Safety of the proposed amendment of the specifications for microcrystalline cellulose (E 460(i)) as a food additive

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)

Abstract

Following a request from the European Commission, the EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS) provided a scientific opinion regarding the safety of an amendment of the specifications for the food additive microcrystalline cellulose (E 460(i)). The scope of the current application was to amend the solubility of the food additive to ‘practically insoluble or insoluble in sodium hydroxide solution’. Currently, the existing EU specifications describe microcrystalline cellulose as ‘slightly soluble in sodium hydroxide’. In support of the request, the applicant carried out solubility tests on four batches of microcrystalline cellulose (E 460(i)). Because the concentration of sodium hydroxide solution to be used for the solubility tests is not indicated in the applicable JECFA testing procedures, the applicant performed the test using a concentration (50 g/L) as specified in the European Pharmacopeia. The tests indicated that the quantity of sodium hydroxide solution required to dissolve 1 g of the sample is more than 10,000 mL. The Panel noted that no analytical measurements of the solubility in a range of concentrations of sodium hydroxide solution were submitted in the application dossier and that, according to published information, the solubility of microcrystalline cellulose depends on the concentration of sodium hydroxide solution. The Panel also noted that in the current EU specifications for microcrystalline cellulose (E 460(i)) the concentration of sodium hydroxide solution to be used for testing solubility is not given. Therefore, the Panel concluded that the amendment to the specifications as regards the solubility of microcrystalline cellulose (E 460(i)) proposed by the applicant would not give rise to a safety concern. However, the Panel recommended that the concentration of sodium hydroxide solution to be used in the solubility test should be indicated in the EU specifications.

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1. Introduction

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

1.1.1. Background

The use of food additives is regulated under the European Parliament and Council Regulation (EC) No 1333/2008 on food additives. Only food additives that are included in the Union list, in particular in Annex II to that Regulation, may be placed on the market and used in foods under conditions of use specified therein. Moreover, food additives shall comply with the specifications as referred to in Article 14 of Regulation and laid down in Commission Regulation (EU) No 231/2012.

Microcrystalline cellulose (E 460(i)) is an authorised food additive in the European Union (EU) for use in several food categories and specifications have been adopted for it. Presently, those specifications stipulate for the parameter ‘Solubility’ that the food additive is ‘Insoluble in water, ethanol, ether and dilute mineral acids. Slightly soluble in sodium hydroxide solution’.

The European Commission received a request vis-à-vis an amendment of the present specifications of microcrystalline cellulose (E 460(i)) for that parameter ‘Solubility’ as follows: ‘Insoluble in water, ethanol, ether and dilute mineral acids. Practically insoluble or insoluble in sodium hydroxide solution’.

1.1.2. Terms of Reference

The European Commission requests the European Food Safety Authority (EFSA) to provide a scientific opinion as regards a proposed amendment of the specifications of the food additive microcrystalline cellulose (E 460(i)) in accordance with Regulation (EC) No 1331/2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings.

1.2. Interpretation of the Terms of Reference

In order to address the safety of this proposed change in specifications, the Panel decided that an evaluation of the possible impact of this proposed change on the characteristic of the product and on its safety profile would be adequate.

The Panel considered that this change was not due to a modification in the manufacturing process of microcrystalline cellulose (E 460(i)).

The safety of microcrystalline cellulose (E 460(i)) as food additive will be considered under the re-evaluation programme for food additives already permitted in the EU before 20 January 2009, as envisaged by Commission Regulation (EU) No 257/2010. Meanwhile, the Panel considered that the available toxicological assessment of microcrystalline cellulose would remain valid and in principle there would be no need to reconsider this to address the Terms of Reference.

1.2.1. Information on existing evaluations and authorisations

Currently, microcrystalline cellulose (E 460(i)) is an authorised food additive in the EU at quantum satis (QS), in almost all authorised food categories. It is also included in Group I of food additives authorised at QS.

The safety of microcrystalline cellulose (E 460(i)) as a food additive is currently being re-evaluated by EFSA.

2. Data and methodologies

2.1. Data

The applicant has submitted a dossier requesting changes to existing specifications. The application was supported by data related to the solubility of the food additive microcrystalline cellulose (E 460(i)) (Documentation provided to EFSA n. 1).

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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 Regulation (EC) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council. OJ L 83, 22.3.2012, p. 1-295.
3 EFSA Register of Questions: http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2011-00545
2.2. Methodologies

The current ‘Guidance for submission for food additive evaluations’ (EFSA ANS Panel, 2012) has been followed by the Panel for evaluating the proposed change in specifications, with regard to the solubility.

The assessment was conducted in line with the principles described in the EFSA Guidance on transparency in the scientific aspects of risk assessment (EFSA SC, 2009) and following the relevant existing Guidances from the EFSA Scientific Committee.

The interpretation of the descriptive term for approximate solubility ‘practically insoluble or insoluble’ in the Identification Tests in JECFA specifications means that more than 10,000 parts of solvent is required for 1 part of solute (JECFA, 2006).

3. Assessment

3.1. Technical data

3.1.1. Specifications

The proposed amendment by the applicant to the existing EU specifications for the food additive microcrystalline cellulose (E 460(i)), is given in Table 1.

Table 1: Existing EU specifications for food additive microcrystalline cellulose (E 460(i)) according to Commission Regulation (EU) No 231/2012 and proposal for amendment as requested by the applicant

| Specifications according to Commission Regulation (EU) No 231/20102 | Requested amendment by the applicant |
|---------------------------------------------------------------|-------------------------------------|
| **Synonyms** | Cellulose gel | None |
| **Definition** | Microcrystalline cellulose is purified, partially depolymerised cellulose prepared by treating alpha-cellulose, obtained as a pulp from strains of fibrous plant material, with mineral acids. The degree of polymerisation is typically less than 400 | None |
| Einecs | 232-674-9 | None |
| Chemical name | Cellulose | None |
| Chemical formula | (C₆H₁₀O₅)ₙ | None |
| Molecular weight | About 36,000 | None |
| Assay | Not less than 97% calculated as cellulose on an anhydrous basis | None |
| Particle size | Not less than 5 μm (not more than 10% of particles of less than 5 μm) | None |
| Description | A fine white or almost white odourless powder | None |
| Identification | | |
| Solubility | Insoluble in water, ethanol, ether and dilute mineral acids. Slightly soluble in sodium hydroxide solution | Insoluble in water, ethanol, ether and dilute mineral acids. Practically insoluble or insoluble in sodium hydroxide solution |
| Colour reaction | To 1 mg of the sample, add 1 mL of phosphoric acid and heat on a water bath for 30 min. Add 4 mL of a 1 in 4 solution of pyrocatechol in phosphoric acid and heat for 30 min. A red colour is produced | None |
| Infrared absorption spectroscopy | To be identified | None |
The applicant provided data related to solubility of microcrystalline cellulose in sodium hydroxide solution as part of the dossier. The tests were performed on four different batches and in compliance with the JECFA testing procedures for solubility (JECFA, 2006). Because the concentration of sodium hydroxide solution to be used for the solubility tests is not indicated in the JECFA testing procedures, the applicant performed the test using a concentration (50 g NaOH/L) as specified in the European Pharmacopeia (Ph.Eur. 8.0, 2014).

The analyses were performed as follows: four individual quantities of microcrystalline cellulose, i.e. 0.0089, 0.0088, 0.0089 and 0.0088 g, respectively, were mixed with 100.0 mL of sodium hydroxide solution (concentration: 50 g NaOH/L), corresponding to 1 g of the sample mixed in 10,000 mL of sodium hydroxide solution.

3.1.2. Manufacturing process

The Panel noted that the applicant has submitted information on the manufacturing process used to produce microcrystalline cellulose which is consistent with the manufacturing process in the definition of the food additive according to Regulation (EU) No 231/2012.

4. Discussion

No analytical measurements of the solubility in a range of sodium hydroxide solution were submitted in the application dossier.

The Panel noted that according to published information (Kuo and Hong, 2005), the solubility of microcrystalline cellulose depends on the concentration of sodium hydroxide solution.

The Panel considered that this proposed change in the definition of solubility was not due to a modification in the manufacturing process of microcrystalline cellulose (E 460 (i)).

In the current EU specifications for microcrystalline cellulose (E 460(i)) the concentration of sodium hydroxide solution to be used for testing solubility is not given.
5. **Conclusions**

Following the request by the European Commission, the Panel considered that the change in the specifications as regards the solubility of microcrystalline cellulose (E 460(i)) proposed by the applicant would not give rise to a safety concern.

6. **Recommendations**

The Panel recommended that the concentration of sodium hydroxide solution to be used for the solubility test should be indicated in the EU specifications.

**Documentation provided to EFSA**

1) Dossier ‘Application for a modification of the specifications of an already authorised food additive – MICROCRYSTALLINE CELLULOSE, CELLULOSE GEL, E 460 (i)’. Submitted by ASAHI KASEI Chemicals Corporation on 26 January 2016.

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EFSA SC (Scientific Committee), 2009. Guidance of the Scientific Committee on transparency in the scientific aspects of risk assessment carried out by EFSA. Part 2: general principles. EFSA Journal 2009;7(5):1051, 22 pp. doi:10.2903/j.efsa.2009.1051.

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 2006. Analytical methods, test procedures and laboratory solutions used by and referenced in the food additive specifications. Combined Compendium of Food Additive Specifications, Vol. 4. Food and Agriculture Organization of the United Nations, Rome, 41 pp.

Kuo YN and Hong J, 2005. Investigation of solubility of microcrystalline cellulose in aqueous NaOH. Polymers for Advanced Technologies, 16, 425–428.

Ph.Eur. 8.0, 2014. Microcrystalline Cellulose. European Pharmacopoeia, pp. 1824–1828.

**Abbreviations**

| Abbreviation | Description |
|--------------|-------------|
| ANS Panel    | EFSA Panel on Food Additives and Nutrient Sources added to Food |
| JECFA        | Joint FAO/WHO Expert Committee on Food Additives |
| QS           | quantum satis |