European Food Safety Authority

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## SCIENTIFIC OPINION

# Scientific Opinion on the safety evaluation of the substance zinc oxide, nanoparticles, uncoated and coated with [3-(methacryloxy)propyl] trimethoxysilane, for use in food contact materials[1]

**EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)**[2,3]

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## ABSTRACT

This scientific opinion of the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) deals with the safety assessment of zinc oxide, nanoparticles, uncoated (FCM No 1050) and coated with [3-(methacryloxy)propyl] trimethoxysilane (FCM No 1046), for use as a transparent ultraviolet light absorber in all polyolefins at a maximum content of 2 % and 3 % for the uncoated and the coated species, respectively. The substance is used as a powder in nanoform. In the final polymer, nanoparticles are still present but largely aggregated. The specific migration of the substance was tested from low-density polyethylene films, containing the maximum use level of the substance, into 3 % acetic acid and 10 % and 50 % ethanol for 10 days at 60 °C. Data from a stress test with iso-octane for 10 days at 20 °C was provided. Migration values into the different simulants and the microscopic analysis of swollen polymers demonstrate that there is no mass transfer of the zinc oxide in nanoform. In 2003 the Scientific Committee on Food established for zinc a no observed adverse effect level of 50 mg/day and an upper limit of 25 mg/person per day was recommended. The CEF Panel concluded that zinc oxide, nanoparticles, uncoated or coated with [3-(methacryloxy)propyl]trimethoxysilane, does not migrate in nanoform, and therefore the safety evaluation focuses on the migration of soluble ionic zinc. Available migration data for ionic zinc coming from the intended application are in compliance with the current specific migration limit (SML), but in combination with the dietary exposure from other sources the upper limit of 25 mg/person per day could be exceeded. For use of the coated form of zinc oxide, migration of [3-(methacryloxy)propyl]trimethoxysilane should be within the existing SML for this substance of 0.05 mg/kg.



## KEY WORDS

zinc oxide nanoparticles, FCM No 1046, FCM No 1050, food contact materials, safety assessment, evaluation

[1] On request from the Ministry of Health, Welfare and Sport, the Netherlands, Question No EFSA-Q-2014-00308, adopted on 18 March 2015.

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## SUMMARY

Within the general task of evaluating substances intended for use in materials in contact with food, according to Regulation (EC) No 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with foodstuffs, the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel) received a request from the Ministry of Health, Welfare and Sport, the Netherlands, for a safety assessment of the substance zinc oxide, nanoparticles, uncoated and coated with [3-(methacryloxy)propyl] trimethoxysilane, following a corresponding application submitted on behalf of Umicore Zinc Chemicals, Belgium.

The zinc oxide nanoparticles are intended to be used as a transparent ultraviolet light (UV) absorber in all types of polyolefins. When coated with [3-(methacryloxy)propyl] trimethoxysilane, the coating is up to 2 % by weight of the zinc oxide. The additive is to be used in the polymer at a maximum content of 2 % and 3 % by weight for the uncoated and the coated species, respectively. The plastics are intended to be used in contact with all types of foodstuffs for long-term storage at room temperature.

The substance is used as a powder in nanoform. In the final polymer the nanoparticles are still present but largely aggregated. Zinc oxide particle clusters were present with a median number-based size of 205 nm for low-density polyethylene (LDPE) with 2 % of uncoated zinc oxide and of 120 nm for LDPE with 3 % of coated zinc oxide.

Specific migration of the substance was tested from LDPE films (thicknesses 30–40 µm), containing the maximum use level of uncoated and coated species, into 3 % acetic acid and 10 % and 50 % ethanol for 10 days at 60 °C. Migration of zinc into 3 % acetic acid was high: up to 7.6 mg/kg (2 % zinc oxide), and up to 17.3 mg/kg (3 % coated zinc oxide). Migration of zinc into 10 % and 50 % ethanol was up to 80 µg/kg for the coated and uncoated species.

The applicant provided data from a stress test on the migration test samples, which were in contact with iso-octane for 10 days at 20 °C to generate polymer swelling. The absence of any detectable zinc (< 0.1 µg/kg) in the swelling simulant iso-octane suggests that the up to 80 µg/kg of zinc detected in the 10 % and 50 % ethanol simulants is due to slight solubilisation of zinc oxide releasing ionic zinc. This would be consistent with current scientific understanding on the lack of the diffusion potential of nanoparticles in polymers (Bott et al., 2014a, b, c). No direct evidence is available, however, on the physical form of this released zinc. In the event that it was in particulate form, it would nonetheless be expected to dissolve immediately into ionic zinc on contact with acid foods or stomach acid. For the 3 % acetic acid simulant, based on the solubility results, the high level of migration is clearly driven by solubilisation of zinc by the acidic media with dissolution of zinc oxide to the soluble ionic form (i.e. $Zn^{2+}$).

In 2003 the Scientific Committee on Food (SCF) established a no observed adverse effect level (NOAEL) of 50 mg/day for zinc, subsequently confirmed by EFSA in 2006 and 2014. The NOAEL of 50 mg/day is based on the absence of any adverse effects on a wide range of relevant indicators of copper status. An upper limit (UL) of 25 mg/person per day was recommended.

The CEF Panel, after having considered the above-mentioned data, concluded that the substance zinc oxide in nanoform, uncoated or coated with [3-(methacryloxy)propyl]trimethoxysilane, does not migrate in nanoform, and therefore the safety evaluation focuses on the migration of soluble ionic zinc. The available migration data for ionic zinc coming from the intended application comply with the current specific migration limit (SML), but in combination with dietary exposure from other sources the UL of 25 mg/person per day could be exceeded. For the coated form of zinc oxide, migration of [3-(methacryloxy)propyl]trimethoxysilane should be within the existing SML for this substance, namely 0.05 mg/kg. The Panel recommends that the Commission reconsiders the SML of 25 mg/kg for zinc, taking into account the fact that consumers are exposed to zinc from sources other than food contact materials.

## TABLE OF CONTENTS

## BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY REQUESTOR

The European Food Safety Authority was asked by the Ministry of Health, Welfare and Sport, the Netherlands, to evaluate the safety of zinc oxide, nanoparticles, uncoated (FCM No 1050) and coated with [3-(methacryloxy)propyl] trimethoxysilane (FCM No 1046). The request has been registered in the EFSA's register of questions under the number EFSA-Q-2014-00308. The dossier was submitted by Umicore Zinc Chemicals, Belgium.

Before a substance is authorised to be used in food contact materials and is included in a positive list EFSA's opinion on its safety is required. This procedure has been established in Articles 8 and 9 of the Regulation (EC) No 1935/20044 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food.

According to this procedure the industry submits applications to the Member States competent Authorities which transmit the applications to EFSA for their evaluation. The application is supported by a technical dossier submitted by the industry following the Scientific Committee for Food (SCF) guidelines for the 'presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation' (EC, 2001).

In this case, EFSA received an application from the Ministry of Health, Welfare and Sport, the Netherlands, requesting the evaluation of zinc oxide, nanoparticles, uncoated (FCM No 1050) and coated with [3-(methacryloxy)propyl] trimethoxysilane with (FCM No 1046).

According to Regulation (EC) No 1935/2004 of the European Parliament and of the Council on materials and articles intended to come into contact with food EFSA is asked to carry out an assessment of the risks related to the intended use of the substance and to deliver a scientific opinion.

[4] Regulation (EC) No 1935/2004 of the European parliament and of the council of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC. OJ L 338, 13.11.2004, p. 4–17.

## ASSESSMENT

### 1. Introduction

The European Food Safety Authority was asked by the Ministry of Health, Welfare and Sport, the Netherlands, to evaluate the safety of zinc oxide, nanoparticles, uncoated (Food Contact Materials (FCM) No 1050) and coated with [3-(methacryloxy)propyl] trimethoxysilane (FCM No 1046). The request has been registered in the EFSA's register of questions under the number EFSA-Q-2014-00308. The dossier was submitted by Umicore Zinc Chemicals, Belgium.

### 2. General information

According to the applicant, the substance zinc oxide in nanoform, either uncoated or coated with [3-(methacryloxy)propyl]trimethoxysilane, is intended to be used as a transparent ultraviolet light (UV) absorber in all types of polyolefins. When coated with [3-(methacryloxy)propyl] trimethoxysilane the coating is up to 2 % by weight of the zinc oxide. The additive is to be used in the polymer at a maximum content of 2 % and 3 % by weight for the uncoated and the coated species, respectively. The plastics are intended for contact with all types of foodstuff for long-term storage at room temperature.

Zinc oxide in bulk form is authorised as an additive for plastic materials and articles in contact with food (Regulation (EU) No 10/2011[5]), with a specific migration limit (SML) of 25 mg/kg food, expressed as zinc (FCM No 402).

The substance used as the coating agent, [3-(methacryloxy)propyl]trimethoxysilane, is authorised as a monomer for plastic materials and articles in contact with food (Regulation (EU) No 10/2011) with the following restriction: only to be used as a surface treatment agent for inorganic fillers and with a specific migration limit (SML) of 0.05 mg/kg (FCM No 788).

### 3. Data available in the dossier used for this evaluation

The studies submitted for evaluation followed the Scientific Committee on Food (SCF) guidelines for the presentation of an application for safety assessment of a substance to be used in food contact materials prior to its authorisation (EC, 2001).

#### 3.1. Non-toxicity data

- Data on identity, physical and chemical properties
- Data on purity, impurities and thermal stability
- Information on the production technology
- Data on intended use and authorisation
- Data on physical properties of the substance incorporated into the polymer
- Data on migration and residual content of the substance

#### 3.2. Toxicity data

- None

### 4. Evaluation

#### 4.1. Non-toxicological data

Chemical formula: ZnO (molecular weight: 81.4 Da)

[5] Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. Text with EEA relevance. OJ L 12, 15.1.2011, p. 1–89.

The, substance is used as a powder in nanoform, as shown by particle size distribution measurements using the centrifugal particle size technique. The average primary particle size is 60 nm (on a weight basis) or 44 nm (on a particle number basis), with 1 % of the particles being smaller than 30 nm. In the final polymer (low-density polyethylene (LDPE) with the maximum intended use level of coated and uncoated zinc oxide) nanoparticles are still present but largely aggregated. The zinc oxide particle clusters had a median number-based size of 205 nm for the LDPE with 2 % of uncoated zinc oxide and of 120 nm for the LDPE with 3 % of coated zinc oxide. 10 % and 35 % of the zinc oxide particle clusters were smaller than 100 nm in the LDPE with 2 % of uncoated zinc oxide and in the LDPE with 3 % of coated zinc oxide, respectively.

The substance is practically insoluble in water and in alcohol but rapidly soluble in 3 % acetic acid and in 0.07 M solution of hydrochloric acid with dissolution into $Zn^{(2+)}$ ions. This was demonstrated in tests using a nanofilter with a pore size of 30 nm. This trapped the nanoparticles when a suspension of either coated or uncoated forms was prepared in water and then filtered. In contrast, when the nanoparticles were added to 3 % acetic acid or 0.07 M hydrochloric acid and filtered immediately, all of the zinc passed through in the filtrate and none was trapped on the filter, indicating that full dissolution had occurred rapidly. Zinc oxide is thermally stable far above the processing conditions of polymers.

Specific migration was tested from LDPE films (thicknesses 30–40 µm), containing 2 % of the uncoated substance and 3 % of the coated species, into 3 % acetic acid and 10 % and 50 % ethanol under contact conditions of 10 days at 60 °C. Zinc was measured by inductively coupled plasma mass spectrometry and inductively coupled plasma atomic emission spectrometry.

Migration of zinc into 3 % acetic acid was high: up to 7.6 mg/kg (for the 2 % uncoated zinc oxide), and up to 17.3 mg/kg (for the 3 % coated zinc oxide sample). Migration of zinc into 10 % and 50 % ethanol was up to 80 µg/kg for the coated and uncoated species.

The applicant provided data from a stress test on the migration test samples, which were in contact with iso-octane for 10 days at 20 °C to generate polymer swelling. The exposed simulant contains less than 0.1 µg/kg of zinc. Scanning electron microscope and energy-dispersive X-ray spectroscopy (examination of the surface of the test specimens before and after exposure to the swelling simulant detected no difference in the concentration of zinc oxide at the surface.

The absence of any detectable zinc (< 0.1 µg/kg) in the swelling simulant iso-octane suggests that the zinc (up to 80 µg/kg) detected in the 10 % and 20 % ethanol simulants is due to slight solubilisation of zinc oxide giving release of ionic zinc. This would be consistent with current scientific understanding on the lack of the diffusion potential of nanoparticles in polymers (Bott et al., 2014a, b, c). No direct evidence is available, however, on the physical form of this released zinc. In the event that it was in particulate form, it would nonetheless be expected to dissolve immediately into ionic zinc on contact with acid foods or stomach acid. For the 3 % acetic acid simulant, based on the solubility results, the high level of migration is clearly driven by solubilisation of zinc by the acidic media with dissolution of zinc oxide to the soluble ionic form (i.e. $Zn^{2+}$).

The solubilisation of zinc by acidic media, with dissolution of the zinc oxide to the soluble ionic form, could give rise to the organic coating (which can be up to 2 % by weight of the additive for the coated form) being liberated from the zinc oxide surface. This organic coating is not likely to dissolve in the aqueous acidic media, but rather it is to be expected to remain bound to the polyolefin plastic. In any case, the existing SML of 0.05 mg/kg for the coating agent, [3-(methacryloxy)propyl] trimethoxysilane, would need to be respected.

### 4.2. Toxicological data

Zinc is an essential element with an average requirement of up to 10.2 mg/day for women and up to 12.7 mg/day for men (EFSA NDA Panel, 2014).

In 2003 the SCF established a no observed adverse effect level (NOAEL) of 50 mg/day for zinc, subsequently confirmed by EFSA in 2006 and 2014 (EC, 2003; EFSA Scientific Committee and NDA Panel, 2006; EFSA NDA Panel, 2014). The NOAEL of 50 mg/day is based on the absence of any adverse effects on a wide range of relevant indicators of copper status (as the critical endpoint) in the studies by Davis et al. (2000), Milne et al. (2001) and Bonham et al. (2003a, b). An uncertainty factor of 2 was applied owing to the small number of subjects included in these relatively short-term studies but acknowledging the rigidly controlled metabolic experimental conditions employed. An upper limit (UL) of 25 mg/person per day was recommended.

## 5. Conclusions

The EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF Panel), after having considered the above-mentioned data, concluded that the substance zinc oxide, nanoparticles, uncoated or coated with [3-(methacryloxy)propyl]trimethoxysilane, does not migrate in nanoform, and therefore the safety evaluation focuses on the migration of soluble ionic zinc. Available migration data for ionic zinc coming from the intended application comply with the current SML, but in combination with the dietary exposure from other sources the UL of 25 mg/person per day could be exceeded. For the coated form of zinc oxide, migration of [3-(methacryloxy)propyl]trimethoxysilane should be within the existing SML for this substance, namely 0.05 mg/kg.

## 6. Recommendations

The Panel recommends that the Commission reconsiders the SML of 25 mg/kg for zinc, taking into account the fact that consumers are exposed to zinc from sources other than food contact materials.

## DOCUMENTATION AS PROVIDED TO EFSA

1. Zinc oxide, nanoparticles, uncoated and coated with [3-(methacryloxy)propyl] trimethoxysilane. Dated April 2014. Submitted by Umicore Zinc Chemicals, Belgium.

2. Additional data for dossier: Zinc oxide, nanoparticles, uncoated and coated with [3-(methacryloxy)propyl] trimethoxysilane. Dated January 2015. Submitted by Umicore Zinc Chemicals, Belgium.

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## ABBREVIATIONS

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|---|---|
| CAS | Chemical Abstracts Service |
| CEF | (EFSA Panel on) Food Contact Materials, Enzymes, Flavourings and Processing Aids |
| EC | European Commission |
| EU | European Union |
| FCM | Food Contact Materials |
| LDPE | low-density polyethylene |
| NOAEL | no observed adverse effect level |
| SCF | Scientific Committee on Food |
| SML | specific migration limit |
| UL | upper level |
| UV | ultraviolet (light) |