National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

Dutch Committee for Safety Assessment of Food Contact Materials

CBVV

Opinion

on an application for authorisation under the Dutch Commodities Act Decree on packaging and consumer articles for

N-(1,1-dimethyl-3-oxobutyl)acrylamide

CAS Number: 2873-97-4

Submitting applicant: Covestro Coating Resins BV (transferred from DSM Coating Resins BV)

CBVV-S1029-D0041

Adopted

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1. Introduction

Before a substance is authorised to be used in food contact materials (FCM) and is included in a positive list, an opinion on its safety is required. This is laid down in Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food[1], and implemented in the Dutch Commodities Act Decree on packaging and consumer articles (Warenwetbesluit verpakkingen en gebruiksartikelen)[2] and its corresponding Regulation (Warenwetregeling verpakkingen en gebruiksartikelen)[3]. In case industry seeks authorisation for a substance that is not yet on a positive list and which is used in a material for which so far no harmonized EU legislation applies, it may submit an application for authorisation to the Dutch Committee for Safety Assessment of Food Contact Materials (CBVV) for its evaluation. Such an application may also be submitted for a modification of a current entry on a positive list. The CBVV will carry out an assessment of the risks related to the intended use of the substance and deliver a scientific opinion.

In this case, the CBVV received an application from DSM Coating Resins BV (in 2021 transferred to Covestro Coating Resins BV), requesting the evaluation of the substance N-(1,1-dimethyl-3-oxobutyl)acrylamide (CAS No 2873-97-4) for inclusion in Chapter X (Coatings), subsection a (monomers) of section 3 (Dispersions of macromolecular substances in water) of Part A of the Annex to the Commodities Act Regulation on packaging and consumer articles.

2. Data and methodologies

2.1 Data

The applicant has submitted a dossier in support of their application for the authorisation of N-(1,1-dimethyl-3-oxobutyl)acrylamide (diacetone acrylamide; 4-acrylamido-4-methyl-2-pentanone; DAAM) as a monomer for water-based polymer dispersions. Additional information was provided by the applicant during the assessment process in response to requests from CBVV sent on 16 December 2019 and 11 May 2021 (see 'Documentation provided to CBVV').

Data submitted and used for the evaluation are:

Non-toxicological data and information
- Chemical identity
- Physical and chemical properties
- Manufacturing process
- Intended use
- Existing authorisation(s)
- Impurities and oligomers

[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.

[2] Besluit van 30 mei 2005, houdende vaststelling van het Warenwetbesluit verpakkingen en gebruiksartikelen in verband met Verordening (EG) nr. 1935/2004 van het Europees Parlement en de Raad van de Europese Unie van 27 oktober 2004 inzake materialen en voorwerpen bestemd om met levensmiddelen in contact te komen en houdende intrekking van de richtlijnen 80/590/EEG en 89/109/EEG (PbEU L 338) (Warenwetbesluit verpakkingen en gebruiksartikelen). Staatsblad van het Koninkrijk der Nederlanden, 2005, 420.

[3] Regeling van de Minister van Volksgezondheid, Welzijn [en Sport] van 14 maart 2014, kenmerk 328583-117560-VGP, houdende vaststelling van de Warenwetregeling verpakkingen en gebruiksartikelen die in contact komen met levensmiddelen (Warenwetregeling verpakkingen en gebruiksartikelen). Staatscourant, 2014, 8531.

- Migration of substances
- Residual content of substances

Toxicological data
- Bacterial gene mutation test
- In vitro mammalian cell micronucleus test
- Other information

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) and the Note for Guidance of the European Food Safety Authority (EFSA) for the preparation of an application for the safety assessment of a substance to be used in plastic FCM (EFSA CEF Panel, 2021).

The methodology is based on the characterisation of the substance that is 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 is 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) and the EFSA Scientific Committee recommendations on genotoxicity testing strategies applicable to food and feed safety assessment (EFSA Scientific Committee, 2011).

3. Assessment

The substance DAAM has previously been evaluated by EFSA, who expressed a scientific opinion on the safety of its use as a comonomer for acrylic copolymers with keto side

groups for non-self-supporting coatings on polyolefins used in laminates made from plastics (EFSA CEF Panel, 2015). Since coatings are outside EFSA's mandate and thus not covered by EU legislation, the G4 Commission (the predecessor of the CBVV) adopted EFSA's opinion on this limited claim of intended use without re-assessment when it in 2016 received a dossier from BASF Nederland B.V. for that particular use. This resulted in the following entry in Chapter X, section 3, subsection a of Part A of the Annex to the Commodities Act Regulation on packaging and consumer articles[4]:

> N-(1,1-dimethyl-3-oxobutyl)acrylamide; CAS No 2873-97-4; SML = 0.05 mg/kg; only to be used as co-monomer in acrylic copolymers, to induce keto-side groups crosslinked with adipic acid dihydrazide, in coatings on plastics and not in direct contact with food.

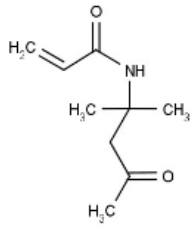
The present application, by a different applicant, was submitted to the CBVV before the above mentioned entry was published, and is intended to have a broader application of DAAM. DAAM is to be used as monomer into acrylic and other (co-)polymers, to provide crosslinking properties by introducing ketone-groups in water-based polymer dispersions. These dispersions are used as binders in primers, printing inks and coatings applied onto both absorbing and non-absorbing substrates intended for food packaging applications. These substrates can be made of paper and board, polyethylene, polypropylene, polyester, aluminium, polyamides etc. DAAM containing polymer is meant for direct and indirect contact with food, with both single and repeated use applications in scope. Contact times with foodstuffs can range from several minutes (paper and board) to more than 6 months (for products with a long shelf life). The packaging materials coated/printed with DAAM functional polymers are not intended to be used for oven applications, but microwave heating of foodstuffs with a maximum of 100°C is possible.

3.1 Non-toxicological data

3.1.2 Identity of the substance

Chemical formula: $C_9H_{15}NO_2$

Chemical structure:



In the dossier it is briefly described that DAAM is converted into polymers through radical polymerization (via its acrylic double bond) in an aqueous emulsion process. This mechanism leaves the C=O ketone group fully intact. The resulting DAAM-containing aqueous polymer dispersion can function as a binder upon film formation by adding a crosslinker. Typically, the crosslinking reaction is a condensation reaction (i.e. a reaction connecting two reactants while splitting off water) between the ketone group introduced

[4] Regeling van de Minister van Volksgezondheid, Welzijn en Sport van 26 april 2022, 3348384-1027396-VGP, houdende wijziging van de Warenwetregeling verpakkingen en gebruiksartikelen in verband met het verwijderen en toevoegen van stoffen aan deel A van de bijlage en enkele technische wijzigingen. Staatscourant, 2022, 11934.

by DAAM and a hydrazide group introduced by a crosslinker. The crosslinking will result in a high-performance film (primer or coating or printing ink layer).

3.1.2 Physical and chemical properties

DAAM has a molecular weight of 169.22 g/mol. It is used at a purity higher than 99%. The substance has hydrophilic characteristics with a log Po/w (octanol/water partition coefficient) determined at 0.321 at 21 °C and a water solubility of 839 g/L at 20 °C. DAAM has a melting point of 57 °C and a boiling point of 310 °C. It decomposes at an onset of 105 °C and a peak of 204 °C. The maximum polymer processing temperature is 95 °C.

3.1.3 Migration data

Based on worst-case calculations, the maximum migration of residual DAAM, impurities and oligomers from a typical DAAM containing product was determined. In these calculations, the highest amounts of residual DAAM, oligomers and acrylamide (one of the impurities) as analytically determined in various commercial binders were used. This resulted in worst-case migrations of 40 ppb, 94 ppb and 0.4 ppb for residual DAAM, oligomers and acrylamide, respectively. So, migration of DAAM was shown to be below 50 ppb, whereas for oligomers it was near the EFSA threshold of 90 ppb for Cramer class III substances (EFSA, 2019). For acrylamide the migration was below the detection limit of 10 ppb set in the Plastics Regulation[5] as SML for substances for which no migration is permitted. For impurities other than acrylamide, the worst-case migration based on supplier specifications was well below their respective SMLs.

3.2 Toxicological data

3.2.1 Genotoxicity

3.2.1.1 Bacterial reverse mutation test

DAAM was tested in a bacterial reverse mutation test with Salmonella typhimurium strains TA97a, TA98, TA100, TA102 and TA1535, with and without metabolic activation. No substantial increases in revertant colony numbers over control counts were obtained with any of the tester strains following exposure to DAAM at any concentration up to and including 5000 µg/plate in either the presence or absence of S9 mix. DAAM thus did not show evidence of mutagenic activity under the test conditions used.

3.2.1.2 In vitro mammalian cell micronucleus assay

DAAM was also tested in an in vitro micronucleus test in cultured peripheral human lymphocytes. No relevant increase in the number of mono- and binucleated cells with micronuclei was observed at concentrations up to and including 1692 µg/mL (0.01 M) in the absence and presence of S9-mix. Under the experimental conditions used, DAAM was considered not clastogenic or aneugenic.

3.2.1.3 Other information

Reference was made to the earlier EFSA opinion on the safety assessment of 4-acrylamido-4-methyl-2-pentanone for use in food contact materials (EFSA, 2015). In this opinion, the results of a bacterial reverse mutation test, an in vitro gene mutation test in Chinese hamster V79 cells, an in vitro chromosome aberration test in Chinese hamster V79 cells, and an in vivo micronucleus test in mice were summarised. DAAM tested negative in all these studies, although with respect to the latter study EFSA remarked that there was no

[5] Commission Regulation (EC) 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.

proof that the bone marrow had been exposed. However, based on the negative results of the in vitro studies on gene mutation and on chromosomal damage, EFSA concluded that DAAM does not give rise to concerns for genotoxicity and that there was no need to demonstrate bone marrow exposure for the in vivo micronucleus test.

3.2.2 General toxicity

3.2.2.1 Other information

In the earlier EFSA opinion on the safety assessment of 4-acrylamido-4-methyl-2-pentanone for use in food contact materials (EFSA, 2015), it was concluded that there is no evidence for neurotoxicity of DAAM in vivo: although some neurotoxic potential was seen in an in vitro study, this was not expressed in different in vivo studies.

3.3.3 Concluding remarks on toxicity

As migration of DAAM was shown to be below 50 ppb, the toxicological data provided in the dossier fulfil the requirements for a substance with low migration (i.e. < 0.05 mg/kg food). Based on the available data, DAAM is concluded to be a non-genotoxic and non-neurotoxic substance.

4. Conclusions

Based on the data submitted, the CBVV concluded that the substance N-(1,1-dimethyl-3-oxobutyl)acrylamide does not raise a safety concern for the consumer under the intended and tested conditions of use as a monomer for water-based polymer dispersions. To CBVV's opinion, the current entry for the substance in part A of the Annex to the Commodities Act Regulation on packaging and consumer articles (see section 3) can be changed as follows:

Chapter	**Section**	**Subsection**
X. Coatings	3. Dispersions of macromolecular substances in water	a. monomers

CAS No	**Name**	**SML mg/kg**	**Restrictions and specifications**
2873-97-4	N-(1,1-dimethyl-3-oxobutyl) acrylamide	0.05	

In Dutch:

Hoofdstuk	**Paragraaf**	**Subparagraaf**
X. Deklagen	3. Dispersies van macromoleculaire stoffen in water	a. monomeren

CAS Nr	**Naam**	**SML mg/kg**	**Restricties en specificaties**
2873-97-4	N-(1,1-dimethyl-3-oxobutyl) acrylamide	0,05	

Documentation provided to CBVV

1) Initial dossier. May 2019. Submitted by DSM Coating Resins BV.
2) Additional data. December 2020. Submitted by DSM Coating Resins BV.
3) Additional data. July/August 2021. Submitted by Covestro Coating Resins BV (following transfer of the dossier).

References

EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2015. Scientific Opinion on the safety evaluation of the substance, 4-acrylamido-4-methyl-2-pentanone, CAS No 2873-97-4, for use in food contact materials. EFSA Journal 2015;13(11):4283, 8 pp. https://doi:10.2903/j.efsa.2015.4283

EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2021. Note for Guidance for the preparation of an application for the safety assessment of a substance to be used in plastic Food Contact Materials (update 2021). EFSA Journal 2008, 6(7):21r, 41 pp. https://doi.org/10.2903/j.efsa.2008.21r

EFSA Scientific Committee, 2011. Scientific Opinion on genotoxicity testing strategies applicable to food and feed safety assessment. EFSA Journal 2011;9(9):2379, 69 pp. https://doi.org/10.2903/j.efsa.2011.2379

EFSA Scientific Committee, 2019. Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment. EFSA Journal 2019;17(6):5708, 17 pp. https://doi.org/10.2903/j.efsa.2019.5708

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 to its authorisation. Available online: https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out82_en.pdf

Abbreviations

CAS	chemical abstracts service
EFSA	European Food Safety Authority
FCM	food contact materials
SCF	Scientific Committee on Food
SML	specific migration limit