SCIENTIFIC OPINION

Scientific Opinion on the safety evaluation of the substance, 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine, CAS No. 6607-41-6, for use in food contact materials[1]

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

European Food Safety Authority (EFSA), Parma, Italy

This Scientific Opinion, published on 16 August 2012, replaces the earlier version published on 24 July 2012[4]

ABSTRACT

This scientific opinion of EFSA deals with the risk assessment of the substance 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine with the CAS No. 6607-41-6 and the FCM substance No 872, for use as a co-monomer for manufacturing polycarbonate polymers intended to be used for single and repeated contacts with all kinds of foodstuffs without restriction in time and temperature. Based on three *in vitro* genotoxicity tests and a mouse micronucleus test *in vivo* on the substance, the Panel considered that there is no concern with respect to genotoxicity of the substance. The CEF Panel concluded that there is no safety concern for the consumer if 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine is used as a co-monomer in polycarbonate copolymer and its migration does not exceed 0.05 mg/kg food. Potential migration of aniline, an impurity of the substance, should be in compliance with the restriction set in the Commission Regulation (EU) No 10/2011, i.e. not detectable.

KEY WORDS

2-Phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine; PPPBP; CAS number 6607-41-6; FCM substance No 872; Food contact materials; Safety assessment; Evaluation.

[1] On request from the Food Standards Agency, United Kingdom, Question No EFSA-Q-2009-00834 adopted on 5 July 2012.

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[3] Acknowledgement: The Panel wishes to thank the members of the Working Group on Food Contact Materials for the preparation of this opinion: Mona-Lise Binderup, Laurence Castle, Riccardo Crebelli, Roland Franz, Nathalie Gontard, Eugenia Lampi, Jean-Claude Lhuguenot, Maria Rosaria Milana, Karla Pfaff, Fatima Poças, Philippe Saillard, Kettil Svensson and Detlef Wölfle for the support provided to this EFSA scientific opinion.

[4] Editorial changes have been made on page 1. The changes do not affect the overall conclusions of the opinion. To avoid confusion, the original version of the Opinion has been removed from the website, but it is available on request.

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SUMMARY

Within the general task of evaluating substances intended for use in materials in contact with food according to the Regulation (EC) No 1935/2004[5] of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with foodstuffs, the CEF Panel received a request from the Food Standards Agency, United Kingdom for safety evaluation of the substance 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine following a corresponding application submitted on behalf of the company SABIC Innovative Plastics.

The safety evaluation of 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine with the CAS number 6607-41-6 and the FCM substance No 872 was requested for use as a co-monomer for manufacturing polycarbonate polymers. Finished articles are intended to be used for single and repeated contact with all kinds of foodstuffs without restriction in time and temperature.

The CEF Panel considered that the specific migration from polycarbonate test samples under adequate test conditions was up to 7 µg/kg food in aqueous food simulants and was not detected in olive oil at the detection limit of 9 µg/kg food simulant. The substance was tested in three *in vitro* genotoxicity tests and in a mouse micronucleus test in vivo. The substance did not induce gene mutations and the clastogenicity observed *in vitro* was not expressed *in vivo*. Therefore, the Panel considered that the substance does not raise a safety concern for genotoxicity.

Migration of the substance containing oligomeric fraction below 1000 Da was not detected with an estimated detection limit of 7 µg/kg both in 3% acetic acid and 50% ethanol. In addition, these oligomers are composed of non-genotoxic monomers. Therefore no toxicological data are requested for the oligomers.

The major impurity, phenolphthalein, is present in the substance but was not detectable in the final copolymer. This supports the fact that structurally related impurities are expected to react in the same way as the monomer and are anticipated to be incorporated into the polymeric structure. Therefore, at the very low migration, if any, of impurities structurally related to the substance, the Panel considered that these were not of safety concern and no toxicological data are requested.

The substance contains also aniline, for which the specific migration was detected only in 50% ethanol at migration up to 7.3 µg/kg food simulant from a sample made with the substance at higher level than the intended use level and which is likely to be due to the aggressiveness of this simulant under these conditions. Therefore, migration for aniline from a copolymer manufactured with the maximum intended use level is expected to be below 0.01 mg/kg food, the limit of detection set for the restriction "not detectable" for primary aromatic amines in the Commission Regulation (EU) No 10/2011[6].

The CEF Panel concluded that there is no safety concern for the consumer if the substance 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine is used as a co-monomer in polycarbonate copolymer and its migration does not exceed 0.05 mg/kg food. Potential migration of aniline should be in compliance with the restriction set in the Commission Regulation (EU) No 10/2011, i.e. not detectable.

[5] 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.

[6] Commission regulation (EU) No 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food, OJ L 12. 15.1.2011, p. 1-89.

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BACKGROUND AS PROVIDED BY THE LEGISLATION

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 1935/2004 of the European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food[7].

According to this procedure the industry submits applications to the Member States competent Authorities which in their turn transmit the applications to the EFSA for their evaluation. The application is supported by a technical dossier submitted by the industry 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).

In this case, EFSA received an application from the Food Standards Agency, United Kingdom, requesting the evaluation of the co-monomer 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine with the CAS number 6607-41-6 and the FCM substance No 872.

TERMS OF REFERENCE AS PROVIDED BY THE LEGISLATION

The EFSA is required by Article 10 of Regulation (EC) No 1935/2004 of the European Parliament and of the Council on materials and articles intended to come into contact with food to carry out risk assessments on the risks originating from the migration of substances from food contact materials into food and deliver a scientific opinion on new substances intended to be used in food contact materials before their authorisation and inclusion in a positive list.

[7] 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 Food Standard Agency, United Kingdom, to evaluate the safety of 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine (PPPBP) with a CAS number 6607-41-6 and a FCM substance No 872. The request has been registered in the EFSA's register of received questions under the number EFSA-Q-2009-00834. The dossier was submitted on behalf of SABIC Innovative Plastics.

2. General information

According to the applicant, the substance 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine is intended to be used as a co-monomer at a maximum content of 33 mol% for manufacturing polycarbonate polymers. Finished articles are intended to be in contact with all types of foodstuffs without restriction in time and temperature for single and repeated uses.

The substance has not been evaluated by the SCF or EFSA in the past.

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 and impurities
- Data on physical and chemical properties
- Data on intended use and authorisation
- Data on migration of the substance and impurities
- Data on overall migration
- Data on characterisation and quantification of migrating oligomers

Toxicity data:

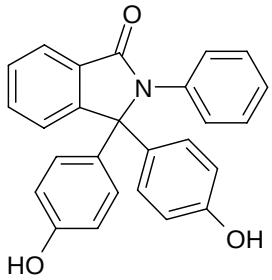
- Bacterial gene mutation test
- *In vitro* mammalian cell gene mutation test
- *In vitro* mammalian chromosome aberration test
- *In vivo* mouse bone marrow micronucleus test

4. Evaluation

4.1. Non-toxicological data

Chemical formulae: $C_{26}H_{19}NO_3$

Chemical structure:



PPPBP has a molecular weight of 393.4 Da. It is thermally stable until 310ºC, well above the maximum polymerisation process temperature. It is poorly soluble in water and well soluble in organic solvents. The log $P_{o/w}$ is 3.8.

Migration tests were performed using polycarbonate test samples manufactured with PPPBP use levels of 25 mol% and 45 mol% which spans the maximum used PPPBP amount of 33 mol%.

Specific migration of the substance from both polycarbonate test samples was determined into 10% ethanol, 3% acetic acid and olive oil which are appropriate for all food types. The test conditions were 121ºC for 2 hours followed by 10 days at 40ºC for 10% ethanol and 3% acetic acid and 180ºC for 4 hours in olive oil. The surface to volume ratio was 6.6 dm^2/L. Under these conditions, the specific migration in aqueous food simulants was up to 7 µg/kg food and no migration in olive oil was observed at the detection limit of 9 µg/kg food simulant.

According to the information provided by the applicant, purity of the substance is 99.9%. The major impurity, phenolphthalein, is present in the substance at a level of 266 mg/kg but was not detectable in the final copolymer based on 45 mol% PPPBP at the detection limit of 0.51 mg/kg polymer. When assuming total mass transfer of the residual content of all structurally related impurities and also assuming that they are present at the level of the detection limit in the copolymer, the worst-case migration is calculated to be 9 µg/kg food. However, due to the low diffusion characteristics of polycarbonate copolymers the realistic migration is expected to be markedly lower. In addition, the structurally related impurities are expected to react in the same way as the monomer and are anticipated to be incorporated into the polymeric structure, which is supported by the fact that the main impurity is no longer detectable in the polymer. Based on these two arguments, the Panel concludes that the migration of structurally related impurities will be negligible.

Aniline was another impurity present in the substance at a level of approx.1.5 mg/kg. Specific migration of aniline was determined from the 45 mol% PPPBP use level copolymer into water, 3% acetic acid and 50% ethanol and from the 25 mol% PPPBP use level sample into 10% and 50% ethanol. The test conditions were 121ºC for 2 hours followed by 10 days at 40ºC. The migration of aniline from the 45 mol% PPPBP use level copolymer was not detected at the limit of detection of about 2 µg/kg food simulant into water and 3% acetic acid and was up to 7.3 µg/kg into 50% ethanol which is likely to be due to the aggressiveness of this simulant under these conditions. The migration from the 25 mol% PPPBP use level sample into 10% and 50% ethanol was not detectable at the limit of detection of 4.5 µg/kg food simulant. Therefore, migration of aniline from a copolymer manufactured with the maximum intended use level (33 mol%) is expected to be below 0.01 mg/kg food, the limit of detection set for the restriction “not detectable” for primary aromatic amines in the Commission regulation (EU) No 10/2011.

Migration of oligomers containing PPPBP from a polycarbonate test sample manufactured with the substance at a nominal amount of 45 mol% PPPBP has not been detected with an estimated detection limit of 7 µg/kg in contact with 3% acetic acid after 2 hours at 121°C followed by 10 days at 40ºC and in contact with 50% ethanol after 2 hours at reflux temperature.

4.2. Toxicological data

The substance was tested in three *in vitro* genotoxicity tests with and without metabolic activation and in a mouse micronucleus test *in vivo*. In the bacterial reversion mutation assays using the *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and the *Escherichia coli* strain WPuvrA, the test substance did not induce gene mutations. In mammalian cells (L5178Y/TK$^{+/-}$ mouse lymphoma cells) the test substance did not induce gene mutations. A chromosomal aberration study with Chinese hamster ovary cells showed clear increases in the number of aberrant cells both in the presence and absence of metabolic activation. However, when given to male and female mice by intraperitoneal injection, the test substance (up to 2000 mg/kg body weight) did not induce micronuclei in erythrocytes; the bioavailability of the substance was demonstrated by a reduced ratio of polychromatic to total erythrocytes in the 24-hour treated groups compared to controls. Thus, the clastogenicity observed *in vitro* was not expressed *in vivo* and the Panel considers that the substance does not raise a safety concern for genotoxicity..

Oligomers with a molecular weight below 1000 Da containing PPPBP are not detected in any of the simulants and are composed of non-genotoxic monomers. Therefore no toxicological data are requested for the oligomers.

Migration of aniline from a copolymer manufactured with the maximum intended use level (33 mol%) is expected to be below 0.01 mg/kg food, therefore in compliance with the limit of detection set for the restriction “not detectable” for primary aromatic amines in the Commission regulation (EU) No 10/2011.

At the very low migration of impurities structurally related to the substance, the Panel considers that these are not of safety concern and no toxicological data are requested.

CONCLUSIONS

The CEF Panel concluded that there is no safety concern for the consumer if the substance 2-phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine is used as a co-monomer in polycarbonate copolymers and its migration does not exceed 0.05 mg/kg food.

Potential migration of aniline should be in compliance with the restriction set in the Commission Regulation (EU) No 10/2011, i.e. not detectable.

DOCUMENTATION PROVIDED TO EFSA

Dossier referenced: GE00366-33. Dated: February 2012. Submitted on behalf of SABIC Innovative Plastics.

REFERENCES

EC (European Commission), (2001). Guidelines of the Scientific Committee on Food for the presentation of an application for safety assessment of a substance to be used in food contact materials prior its authorisation; http://ec.europa.eu/food/fs/sc/scf/out82_en.pdf.

GLOSSARY AND ABBREVIATIONS

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
CAS	Chemical abstracts service
CEF	Food contact materials, enzymes, flavourings and processing aids
Da	Dalton
EC	European Commission
EFSA	European food safety authority
FCM	Food Contact Material(s)
Po/w	Octanol/water partition coefficient
PPPBP	2-Phenyl-3,3-bis(4-hydroxyphenyl)phthalimidine
SCF	Scientific Committee on Food