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SCIENTIFIC OPINION

Safety assessment of mixtures of 1,9-nonanediamine (NMDA) and 2-methyl-1,8-octanediamine (MODA), for use in food contact materials

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Abstract

The EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP) assessed the safety of mixtures of 1,9-nonanediamine (NMDA) and 2-methyl-1,8-octanediamine (MODA) when used to produce polyamide food contact materials for contact with all food types for long-term storage at room temperature and below, including heating up to 121°C for up to 2 h. The polyamide material is also intended to be used for repeated use up to 121°C with short contact (up to 30 min). The polymer typically contains [redacted] of a low molecular weight fraction (LMWF, < 1000 Da). The specific migration was measured with polyamide samples in a set of migration tests with 3% acetic acid and 10% ethanol. NMDA and MODA were not detected at [redacted], respectively. The specific migration of the LMWF consisting of NMDA/MODA-related species was up to [redacted]. The overall migration in olive oil was below the detection limit (3 mg/dm^2). The most abundant migrating LMWF oligomers were identified. Toxicological studies were performed with NMDA, MODA and with polyamide formulations enriched in the LMWF. The results of genotoxicity assays did not raise a concern. From a repeated-dose oral 90-day toxicity study in rats, the Panel identified a no observed adverse effect level (NOAEL) of 1000 mg/kg body weight per day for the migrating LMWF. The CEP Panel concluded that NMDA/MODA mixtures do not raise a safety concern for the consumer when used as comonomer with terephthalic acid to manufacture polyamide articles intended for contact with all food types, except for infant formula and human milk, if the migration of NMDA and MODA does not exceed 0.05 mg/kg food (as a sum of the two substances) and if the migration of the LMWF consisting of NMDA/MODA-related species does not exceed 5 mg/kg food.

KEYWORDS

1,9-nonanediamine (NMDA) and 2-methyl-1,8-octanediamine (MODA), CAS number 646-24-2, 148528-05-6, FCM substance no 1090, food contact materials, polyamide, safety assessment

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1 | INTRODUCTION

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

Before a substance is authorised to be used in food contact materials (FCM) and is included in a positive list, EFSA's opinion on its safety is required. This procedure has been established in Articles 8, 9 and 10 of Regulation (EC) No 1935/2004[1] 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 the European Food Safety Authority (EFSA) for their evaluation.

In this case, EFSA received from the Dutch competent authority (Ministry of Health, Welfare and Sport) one application requesting the evaluation of 1,9-nonanediamine (NMDA) and one application requesting the evaluation of 2-methyl-1,8-octanediamine (MODA). The dossiers were submitted on behalf of Kuraray Eval Europe. The two applications were assessed together as mixtures of NMDA and MODA, with FCM Number No 1090.

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.

2 | DATA AND METHODOLOGIES

2.1 | Data

The applicant submitted a dossier in support of their application for the authorisation of mixtures of NMDA and MODA to be used to manufacture plastic FCM.

Additional information was provided by the applicant during the assessment process in response to the request from EFSA sent on 11 June 2020 (see Section 5).

Data submitted and used for the evaluation are:

Non-toxicological data

- Chemical identity
- Description of manufacturing process of substance/FCM
- Physical and chemical properties
- Intended uses
- Existing authorisation(s)
- Migration of the substance
- Identification and migration of impurities
- Identification and migration of oligomers and reaction products

Toxicological data

- Bacterial gene mutation tests
- In vitro gene mutation tests in mammalian cells
- In vitro chromosome aberration tests
- In vitro micronucleus tests
- A 90-day oral toxicity study in Wistar rats
- Reasoning on potential accumulation in human

2.2 | Methodologies

The assessment was conducted in line with the principles laid down in Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food. This Regulation underlines that applicants may consult the Guidelines of the Scientific Committee on Food (SCF) for the presentation of an application for safety assessment of a substance to be used in FCM prior to its authorisation (European Commission, 2001) including the corresponding data requirements. The dossier that the applicant submitted for evaluation was in line with the SCF guidelines (European Commission, 2001).

[1]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.

The methodology is based on the characterisation of the substance that is/are the subject of the request for safety assessment prior to authorisation, its impurities and reaction and degradation products, the evaluation of the exposure to those substances through migration and the definition of minimum sets of toxicity data required for safety assessment.

To establish the safety from ingestion of migrating substances, the toxicological data indicating the potential hazard and the likely human exposure data need to be combined. Exposure is estimated from studies on migration into food or food simulants and considering that a person may consume daily up to 1 kg of food in contact with the relevant FCM.

As a general rule, the greater the exposure through migration, the more toxicological data are required for the safety assessment of a substance. Currently there are three tiers with different thresholds triggering the need for more toxicological information as follows:

a. In case of high migration (i.e. 5–60 mg/kg food), an extensive data set is needed.
b. In case of migration between 0.05 and 5 mg/kg food, a reduced data set may suffice.
c. In case of low migration (i.e. < 0.05 mg/kg food), only a limited data set is needed.

More detailed information on the required data is available in the SCF guidelines (European Commission, 2001).

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

3 | ASSESSMENT

According to the applicant, mixtures of the substances 1,9-nonanediamine (1,9-nonamethylenediamine, NMDA) and 2-methyl-1,8-octanediamine (MODA) are used in the production of the polyamide PA9T.

PA9T is intended to be used for contact with all types of food for single use applications, [redacted], as well as in repeated use articles, [redacted]. In single use applications, contact may be for long-term storage at room temperature and below, including heating up to 121°C for up to 2 h. In repeated use applications, contact may be long term at room temperature or below, including heating up to 121°C for up to 30 min. The requested uses do not include contact with infant formula and human milk.

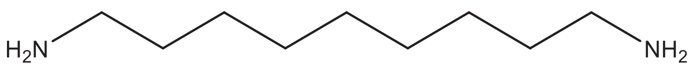
The substances were not evaluated by scientific committee on food and EFSA in the past. They are covered by the US FDA Food Contact Notification FCN No 1966 for the polyamide PA9T with the limitations/specifications 'The finished food-contact article may contact all food types and may be used under Conditions of Use A through H, as described in Tables 1 and 2. The FCS is not for use in contact with infant formula and human milk. Such uses were not included as part of the intended use of the substance in the FCN'.[2]

3.1 | Non-toxicological data

3.1.1 | Identity of the substance[3]

1,9-Nonanediamine (NMDA)

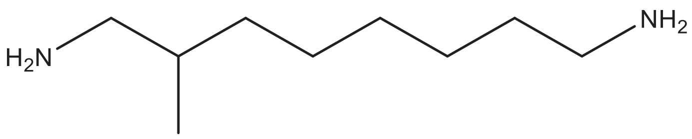
Chemical formula: $C_9N_2H_{22}$
Chemical structure:



CAS number: 646–24-2
Molecular weight: 158.2 Da

2-Methyl-1,8-octanediamine (MODA)

Chemical formula: $C_9N_2H_{22}$
Chemical structure:



[2]https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=FCN&id=1966&sort=Sort_FCS&order=DESC&startrow=1&type=basic&search=1966.

[3]Technical dossier/ 4subm_Consolidated version_Nov2023/Appendix B/Section 1 and Section 3, and Attachments 1, 2, 8, 9, 37, 38, 41, 42.

CAS number: 148528-05-6
Molecular weight: 158.2 Da

NMDA and MODA are manufactured by reaction of [redacted] According to the applicant, two mixtures with different NMDA and MODA proportions are obtained: a mixture where NMDA is the most abundant monomer (NMDA: 80%–100%, MODA: 0%–20%), and another one, where MODA is the most abundant monomer (MODA: 90%–100%, NMDA: 0%–10%). The typical NMDA:MODA proportions are reported to be [redacted] and [redacted], respectively. The two mixtures may then be blended to achieve the desired NMDA:MODA ratio in the formulation used to produce PA9T.

The purity of NMDA and MODA was reported to be 98.5%–99.9% and 98.0%–99.9%, respectively, expressed on the basis of total diamine content.

The impurities detected were related substances present as a result of an incomplete conversion in the manufacturing process. The two corresponding dialdehydes were below the limit of detection [redacted]. [redacted]

The polyamide PA9T is manufactured via polycondensation of NMDA and MODA with terephthalic acid (TA), benzoic acid (BA) as endcap [redacted] According to the applicant, the typical ratio between the diamine comonomers (NMDA + MODA) and the acid comonomers (TA + BA) is approximately [redacted] [redacted], with the fraction of NMDA in the plastic being between [redacted]% and [redacted]% [redacted] and the fraction of MODA in the plastic being between [redacted]% and [redacted]% w/w. The applicant provided the composition of two typical PA9T formulations, 'TS-414' ([redacted] and 'TS-415' ([redacted]).

The weight average molecular weight of the TS-414 polymer was [redacted] with a low molecular weight fraction < 1000 Da (LMWF) of [redacted]. The weight average molecular weight of the TS-415 polymer was [redacted] ([redacted]) with an LMWF of [redacted]. The LMWF constituents were identified in migration tests (see Sections 3.1.3 and 3.1.4) and they consisted largely of the expected oligomers coming from the amine-acid condensation reaction.

3.1.2 | Physical and chemical properties[4]

NMDA is a solid and MODA is a liquid at ambient temperature. The melting and the boiling points were reported as 37°C and 258°C, respectively, for NMDA and as −25°C and 244°C, respectively, for MODA. The log $P_{o/w}$ at 25°C was reported to be 1.8 (NMDA) and 2.0 (MODA). [redacted]

According to the applicant, PA9T is primarily foreseen for high temperature applications due to its high glass transition temperature (125°C) and high resistance to water.

3.1.3 | Specific migration[5]

The specific migration of the substance was determined in three consecutive tests, using two 250 μm-thick PA9T films (TS-414 and TS-415) produced with [redacted] NMDA and [redacted] MODA (TS-414) or with [redacted] NMDA and [redacted] MODA (TS-414). Tests were performed by total immersion at a surface to volume ratio of 2 dm^2/100 mL, using 3% acetic acid and 10% ethanol as food simulants. The samples were kept under reflux conditions (i.e. at boiling temperature) for 4 h. The applicant also provided migration tests in the same simulants under reflux conditions for 30 min in order to simulate the typical use of the polymer in parts of, e.g. coffee machines.

The Panel noted that, in principle, the conditions of the first contact do not cover the conditions required by Regulation (EU) 10/2011[6] for the intended single use, as migration tests should be carried out for 8 h (and not for only 4 h, as done here). However, the Panel noted that the migration of NMDA and MODA in each repeated test was not detected and below [redacted], and that the overall migration and the migration of the LMWF decreased from one test to the subsequent one. Based on these observations, the Panel considered that prolonging the duration of migration tests from 4 to 8 h would not result in higher migration values. Based on theoretical considerations, the Panel also concluded that the accelerated test conditions of 4 h at boiling temperature cover the test conditions of 60°C for 10 days recommended by Regulation (EU) 10/2011. Therefore, the test conditions used were considered adequate to simulate the uses intended by the applicant.

[4]Technical dossier/ 4subm_Consolidated version_Nov2023/Appendix B/Section 2 and Attachments 3, 4, 5, 12, 39.
[5]Technical dossier/ 4subm_Consolidated version_Nov2023/Appendix B/Section 5 and Attachments 11, 47, 48.
[6]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.

The analysis of the exposed food simulants was performed by ultra-performance liquid chromatography-high-resolution-mass spectrometry (UPLC-HR-MS) after derivatisation with fluorescamine. Based on the conditions of the analytical method applied, the derivatised NMDA and MODA eluted at the same retention time. All migration test results were converted from the 2 dm^2/100 mL used in the tests to the conventional ratio of 6 dm^2/kg. In all tests (including after the first contact), the migration of NMDA and MODA was not detected [redacted], respectively (4 h at boiling temperature), and at [redacted] (30 min at boiling temperature).

The migration of TA and BA was determined via ultra-performance liquid chromatography-UV detection (UPLC-UV, 240 nm) analysis of the exposed simulants, using calibration with TA standards and assuming that BA has the same UV response factor as TA. The specific migration of TA and BA was up to [redacted] respectively, hence well below the corresponding specific migration limits (SMLs) listed in Regulation (EU) 10/2011, i.e. 7.5 mg/kg food for FCM No 785 (TA) and 60 mg/kg food for FCM no 116 (BA).

3.1.4 | Screening of migrating oligomers and reaction products related to NMDA and MODA[7]

For the identification of the migrating LMWF, simulants obtained under the conditions of the tests for specific migration were analysed using UPLC-HR-MS with electrospray ionisation (ESI) in positive and negative mode, with and without prior derivatisation with fluorescamine. The LMWF was dominated by oligomers with the most abundant species tentatively identified as [redacted]

UPLC-UV detection using TA standards for calibration (see Section 3.1.3) was applied for semi-quantification of the total migration of the LMWF consisting of NMDA/MODA-related species (i.e. excluding the migration of TA and BA). After the first contact, the migration of the LMWF was [redacted] from TS-414 and TS-415, respectively, in 3% acetic acid, and [redacted] from TS-414 and TS-415, respectively, in 10% ethanol. For the third contact, the migration of the LMWF was [redacted] from TS-414 and TS-415, respectively, in 3% acetic acid, and [redacted] food from TS-414 and TS-415, respectively, in 10% ethanol. The Panel noted that the approach used may cause a consistent underestimation of the migration of the LMWF, as the molecular weight of TA (116 Da) is at least twice smaller than that of the most abundant oligomers. By considering this aspect, the Panel estimated that the migration of the LMWF consisting of NMDA/MODA-related species can be up [redacted] after the first contact and [redacted] after the third contact.

The Panel considered that, if a proper correction factor is applied, the analytical method used by the applicant is appropriate to measure the migration of the LMWF consisting of NMDA/MODA-related species from such a plastic.

3.1.5 | Overall migration[8]

The overall migration was measured under the same conditions as used for the specific migration tests. The highest value was [redacted], determined after first contact with 3% acetic acid for 4 h at boiling temperature.

In addition, the overall migration was determined after contact with olive oil (2 h at 121°C followed by 10 days at 60°C) and contact with isooctane and 50% ethanol (3 consecutive tests for 30 min at boiling temperature). The migration was [redacted] in olive oil (LoD: 3 mg/dm^2) and isooctane ([redacted] The overall migration in 50% ethanol was up to [redacted] in the first contact (corresponding to [redacted]) and up to [redacted] in the third contact (corresponding to [redacted]).

The migration reported for 50% ethanol is [redacted] The Panel attributed this [redacted] migration to a swelling effect under the applied test conditions and, therefore, considered the use of this simulant not appropriate to measure migration.

3.2 | Toxicological data

In accordance with the 'EFSA Note for Guidance for Food Contact Materials' (EFSA AFC Panel, 2008), the applicant provided a battery of genotoxicity studies to demonstrate the absence of concern for genotoxicity for NMDA, MODA and the migrating LMWF. No other tests were provided for NMDA and MODA, as their individual migration was below 0.05 mg/kg food.

As the migration of the LMWF containing NMDA/MODA-related species exceeded 0.05 mg/kg of food, the applicant additionally provided a 90-day oral toxicity study and data to demonstrate the absence of potential for accumulation in humans.

[7]Technical dossier/4subm_Consolidated version_Nov2023/Appendix B/Section 5.3 and Attachments 11, 47, 48.
[8]Technical dossier/4subm_Consolidated version_Nov2023/Appendix B/Section 5.2 and Attachments 11, 47, 48.

3.2.1 | Genotoxicity[9]

3.2.1.1 | *NMDA*

3.2.1.1.1 | *Bacterial reverse mutation test*

NMDA (purity 99.99%) was tested in a bacterial reversion assay with tester strains Salmonella Typhimurium TA1535, TA1537, TA98, TA100 and *Escherichia coli* WP2 *uvrA*, with and without metabolic activation (S9) using the pre-incubation procedure with duplicate plating (triplicate for negative controls). The study was performed under GLP conditions, following the Japanese guidelines for bacterial mutagenicity testing. [redacted] Based on the results obtained, NMDA is evaluated as negative in this bacterial reversion assay.

The Panel noted that duplicate plating was used instead of triplicate as recommended by the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 471 (OECD, 1997a) for an adequate estimation of variability. However, the Panel also noted that no indication of treatment-related increase of revertants was obtained in fully replicated experiments: The available data are thus considered acceptable, as stipulated in the OECD TG 471. Based on the 'Harmonised approach for reporting reliability and relevance of genotoxicity studies' (EFSA, 2023), the Panel considered the study reliable without restrictions, and the results of high relevance.

3.2.1.1.2 | *In vitro gene mutation test in mammalian cells*

NMDA (purity 99.5%) was tested in the forward gene mutation assay at the thymidine kinase locus in L5178Y mouse lymphoma cells. The study was performed under GLP conditions, following the OECD TG 476 (OECD, 1997c). The [redacted] and tested at the following concentrations [redacted]: 0.05, 0.1, 0.2 and 0.4 mg/mL, both without and with metabolic activation (S9), [redacted] Treatments produced [redacted] NMDA is evaluated as non-mutagenic in this forward mutation assay. The Panel considered the study reliable without restrictions and the results of high relevance.

3.2.1.1.3 | *In vitro mammalian chromosomal aberration test*

NMDA (purity 99.5%) was tested in a chromosomal aberration assay in the Chinese hamster ovary cell line CHO-K1. The study was performed under GLP conditions and following the OECD guideline TG 473 (OECD, 1997b). The test item was dissolved in distilled water. [redacted], the following concentrations were selected for the main mutagenicity assay: 0.30, 0.15 and 0.08 mg/mL. [redacted]

[redacted] These findings are therefore evaluated as equivocal instead of negative, as suggested by the study authors. The Panel evaluated the study as reliable with restrictions and the equivocal results reported of low relevance.

3.2.1.1.4 | *In vitro micronucleus test*

NMDA (purity 99.8%) was tested in an in vitro micronucleus assay in the human lymphoblastoid cell line TK6. The study was performed under GLP conditions and following the OECD TG 487 (OECD, 2016). [redacted]

[9]Technical dossier/4subm_Consolidated version_Nov2023/Appendix B/Section 8.1 and Attachments 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 50.

[redacted] Overall, NMDA is evaluated as negative in this in vitro micronucleus assay. The Panel considered the study reliable without restrictions and the results of high relevance.

3.2.1.2 | *MODA*

3.2.1.2.1 | *Bacterial reverse mutation test*

MODA (purity 99.9%) was tested in a bacterial reversion assay with tester strains Salmonella Typhimurium TA1535, TA1537, TA98, TA100 and *Escherichia coli* WP2 *uvrA*, with and without metabolic activation, using the plate incorporation method with duplicate plating. The study was performed under GLP conditions, following the Japanese guidelines for bacterial mutagenicity testing. A range-finding experiment was performed with all strains, with and without metabolic activation (S9), [redacted] with all strains, with and without S9. Inhibition of bacterial growth was observed at [redacted] Based on the results obtained, MODA is evaluated as negative in this bacterial reversion assay.

The Panel noted that duplicate plating was used instead of triplicate as recommended by the OECD TG 471 (OECD, 1997a) for an adequate estimation of variability. However, the Panel also noted that no indication of treatment-related increase of revertants was obtained in fully replicated experiments: The available data are thus considered acceptable, as stipulated in OECD TG 471 (1997a). Therefore, the panel considered the study reliable without restrictions and the negative results of high relevance.

3.2.1.2.2 | *In vitro gene mutation test in mammalian cells*

MODA (purity 98.6%) was tested in the forward gene mutation assay at the thymidine kinase locus in L5178Y mouse lymphoma cells. The study was performed under GLP conditions, following the OECD TG 476 (OECD, 1997c). The test item, dissolved in distilled water, was tested at the following concentrations, selected after a preliminary toxicity assay: 2.5, 1.25, 0.625 and 0.3125 µg/mL, both without and with metabolic activation, [redacted] Overall, MODA is evaluated as negative in this mammalian gene mutation assay. The Panel considered the study reliable without restrictions and the results of high relevance.

3.2.1.2.3 | *In vitro mammalian chromosomal aberration test*

MODA (purity 99.9%) was tested in a chromosomal aberration assay in the Chinese hamster lung-derived fibroblast cell line CHL-IU. The study was performed under GLP conditions and following the Japanese guidelines for in vitro cytogenetic testing. The test item was dissolved in saline water. [redacted]

In the tests conducted with a continuous treatment without metabolic activation, a distinct and concentration-related increase of cells with chromosomal aberrations was observed both after 24 and 48 h: [redacted]

[redacted] After the short treatments (6 h), the incidence of cells with structural aberrations was clearly increased in the absence of metabolic activation, [redacted] at the top dose ([redacted] in the concurrent negative control). [redacted]

Overall, the results of this study indicate that MODA can exert a clastogenic effect and arrest mitosis in experimental conditions without metabolic activation. However, the Panel noted that toxicity elicited by treatments was not adequately controlled during the study [redacted]. Therefore, the possibility that the positive effects recorded were associated with the levels of toxicity higher than recommended (55 ± 5% according to OECD TG 473, 2014a) cannot be discarded. Overall, the panel considered the study reliable with restrictions and the inconclusive results reported of low relevance.

3.2.1.2.4 | *In vitro micronucleus test*

MODA (purity 98.6%) was tested in the in vitro micronucleus assay in human binucleated lymphocytes. The study was performed under GLP conditions and in compliance with the OECD TG 487 (OECD, 2014b). Two experiments were performed with blood cells obtained from different donors. [redacted] experiments were performed with and without metabolic activation with treatment/recovery times of 4/20 h. With metabolic activation, the following concentrations were evaluated: 317, 633 and 1266 μg/mL; the same concentrations were applied without metabolic activation in the first experiment, [redacted] Overall, MODA is evaluated as negative in this in vitro micronucleus assay. The Panel evaluated the study as reliable without restrictions and the results of high relevance.

3.2.1.3 | *PA9T oligomers*

The test item 'PA9T oligomer' for the genotoxicity tests was obtained by [redacted] extraction of plastic [redacted] using 10% and 50% ethanol under time–temperature conditions that mimicked the migration testing reported in Section 3.1.3. [redacted] The test item was analysed by gel permeation chromatography (GPC) [redacted] and the LMWF (< 1000 Da) was reported to be [redacted]

The Panel noted that plastic [redacted] is a good choice as the source polymer since it is made using an acceptable ratio of the four co-monomers involved in the production of PA9T plastics. [redacted] The Panel also noted that the same simulants and time/temperature conditions were used to obtain the PA9T oligomer mixture as had been used in the migration tests and that the characterisation by GPC was satisfactory. The Panel concluded that for the purpose of hazard identification, the test item 'PA9T oligomer mixture' is sufficiently similar to the LMWF to which the consumer may be exposed as a result of migration from PA9T plastics.

3.2.1.3.1 | *Bacterial reverse mutation test*

PA9T oligomers [redacted] were tested in a bacterial reversion assay with tester strains S. Typhimurium TA1535, TA1537, TA98, TA100 and *E. coli* WP2 *uvrA*, with and without metabolic activation using the pre-incubation procedure. The study was performed under GLP conditions and following the OECD TG 471 (OECD, 1997a). [redacted] Based on the results obtained, the mixture of PA9T oligomers is evaluated as negative in this bacterial reversion assay. The Panel evaluated the study as reliable without restrictions and the results reported of high relevance.

3.2.1.3.2 | *In vitro mammalian chromosomal aberration test*

PA9T oligomers [redacted] were tested in a chromosomal aberration assay in the Chinese hamster lung-derived fibroblast cell line CHL-IU. The study was performed under GLP conditions and following the OECD TG 473 (OECD, 2016). [redacted]
Overall, PA9T oligomers are evaluated as directly clastogenic under the conditions of this study. The Panel considered the study as reliable without restrictions and the results of high relevance.

3.2.1.3.3 | *In vitro micronucleus test*

As a follow-up of the in vitro chromosomal aberration assay, an in vitro micronucleus assay in the p53-proficient human lymphoblastoid TK6 cells was performed with PA9T oligomers [redacted] The study was conducted under non-GLP conditions with a limited experimental protocol tailored on the results of the chromosomal aberration test, i.e. only with [redacted] The Panel considered the study as reliable with restrictions and the results of limited relevance.

3.2.1.3.4 | *In vitro micronucleus test*

An in vitro micronucleus assay in the human lymphoblastoid cell line TK6, performed with PA9T oligomers under GLP conditions and following the OECD TG 487 (OECD, 2014b) was also available for evaluation. [redacted] There was no concentration-related and/or statistically significant increase of micronucleated cells at any dose. PA9T oligomers were evaluated as negative under the conditions of this study. The Panel considered the study as reliable without restrictions and the results of high relevance.

3.2.1.4 | *Conclusion on genotoxicity*

Negative results of high relevance were obtained with NMDA, MODA and PA9T oligomers in in vitro gene mutation assays in bacteria and in mammalian cells, and in the in vitro micronucleus assay in human cells. Equivocal/inconclusive (for NMDA and MODA) or positive (for PA9T oligomers) results were obtained in in vitro chromosomal aberration tests in rodent cell lines (CHO and CHL-IU).

The Panel considered that the negative results obtained in robust in vitro micronucleus assays in human cells overrule the findings obtained in chromosomal aberration tests with rodent p-53-deficient cell lines (Fowler et al., 2012; Fujita & Honda, 2022), and concluded that the available data were sufficient to rule out a genotoxic concern for NMDA, MODA and PA9T oligomers.

3.2.2 | Subchronic toxicity[10]

A repeated dose 90-day oral toxicity study was conducted following the most recent version of the OECD TG 408 (OECD, 2018) and under GLP.

A sufficient quantity of test item needed for a 90-day repeated oral dose toxicity study could not reasonably be prepared using the same migration/extraction approach as described above (Section 3.2.1.3). Consequently, a [redacted] method was used [redacted] PA9T oligomer mixture were prepared. These nine samples of PA9T oligomer mixtures were characterised by UPLC-HR-MS (positive and negative ESI) [redacted] GPC analysis [redacted] indicated that the LMWF (< 1000 Da) was ca. [redacted] The Panel noted that based on the comprehensive UPLC-HR-MS characterisation report, the oligomer mixture of the test item was a good representation of the migrating LMWF. It contained the oligomers [redacted] at high percentage levels that were comparable to the migrate mixtures. The Panel concluded that, for the purpose of hazard identification and characterisation, the test item is sufficiently similar to the LMWF to which the consumer may be exposed as a result of migration from PA9T plastics.

The test item was administered to Sprague–Dawley rats [Crl:CD(SD)] for 90 consecutive days by gavage at doses of 0, 250, 500 and 1000 mg/kg body weight (bw) per day.

[redacted]

Under the conditions and the procedure followed in this study, the Panel identified a no observed adverse effect level (NOAEL) of 1000 mg/kg bw per day, the highest dose tested.

3.3 | DISCUSSION

The Panel noted that the specific migration of NMDA and MODA into acidic and aqueous food simulants was below [redacted] for the migration tests conducted for 4 h at boiling temperature. The results of the genotoxicity assays did not raise a concern.

The migration of the LMWF consisting of NMDA/MODA-related species was calculated by the Panel to be up to [redacted]. The Panel concluded that the migrating oligomers and reaction products were adequately represented in the toxicity studies provided, which used either a low molecular mass test item prepared from extracts of PA9T (for the genotoxicity tests) or a PAT9 oligomer mixture with a large LMWF (for the repeated-dose 90-day study). The results of genotoxicity assays did not raise any concern. As regards subchronic toxicity, the results of a 90-day repeated oral toxicity study performed in Wistar rats allowed to identify an NOAEL of 1000 mg/kg bw per day, the highest dose tested. The Panel

[10]Technical dossier/4subm_Consolidated version_Nov2023/Appendix B/Section 8.2 and Attachment 43.

considered that there was no concern on the accumulation potential of PA9T oligomers in view of their poor solubility in the fatty food simulant olive oil.

4 | CONCLUSIONS

Based on the above-mentioned data, the Panel concluded that mixtures of 1,9-nonanediamine (NMDA) and 2-methyl-1,8-octanediamine (MODA) are not of safety concern for the consumer when used as a co-monomer with terephthalic acid to manufacture polyamide materials and articles intended for contact with all types of food, except for infant formula and human milk, if the migration of NMDA and MODA does not exceed 0.05 mg/kg food (as a sum of both substances) and if the migration of the LMWF (< 1000 Da) that contains NMDA/MODA-related species does not exceed 5 mg/kg food.

5 | DOCUMENTATION PROVIDED TO EFSA

1. Initial dossier. February 2020. Submitted by Kuraray Eval Europe.
2. Additional data. January 2024. Submitted by Kuraray Eval Europe.

ABBREVIATIONS

ANO	8-amino-1-nonanol/9-amino-1-nonanol
BA	benzoic acid
bw	body weight
CAS	Chemical Abstracts Service
CEF	EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CEP	EFSA Panel on Food Contact Materials, Enzymes and Processing Aids
ESI	electrospray ionisation
FCM	food contact materials
FDA	Food and Drug Administration
GLP	good laboratory practice
GPC	gel permeation chromatography
LDL	low-density lipoprotein
LMWF	low molecular weight fraction
LoD	limit of detection
MODA	2-methyl-1,8-octanediamine
NOAEL	no observed adverse effect level
NMDA	1,9-nonanediamine
PA-9T	polyamide-9T
PD	population doubling
PMMA	poly(methyl methacrylate)
Po/w	octanol/water partition coefficient
OECD	Organisation for Economic Co-operation and Development
RPD	relative population doubling
SP	sodium phosphinate
SCF	Scientific Committee on Food
SML	specific migration limit
TA	terephthalic acid
UPLC-HR-MS	Ultra-Performance Liquid Chromatography–High-Resolution Mass Spectrometry
UPLC-UV	Ultra-Performance Liquid Chromatography–UV detection

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CONFLICT OF INTEREST
If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR
Dutch competent authority (Ministry of Health, Welfare and Sport)

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