

SCIENTIFIC OPINION

Scientific Opinion on the safety evaluation of the substance, N-(2-aminoethyl)ethanolamine, CAS No. 111-41-1, for use in food contact materials¹

**EFSA Panel on food contact materials, enzymes,
flavourings and processing aids (CEF)^{2, 3}**

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ABSTRACT

This scientific opinion of EFSA deals with the risk assessment of the co-monomer N-(2-aminoethyl)ethanolamine (CAS No 111-41-1, Ref. No 35284 and FCM substance No 262). The CEF Panel concluded that the use of N-(2-aminoethylamino)ethanol in manufacturing of can coatings in direct contact with food does not raise a safety concern for the substance itself if migration does not exceed 0.05 mg/kg food. The Panel, however, noted that many oligomers are formed during the manufacturing process which may migrate into the food. Only limited information was provided on the identities of the oligomers in the fraction below 1000 Da. Further structural and quantitative information is needed for a conclusion to be drawn concerning genotoxicity or other toxicity end points of the oligomeric fraction. The toxicological data needed will depend on the identity and level of migration of the oligomers in the food.

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KEY WORDS

N-(2-aminoethyl)ethanolamine; CAS No 111-41-1; Ref. No 35284; FCM substance No 262; Food contact materials; Coatings; Safety assessment; Evaluation.

1 On request from the Ministry for Health, Welfare and Sports, the Netherland, Question No EFSA-Q-2011-00968 adopted by Written Procedure on 4th April 2012..

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SUMMARY

The CEF Panel received a request from the Ministry for Health, Welfare and Sports, the Netherlands, for safety evaluation of a substance following a corresponding application from the company Valspar Packaging Corp AG, Switzerland.

The safety evaluation of N-(2-aminoethyl)ethanolamine, CAS number 111-41-1, was requested to extend its initial use as additive in plastics to a new use as a co-monomer in modified polyester coatings at levels up to 1.5% (w/w) intended for direct contact with foodstuffs. The coatings are intended to be used in easy opening ends of cans for aqueous foods such as non-acidic, acidic and alcoholic beverages. Maximum contact temperature would be 100°C in the case of hot-filled products followed by long term storage at room temperature.

The substance has already been evaluated as an additive in plastics (Ref. No 35284; FCM substance No 262) by the SCF in 2000. It was classified in SCF_List 3 with a restriction of 0.05 mg/kg food and not for use in polymers contacting foods for which simulant D is laid down in Directive 85/572/EEC and for indirect food contact only, behind a PET layer.

For the new use as co-monomer to manufacture coatings, the worst case migration of the substance was calculated from the total mass transfer of its residual content in the coating under the most unfavourable contact area-to-food volume to be 0.14 µg/kg food. The substance was confirmed to be negative in three adequately performed *in vitro* genotoxicity tests hence non-genotoxic.

From an exhaustive solvent extraction of the coating, oligomers containing and not containing the substance were determined. In total, the fraction below 1000 Da constitutes 1.1 mg/dm² which corresponds to 1.49 mg/kg food for the most unfavourable can size with a contact area-to-food volume ratio of 1.35 dm²/L. Out of those oligomers, eight major oligomers containing the substance were found, which when expressed as N-(2-aminoethyl)ethanolamine would migrate at levels higher than 9 µg/kg food and in total up to 100 µg/kg food. This value may be 2 to 3 times higher if expressed as mass of oligomers depending on the structure of the oligomers. The chemical composition and structure of these oligomers is very complex and not entirely clarified regarding the sequence and the identity of the monomers. The CEF Panel concluded that the use of N-(2-aminoethylamino)ethanol in manufacturing of can coatings in direct contact with food does not raise a safety concern for the substance itself if migration does not exceed 0.05 mg/kg food.

The Panel, however, noted that many oligomers are formed during the manufacturing process which may migrate into the food. Only limited information was provided on the identities of the oligomers in the fraction below 1000 Da. Further structural and quantitative information is needed for a conclusion to be drawn concerning genotoxicity or other toxicity end points of the oligomeric fraction. The toxicological data needed will depend on the identity and level of migration of the oligomers in the food.

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BACKGROUND

The industry, Valspar Packaging Corp AG, Switzerland, has submitted a technical dossier to the Ministry for Health, Welfare and Sport, the Netherlands, with the request to evaluate the safety of the substance N-(2-aminoethyl)ethanolamine for use as a co-monomer for the manufacture of polymeric coatings which can be in direct contact with food. The dossier was compiled following the 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).

The substance N-(2-aminoethyl)ethanolamine is intended to be used as a co-monomer in modified polyester coatings. The coatings are used in the ends of easy opening cans for aqueous foods such as non-acidic, acidic and alcoholic beverages. Food contact area of the can end depends on the size and geometry of the can. For substances used in the manufacture of coatings there is no specific Community measure. Therefore no authorisation is foreseen at EU level for substances used in coatings.

The Ministry for Health, Welfare and Sport, the Netherlands, transmitted this request for the safety evaluation of the substance to the EFSA.

TERMS OF REFERENCE

The EFSA was requested by the Ministry for Health, Welfare and Sport, the Netherlands, to evaluate the safety of the substance N-(2-aminoethyl)ethanolamine, CAS number 111-41-1, for use in polymeric coatings which can be in direct contact with food.

ASSESSMENT

1. Introduction

The European Food Safety Authority was asked by the Ministry for Health, Welfare and Sport, the Netherlands, to evaluate the safety of N-(2-aminoethyl)ethanolamine with the CAS number 111-41-1, the Ref. No 35284 and the FCM substance No 262. The request has been registered in the EFSA's register of received questions under the number EFSA-Q-2011-00968. The dossier was submitted on behalf of Valspar Packaging Corp AG, Switzerland.

2. General information

According to the applicant, the substance N-(2-aminoethyl)ethanolamine is intended to be used as a co-monomer in modified polyester coatings at levels up to 1.5% w/w. These particular coatings are typically applied with a mass per area of 10 g/m² which corresponds to a thickness of about 10 µm. The coating is polymerised at maximum process temperature of 60°C then cured on the final article for 10-26 seconds at 232-241°C. The coatings are used in the ends of easy opening cans for aqueous foods such as non-acidic, acidic and alcoholic beverages. Food contact area of the can end depends on the size and geometry of the can. Typical ratios of food contact area to product volume are ranging from 0.57 to 1.35 dm²/L. Maximum contact temperature would be 100°C in the case of hot-filled products followed by long term storage at room temperature.

The substance has been already evaluated as an additive in plastics (Ref. No 35284; FCM substance No 262) by the SCF in 2000 (EC, 2000). Based on migration data, residual content, genotoxicity assays which were concluded to be negative and the requested use, the substance was classified in SCF_List 3 with a restriction of 0.05 mg/kg and not for use in polymers contacting foods for which simulant D is laid down in Directive 85/572/EEC and for indirect food contact only, behind a PET layer.

In this petition, re-evaluation of the substance is requested for the use as a co-monomer in polymeric coatings intended for direct contact with foodstuffs.

3. Data available in the dossier used for this evaluation

The studies submitted for evaluation followed the 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).

Non-toxicity data:

- Data on identity
- Data on physical and chemical properties
- Data on intended use and authorisation
- Data on migration of the substance
- Data on residual content of the substance and worst case migration

- Data on oligomers

Toxicity data:

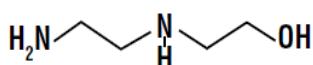
- Bacterial gene mutation test
- *In vitro* mammalian cell gene mutation test
- *In vitro* mammalian chromosome aberration test

4. Evaluation

4.1. Non-toxicological data

Chemical formula: C₄H₁₂N₂O

Molecular weight: 104.15 Da



Chemical structure:

The substance N-(2-aminoethyl)ethanolamine (AEEA) has a log Po/w = - 1.46 and is miscible with water. With a pH of 11.4 for a 1% solution in water it has a basic chemical nature. The substance has a boiling point of 238-240°C at normal pressure. Thermal decomposition of the substance during the manufacturing conditions (up to 241°C for final curing) and during the proposed end use is not expected.

Specific migration of the substance was not measured. Instead the residual content of the substance was determined in the final coating. Assuming total mass transfer of the residual content into food and the most unfavourable contact area-to-food volume ratio of 1.35 dm²/L, worst case migration was calculated to be 0.14 µg/kg food.

Overall migration was not measured. Instead, an exhaustive solvent extraction of the coating was performed and extracts were measured to be 4.7 mg/dm². Overall migration can be expected to be in a similar range. Out of this extraction, the low molecular weight fraction below 1000 Da (LMWF) was determined by gel permeation chromatography (GPC) and found to be up to 1.1 mg/dm².

Oligomers, present in this fraction at a level of 1.1 mg/dm², were investigated by liquid chromatography with time of flight mass spectrometry (LC- TOF-MS) with the objective to determine the quantities of oligomers containing the moiety of the substance. Altogether, a mixture of 185 peaks was detected out of which 41 compounds were found not to contain the substance and were not further considered. Then those oligomers that might contain one or more substance units and that were detected at a level ≥ 40 µg/6 dm² which equals in the actual worst case application (for the 1.35 dm²/L ratio) to ≥ 9 µg/kg food were selected for further consideration. This resulted in 8 major peaks that were further investigated. The individual concentrations, expressed as mass of the substance (AEEA), were found to be in the range up to 29 µg/L. In total, all substance-containing oligomers would make up 100 µg/kg food. The sequence and the identity of all monomers in these oligomers was not identified. Depending on the chemical structure their concentrations can be estimated to be 2 to 3 times higher when expressed as mass of oligomers rather than the AEEA mass expressed values.

Due to a lack of appropriate oligomer standards, the applied quantification method includes an associated uncertainty which is not fully known. Therefore the established concentration of substance-containing oligomers is only an estimate. The Panel noted also the very complex composition of oligomers formed due to the manufacturing process which makes, besides the substance, use of altogether eleven authorised monomers and starting substances to form the above mentioned 185 substance peaks out of which only a marginal number was tentatively identified.

4.2. Toxicological data

N-(2-Aminoethylamino)ethanol was negative in the three new adequately performed *in vitro* genotoxicity assays with and without metabolic activation as currently required by the SCF Guidelines on Food Contact Materials (EC, 2001), viz. a bacterial reverse mutation assay, a mouse lymphoma forward mutation assay and a chromosomal aberration test in Chinese hamster ovary cells. Therefore, the Panel concluded that the substance is non-genotoxic.

As a secondary amine, AEEA may undergo nitrosation to form the genotoxic and carcinogenic N-nitroso-(2-aminoethyl)ethanolamine (NAEEA). The CEF Panel has already evaluated a similar substance, diethanolamine, and the issue of formation of nitrosamines was also considered (EFSA, 2010). Up to a migration of 0.3 mg/kg food, the margin of exposure to endogeneously-formed N-nitrosodiethanolamine would be 10^9 or greater, indicating a negligible human risk. By read-across the Panel considers that possible formation of NAEEA from AEEA migrating up to 0.05 mg/kg food indicates a negligible human risk.

Overall extraction data highlighted the presence of eight major peaks, representing oligomers and/or reaction products, which contain the moiety of N-(2-aminoethylamino)ethanol. The chemical composition and structure of these oligomers is very complex and only tentatively identified regarding the sequence and type of the monomers. Thus, the question of whether their migration into food under the proposed conditions of use would or would not raise a toxicological concern cannot be clarified with the current level of structural and quantitative information.

CONCLUSIONS

After having considered the above-mentioned data, the CEF Panel concluded that the use of N-(2-aminoethylamino)ethanol in manufacturing of can coatings in direct contact with food does not raise a safety concern for the substance itself if migration does not exceed 0.05 mg/kg food.

The Panel, however, noted that many oligomers are formed during the manufacturing process which may migrate into the food. Only limited information was provided on the identities of the oligomers in the fraction below 1000 Da. Further structural and quantitative information is needed for a conclusion to be drawn concerning genotoxicity or other toxicity end points of the oligomeric fraction. The toxicological data needed will depend on the identity and level of migration of the oligomers in the food.

DOCUMENTATION PROVIDED TO EFSA

Dossier referenced: B026 – Val_AEEA. Dated: July 2011. Submitted on behalf of Valspar Packaging Corp AG, Switzerland.

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APPENDIX

TERMS USED RELEVANT TO MIGRATION:

Overall migration: The sum of the amounts of volatile and non volatile substances, except water, released from a food contact material or article into food or food simulant

Specific migration: The amount of a specific substance released from a food contact material or article into food or food stimulant

ABBREVIATIONS

AEEA	N-(2-aminoethyl)ethanolamine
CAS	Chemical abstracts service
CEF	Scientific Panel on food contact materials, enzymes, flavourings and processing aids
Da	Dalton
EC	European Commission
EFSA	European food safety authority
FCM	Food Contact Material(s)
GPC	Gel permeation chromatography
LC-TOF-MS	Liquid chromatography with time of flight mass spectrometry
LMWF	Low molecular weight fraction, below 1000 Da
NAEEA	N-nitroso-(2-aminoethyl)ethanolamine
PET	Poly(ethylene terephthalate)
Po/w	Octanol/water partition coefficient
REF No	Reference Number
SCF	Scientific Committee on food
w/w	Weight by weight