as part of the safety assessment of food additives under re-evaluation

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Abstract

This statement describes the approach followed by the EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) for performing refined exposure assessment in the framework of the re-evaluation of already permitted food additives. Estimation of exposure is obtained through combination of different type of data originating from different sources: food additive concentration is obtained from information provided to EFSA on use levels and/or information obtained by means of analytical measurements. In recent years, the use of market research data has also been used. The statement provides also a description of the three different scenarios used for the exposure assessment of food additives under re-evaluation, from the more conservative regulatory maximum level exposure assessment scenario to more refined ones. Lastly, a description is provided on the approach used for the uncertainty analysis which accompanies the exposure assessment.

Keywords: dietary exposure, concentration data, Comprehensive European Food Consumption Database, food additives

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1. Introduction

This statement describes the approach followed by the EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) for performing refined exposure assessment in the framework of the re-evaluation of already permitted food additives. Current best practices, which are subject to continuous review and refinement based on the experience gained during evaluations, are also presented.

1.1. Background and Terms of Reference as provided by the requestor

1.1.1. Background

Food additives that can be placed on the market as such or used in foods under specified conditions of use are included in the Union lists in Annex II and III to Regulation (EC) No 1333/2008[1]. Food additives permitted before 20 January 2009 must go through a new risk assessment by the European Food Safety Authority (EFSA) as required by Regulation (EU) No 257/2010[2].

Annex II and III to Regulation 1333/2008 specify the name of the food additive and its E number, the foods, the food additives, food enzymes, flavourings and nutrients to which the food additive may be added, the conditions under which the food additive may be used, and if appropriate, whether they are any restrictions on the sale of the food additive directly to the final consumer. This information is essential to estimate dietary exposure.

In 2010, the Working Group of the ANS Panel on exposure assessment was set and started to develop a refined methodology to estimate dietary exposure to food additives. At the time, exposure assessment of food additives was based on budget method and summary statistics from few European Union (EU) countries.

This was also made possible with the development of the EFSA Comprehensive European Food Consumption Database (EFSA, 2011a), which includes food consumption data on all populations over 22 different Member States (MSs), thus allowing having a more complete picture of dietary exposure across Europe covering all almost age classes.

Since 2013, specific calls for occurrence data (use levels from industry and analytical data) on food additives are regularly launched. Given the range of data that have been made available through these recent calls, it was considered that all data should be used in distinct scenarios intended to provide more realistic exposure estimates.

Thus, in 2014, the Working Group (WG) on exposure assessment defined scenarios, still applied, in an approach document on food additive exposure assessment (not published).

This first methodology approach is now deemed necessary to be revised, e.g. by adding refined exposure scenarios on specific population groups such as infants and young children consuming food for special medical purposes. Clarifications on the use of the data received through the call for data will also be included in the updated approach. In addition, since 2015, EFSA has access to a food market research database which is used in exposure assessment of food additives in order to cross-check the usage of the food additives which are on the market. How the ANS Panel makes use of this database will also be part of the statement.

1.1.2. Terms of Reference

In accordance with Article 29(1) of Regulation (EC) No 178/2002[3], EFSA asks its scientific ANS Panel to provide a Panel statement on the approach followed for the refined exposure assessment as part of the safety assessment of food additives under re-evaluation.

[1] Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354, 31.12.2008, p. 16–33.

[2] Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, p. 19–27.

[3] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.

2. Data and methodologies

2.1. Data

2.1.1. Food additive concentration data availability

In the framework of the re-evaluation programme, EFSA has issued several public calls for usage and/or concentration data (analytical data) on food additives to be re-evaluated since 2013.[4]

Data on use levels of food additives have been provided by the food industry, food industry associations and food additive(s) producers. Mainly national food authorities of the MSs have provided analytical data.

2.1.1.1. Information submitted on use levels

The amount of information received for each food additive or group of food additives varies considerably, ranging from no data provided for authorised uses laid down in Annex II to Regulation (EC) No 1333/2008 on food additives, to data covering nearly all authorised uses.

The majority of the information provided so far has been made available by food industry associations that collect data from their members.

To use these data for the exposure assessment, data providers should categorise the product items according to the food categorisation of Annex II, Part D (Reg (EC) No 1333/2008), including the original name of each product.

Typically, very limited information is provided about the representativeness of the use levels submitted with respect to the food market share. In some case, data providers specify whether a level refers to a niche product (a niche product is identified by industry, e.g. as only used by a specific population group). In the case that a reported use level refers to a niche product which belongs to a food category for which additional reported use levels are available, that reported use level is excluded from the exposure assessment. If no other levels, usage or analytical data, are available, the reported use level for a niche product can be taken into account. The possible under/overestimation of the contribution of the food category to which the niche product belongs to the overall exposure should be stated in the opinion.

It should also be noted that industry (food industry, food industry associations and food additive producers) may provide additional information about the 'non-use' of a food additive in a food category in which the additive is authorised. This information is of high relevance for the exposure assessment, but it has been rarely provided up to now. However, if explicitly stated by industry that the food additive is not used in a specific food category, this food category will not be taken into account in the refined scenarios and this information will be made explicit in the opinion.

2.1.1.2. Information submitted on analytical data

Analytical data for food additives are mainly submitted by MSs. The number of data provided per food additive can vary, ranging from no analytical data up to several thousands.

A significant part of these analytical data may be left censored (i.e. either below the limit of detection (LOD) or the limit of quantification (LOQ)), or qualitative (only an indication of the presence or absence of the food additive in the sample). In addition, analytical data may be provided for food categories in which a given food additive is not authorised according to Annex II to Regulation (EC) No 1333/2008. The presence of the food additive in those food categories could be for instance due to carry-over or natural occurrence.

To consider left-censored analytical data, the substitution method as recommended in the 'Principles and Methods for the Risk Assessment of Chemicals in Food' (WHO, 2009) and the EFSA scientific report 'Management of left-censored data in dietary exposure assessment of chemical substances' (EFSA, 2010) is used and the mean or median, whichever is highest, middle-bound concentration is calculated.

For the same reason mentioned above (carry-over, natural occurrence), it can also be that analytical data exceed the maximum permitted levels (MPL) as defined in Annex II to Regulation (EC) No 1333/2008. In the refined dietary exposure estimates, only authorised uses with analytical data at or below the MPL are considered because results above MPL are part of risk management measures, e.g. non-compliance purpose. For this reason, such results are not taken into account, except in specific cases as appropriate (e.g. in case of natural occurrence).

[4] http://www.efsa.europa.eu/en/calls/data

2.1.2. Market research data: use of the Mintel GNPD

EFSA has access to the food label database developed by Mintel, the Global New Products Database (GNPD).[5] This database is an online database, which observes product introductions in consumer packaged goods markets worldwide. The Mintel GNPD contains data of EU food markets since 1996 and currently 20 of its 28 member countries and Norway are presented in the Mintel GNPD.[6] New foods are regularly added to the database.

For the purpose of exposure assessments in the scientific opinions of the ANS Panel, the Mintel GNPD is used to check food product labels for food additives as GNPD shows the compulsory ingredient information presented on product labels. Only the food additives authorised under Annex II to Regulation (EC) No 1333/2008 are mandatory to be labelled on the ingredient information. When information on a food additive is available in the GNPD, the number (and percentage) of foods labelled with the food additive per food category is reported in the opinion stratified according to food categories.

The aim of using the Mintel GNPD is to compare the food categories for which use and analytical data were reported to EFSA with the list of foods labelled to contain the food additive, together with the list of authorised uses by the EU legislation.

The Panel agreed to use this database as a qualitative tool according to the decision tree as presented in the 64th ANS plenary meeting during the discussion of the karaya gum scientific opinion[7] and summarised below:

- There is sufficient usage/analytical data and sufficient information from the Mintel GNPD: GNPD will be used to confirm that the food additive is used in all food categories, and a table will be added listing the number and percentages of products in which the food additive is labelled per food (sub-) category according to the Mintel GNPD food classification and over all foods categories analysed in the opinion.
- There is an insufficient amount of usage/analytical data but abundant products labelled to contain the food additive in the Mintel GNPD: a refined exposure assessment based on the occurrence data provided by industry and/or MSs will be conducted. Acknowledgement of the possible underestimation will be done. A table will be added as in previous bullet in opinions.
- There is a sufficient amount of usage/analytical data but only a few products labelled to contain the food additive in the Mintel GNPD: a refined exposure assessment based on the concentration data provided by industry and/or MSs will be conducted. The possible overestimation in relation to the Mintel GNPD data used will be acknowledged. This should be done on case-by-case basis when dealing with food categories with less food in the Mintel GNPD. Refinement of the exposure assessment based on Mintel information, i.e. not taking into account food (sub-)categories for which no foods were labelled with the food additive in GNPD will be done when further refinement of exposure assessment is needed.
- There is insufficient usage/analytical data and only a few products presented in the Mintel GNPD: The Mintel GNPD can be used to confirm the low use of the food additive. In this case, only the MPL scenario can be calculated, given MPLs are available. If the MPL scenario does not raise a health concern, the exposure assessment does not have to be refined further. In case the MPL scenario raise a health concern, a refined scenario based on the Mintel GNPD information, i.e. by removing food categories/subfood categories for which no foods were labelled with the food additive can be performed. When MPLs are set according to *quantum satis* (QS), no exposure assessment can be done; only qualitative information from the Mintel GNPD will be given.

2.1.3. Food consumption database

The EFSA Comprehensive European Food Consumption Database (Comprehensive Database) (EFSA, 2011a) is used to estimate exposure for the six following population groups: infants (from 12 weeks of age), toddlers (also named young children), children, adolescents, adults and the elderly.

Consumption records were codified according to the FoodEx classification system (EFSA, 2011a). Nomenclature from the FoodEx classification system has been linked to the food categories as presented in Annex II, Part D, of Regulation (EC) No 1333/2008, to perform exposure estimates. In practice, FoodEx food codes were matched to the food categories.

[5] http://www.gnpd.com/sinatra/home/
[6] Missing Bulgaria, Cyprus, Estonia, Latvia, Lithuania, Luxembourg, Malta and Slovenia.
[7] http://www.efsa.europa.eu/sites/default/files/event/160426-m.pdf

Food categories in which the use of the food additive is authorised are selected from the nomenclature of the EFSA Comprehensive Database (FoodEx classification system) (EFSA, 2011b).

2.2. Methodologies

2.2.1. Exposure assessment of food additives under re-evaluation

The Panel estimates chronic exposure to food additives. Exposure assessments of food additives under re-evaluation are carried out by the ANS Panel based on two different sets of concentration data: (a) MPLs of use set down in the EU legislation (defined as *regulatory maximum level exposure assessment scenario*) and (b) use levels and/or analytical data provided through the calls for data (defined as *refined exposure assessment scenario*).

The *regulatory maximum level exposure assessment scenario* is based on the MPLs as set in Annex II to Regulation (EC) No 1333/2008. For the food additives authorised according to QS in all or part of food categories, a *maximum level exposure assessment* scenario is estimated instead based on concentration data provided to EFSA, as described in the EFSA Conceptual framework (EFSA ANS Panel, 2014).

In both exposure assessment scenarios, food additive concentration values (MPL, usage or analytical data) are combined, at individual level, with national food consumption data from the EFSA Comprehensive Database[8] considering the six different population groups above mentioned.

Qualitative information from the Mintel GNPD is considered in the refined exposure assessment scenario to validate the data submitted by industry.

In the refined exposure assessment scenario, the concentration levels considered by the Panel are extracted from the whole data set received (i.e. reported use levels and analytical data).

Use levels reported by food additive producers are not considered at the same level as those provided by food industry. The ANS Panel considered that food additive producers might recommend use levels to the food industry, but the final levels used might, ultimately, be different. Therefore, unless food additive producers confirm that the recommended levels are used by food industry, they are not considered in the refined exposure scenario. Data from food additive producers will only be used in the *maximum level exposure assessment* scenario in case of QS authorisation when no data are available from food industry. In this way, the most comprehensive exposure estimates are calculated. All reported usage data will be presented in the appendixes of the scientific opinion for acknowledgment and information.

The main food categories contributing to the total mean exposure to the food additives are provided in each opinion for each scenario.

The two exposure scenarios do not consider the exposure to food additives via their use in food supplements and foods for special medical purposes (FSMP). Potential exposure to food additives via the consumption of food supplements is covered in specific exposure scenarios, considering consumers only, in order to reflect additional exposure to food additives from food supplements compared to exposure to food additives from food. According to Regulation (EC) No 1333/2008, the food supplement category excludes 'food supplements for infants and young children'. Therefore, exposure to food additives from food supplements will only be considered for the following population groups: children, adolescents, adults and the elderly.

Exposure to food additives from FSMP can only be considered for infants and toddlers assuming that the amount consumed of FSMP in these populations is similar to the consumption of comparable foods (e.g. infant formula) in infants and toddlers from the general population. FSMP consumed in other population groups cannot be considered because of very limited information on consumption from EFSA Comprehensive Database.

2.2.1.1. Regulatory maximum level exposure assessment scenario

The regulatory maximum level exposure assessment scenario is based on MPLs of use as set in Annex II to Regulation No 1333/2008. Therefore, it only includes food categories authorised according to this Annex or any other legislation clearly defining the food or food category in which the food additive might be added with an MPL as a numerical level (e.g. Annex III of the same Regulation, Regulation No 606/2009 on wines[9]).

[8] http://www.efsa.europa.eu/en/food-consumption/comprehensive-database

[9] Commission Regulation (EC) No 606/2009 of 10 July 2009 laying down certain detailed rules for implementing Council Regulation (EC) No 479/2008 as regards the categories of grapevine products, oenological practices and the applicable restrictions. OJ L 193, 24.7.2009, p. 1–59.

As mentioned above, for food additives authorised according to QS in all or part of the food categories, a maximum level exposure assessment scenario is performed based on the maximum reported use levels provided by industry or on the highest percentile different from the maximum (p95/p90 depending of the number of observations) of analytical data provided by MSs whichever is highest or available, as described in the EFSA Conceptual framework (EFSA ANS Panel, 2014). Food categories authorised at QS and for which usage or analytical data are not available or adequate, are not considered in this scenario. Therefore, the safety assessment carried out by the ANS Panel will be limited to those food categories for which either an MPL or analytical/usage data are available.

The exposure estimates derived following this scenario should be considered as the most conservative for the food categories considered as it assumes that the population group will be exposed to a food additive present in food at the MPL or maximum reported use level in case of QS authorisation, over a longer period of time. However, when a low percentage of authorised food categories is considered in this scenario, it is uncertain whether the regulatory maximum level scenario is also conservative for overall dietary exposure or just for the food categories considered. This may apply especially to situations with many food categories in which the additive is authorised at QS.

2.2.1.2. Refined exposure assessment scenarios

The refined exposure assessment scenario is based on information on use levels and/or analytical data and can only be carried out if sufficient and adequate data have been reported. These refined scenarios should be performed taking into account the authorised food categories according to Annex II to Regulation No 1333/2008. Food additives authorised according to Annex III but not to Annex II are addressed in additional scenarios as described in section 4.3.

During its 52nd plenary meeting, the ANS Panel agreed to provide two refined exposure estimates based on different model populations as follows:

The brand-loyal population:

This estimate is based on the assumption that an individual is a long-term brand-loyal consumer of one food category containing the food additive at the highest level reported/highest percentile different from the maximum level analysed and non-brand-loyal to the other food categories in the diet, which contain the food additive at the mean/median of typical reported use level or analytical data.

The general population:

This estimate is based on the assumption that an individual is not brand-loyal to any specific brand available on the market and exposed to the food additive via the diet containing the food additive at the mean/median of typical reported use level or analytical data (non-brand-loyal scenario).

If both usage and analytical data are available for the same food group, the highest reliable value (based on expert judgement) for the food category under consideration is used.

As mentioned previously, food categories for which none or inadequate information regarding the use/occurrence of a food additive is available to EFSA (obtained from industry or from MSs) cannot be included in the refined exposure assessment. Consequently, the exposure assessment carried out by the ANS Panel will be limited to those food categories for which information is available. Exclusion of food categories for which data is not available might result in underestimation of the true exposure. The percentage of the food taken into account in the refined exposure estimates out of all food categories authorised should be provided.

Overall, the refined exposure assessment scenario is suitable to calculate the most realistic exposure estimates to food additives given the available data as the exposure is estimated for both brand- and non-brand-loyal consumers. Moreover, assigning the mean concentration of the food additive to processed food consumed by a given population is consistent with general chronic exposure approaches.

Which of the refined exposure scenario is used for the risk characterisation will be determined on a case-by-case basis.

It should also be noted that refined exposure scenarios may result in an underestimation of the true exposure for brand-loyal consumers or the general population in certain case, e.g. when not all food categories could be taken into account. Furthermore, these estimates will not cover future changes of food additive use in the market.

2.2.1.3. Other exposure assessment scenarios

Additional exposure scenarios might be considered when concentration levels are made available to EFSA on food categories which are not authorised according to Annex II to Regulation No 1333/2008. In order to consider the presence of food additives due to carry-over or due to natural occurrence, additional exposure scenarios can be performed taking into account the availability of data.

As a general basis, exposure to impurities and by-products, e.g. heavy metals and process contaminants, will not be estimated by default.

2.2.2. Uncertainty analysis

In accordance with the guidance provided in the EFSA opinion related to uncertainties in dietary exposure assessment (EFSA, 2007), the sources of uncertainties considered are summarised in each opinion in a table. They are related to the food consumption data and to the concentration data (usage or analytical data) used, and to the scenarios presented in the opinions.

An uncertainty paragraph summarises the uncertainties listed in the table and indicates whether the exposure estimates can be considered as under- or overestimations of the true exposure.

References

EFSA (European Food Safety Authority), 2007. Scientific opinion of the Scientific Committee related to uncertainties in dietary exposure assessment. EFSA Journal 2007;5(1):438, 54 pp. https://doi.org/10.2903/j.efsa.2007.438

EFSA (European Food Safety Authority), 2010. Management of left-censored data in dietary exposure assessment of chemical substances. EFSA Journal 2010;8(3):1557, 96 pp. https://doi.org/10.2903/j.efsa.2010.1557

EFSA (European Food Safety Authority), 2011a. Use of the EFSA Comprehensive European Food Consumption Database in Exposure Assessment. EFSA Journal 2011;9(3):2097, 34 pp. https://doi.org/10.2903/j.efsa.2011.2097

EFSA (European Food Safety Authority), 2011b. Evaluation of the FoodEx, the food classification system applied to the development of the EFSA Comprehensive European Food Consumption Database. EFSA Journal 2011; 9(3):1970, 27 pp. https://doi.org/10.2903/j.efsa.2011.1970

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources), 2014. Statement on a conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010. EFSA Journal 2014;12(6):3697, 11 pp. https://doi.org/10.2903/j.efsa.2014.3697

WHO (World Health Organization), 2009. Principles and methods for the risk assessment of chemicals in food, International Programme on Chemical Safety, Environmental Health Criteria 240. Chapter 2: risk assessment and its role in risk analysis.

Abbreviations

ANS Panel	EFSA Panel on Food Additives and Nutrient Sources added to Food
FSMP	foods for special medical purposes
GNPD	Mintel's Global New Products Database
LOD	limit of detection
LOQ	limit of quantification
MPL	maximum permitted level
MSs	Member States
QS	*quantum satis*
WG	Working Group
WHO	World Health Organization