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

alpha-D-Glucan, (1,3),(1,6)-, modified with 2,3-epoxypropyl trimethylammonium chloride or 3-chloro-2-hydroxypropyl trimethylammonium chloride

CAS Number: 1803472-20-9

Submitting applicant: Keller and Heckman LLP

CBVV-S1035-D0048

Final

Adopted

25 February 2026

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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 Keller and Heckman LLP, requesting the evaluation of the substance alpha-D-glucan, (1,3),(1,6)-, modified with 2,3-epoxypropyl trimethylammonium chloride or 3-chloro-2-hydroxypropyl trimethylammonium chloride (hereafter “Cationic GT glucan”; CAS No 1803472-20-9) for inclusion in Chapter II (Paper and cardboard), subsections m (agents for improving the wet strength) and b (precipitation, fixation, retention and drainage agents) of section 1.2.2 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 cationic GT glucan to be used in industrial and food-contact paper and paperboard applications. This dossier has also been submitted to the German authorities, for inclusion into BfR Recommendation XXXVI (Paper and board for food contact).

Data submitted and used for the evaluation are:

Non-toxicological data
- Data on chemical identity
- Data on physical and chemical properties
- Data on intended use and existing authorisation(s)
- Data on the manufacturing process of the substance/FCM
- Data on residual content of the substance
- Data on the potential migration of the substance

[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.

Toxicological data

- Published in vitro and in vivo genotoxicity data on 2,3-epoxypropyl trimethylammonium chloride (EPTAC) and 3-chloro-2-hydroxypropyl trimethylammonium chloride (CHPTAC)
- Published in vitro genotoxicity data and 90-d study on the diol 2,3-dihydroxypropyl trimethylammonium chloride (DHPTAC)
- Read-across and in silico data on the olefin 3-hydroxypropenyltrimethylammonium chloride (HPTAC) and DHPTAC-related oligomers

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 requires applicants to submit an application accompanied by a technical dossier containing the information specified in the guidelines for the safety assessment of a substance to be published by EFSA. In practice, the technical dossier should contain the information required in the EFSA Note for Guidance for the preparation of an application for the safety assessment of a substance to be used in food contact materials (EFSA, 2008) and relevant cross-cutting documents from the EFSA Scientific Committee.

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.

The above tiered approach to toxicity testing applies to all migrating substances.

For impurities, oligomers and reaction and degradation products which migrate into foods, non-testing methods may be taken into account to assess the genotoxic potential (EFSA CEF Panel, 2016).

More detailed information on the required data is available in the above-mentioned EFSA documents and in the EFSA Scientific Committee recommendations on genotoxicity testing strategies applicable to food and feed safety assessment (EFSA Scientific Committee, 2011).

3. Assessment

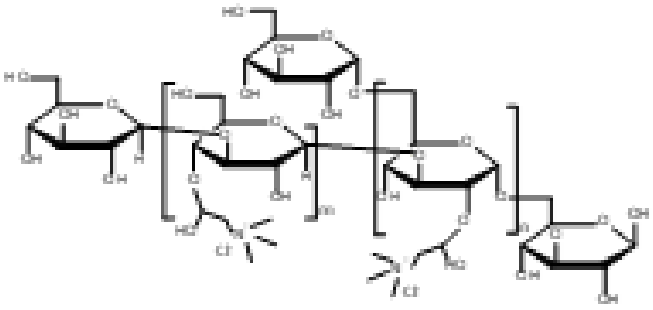
The substance has not been evaluated in the past by the SCF or EFSA, and it is not listed in the Dutch Commodities Act Regulation on packaging and consumer articles. However, the German Federal Institute for Risk Assessment (BfR) has evaluated an identical application for cationic GT glucan, resulting in an inclusion in BfR Recommendation XXXVI (Paper and board for food contact) as per 1 October 2025[4].

The purpose of the present application is to get authorisation for the use of cationic GT glucan as a dewatering agent and a wet strength agent in paper and paperboard manufacture. The finished materials/articles may be used in contact with all food types, under conditions of up to 80 °C, excluding microwave, baking, and hot filter applications.

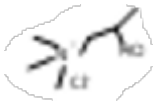
3.1 Non-toxicological data

3.1.2 Identity of the substance

Cationic GT glucan is manufactured by reacting the base polysaccharide polymer alpha-D-glucan, (1,3),(1,6)- (CAS No 83513-22-8; prepared from the polymerization of glucose) with a cationizing agent, 2,3-epoxypropyl trimethylammonium chloride (EPTAC; CAS No 3033-77-0) or 3-chloro-2-hydroxypropyl trimethylammonium chloride (CHPTAC; CAS No 3327-22-8), in the presence of a catalytic amount of sodium hydroxide. A representative structure of the cationic GT glucan is shown below.



where:



and

represent:
$-CH_2CH(OH)CH_2N^+(CH_3)_3Cl^-$

Similar to cationic starches (which are already listed the Dutch Commodities Act Regulation on packaging and consumer articles5), the applicant aims to market several grades of glucan-based polymers in order to cover various functions in the papermaking process. The cationic GT glucan product applied for in the present application contains maximally 3% nitrogen and is to be used at a maximum use level of 0.3%. The molecular weight (mw) is approximately 300 000 Da, with low molecular weight oligomers (< 1000 Da) not present in significant amounts.

It is noted that EPTAC contains epichlorohydrin at an upper limit of 20 ppm. Given that epichlorohydrin is volatile, highly reactive, and water-soluble, it is not expected to be

[4] See BfR Rec. 36.pdf, point 7 in section B (Production aids), subsection IV (Dewatering accelerators) and point 17 in Section C (Special Paper Refining Agents), subsection I (Wet-strength agents).

[5] Cationic starches treated with EPTAC or CHPTAC are listed in Chapter II (Paper and cardboard), subsection h (glues and fibre binding agents) of section 1.2.2, and in Chapter X (Coatings), subsection e (protective colloids and thickening agents) of section 3 (Dispersions of macromolecular substances in water).

present in the final cationic GT glucan product. In the dossier it is plausibly argued that an upper limit of 1 mg epichlorohydrin/kg in the cationic GT glucan can be complied with.

It is further noted that 1,3-dichloro-2-propanol (1,3-DCP) and 3-monochloro-1,2-propanediol (3-MCPD) may end up as contaminants in epichlorohydrin-based polymers, as they can be formed by side reaction of epichlorohydrin with chloride ions under acid condition or by hydrolysis of epichlorohydrin in water.

3.1.2 Physical and chemical properties

Cationic GT glucan is thermally stable at temperatures up to 200 °C. It is insoluble in 95/5 ethanol/water solution. Mixed solutions up to 10/90 ethanol/water and water alone showed increasing solubility. The octanol/water partition coefficient (log Po/w) of the cationic GT polymer is approximated at < -1. Cationic GT glucan is not expected to degrade in gastric juice, saliva simulants or in intestinal fluid simulant.

3.1.3 Migration data

Following measurement of the impurities in commercial cationic GT glucan samples (i.e., residual levels of the cationizing agents EPTAC en CHPTAC and their reaction products), the applicant conducted worst-case migration calculations assuming 100% migration of the residual content amounts from paper. Taking into account the maximum use level for cationic GT glucan and applying a maximum retention factor of 2% for wet-end residues in finished paper, the worst-case migration was calculated to be:

- Below 0.15 µg/kg food for the cationizing agents EPTAC and CHPTAC;
- below 0.05 mg/kg food but above 0.15 µg/kg food for the reaction product 3-hydroxypropenyl-trimethylammonium chloride (HPTAC; CAS No 91725-36-9);
- between 0.05 and 5 mg/kg food for the reaction product 2,3-dihydroxypropyl trimethylammonium chloride (DHPTAC; CAS No 34004-36-9);
- between 0.05 and 5 mg/kg food for the DHPTAC-related oligomers (mainly dimers and trimers).

Migration/extraction data were provided to support that use of the 2% retention factor in the worst-case migration calculations is conservative and does not lead to underestimation of migration.

3.2 Toxicological data

No toxicity data are required for cationic GT glucan as this substance is a large polymer (with a mw typically above 100,000 Da) that is unlikely to be absorbed in the gastrointestinal tract.

The migration of the cationizing agents and reaction product HPTAC was below 0.05 mg/kg food. Therefore, in accordance with the ‘EFSA Note for Guidance’ (EFSA, 2008), the applicant only submitted data on their genotoxic potential. For the reaction product DHPTAC and its related oligomers, with a migration between 0.05 and 5 mg/kg food, the applicant additionally submitted data on general toxicity and on their potential for accumulation. No original toxicity studies were provided, only published study summaries. That was considered acceptable in this case, given that the toxicity studies have been evaluated by a governmental agency under the Australian Industrial Chemicals Introduction Scheme (NICNAS).

3.2.1 Genotoxicity

3.2.1.1 EPTAC and CHPTAC

EPTAC is a genotoxicant[6], with a harmonised classification as Muta. 2 under Regulation (EC) No 1272/2008[7]. CHPTAC is also potentially genotoxic[8]. However, their migration was calculated to be below 0.15 µg/kg food, i.e. the migration level leading to a potential exposure below the threshold of toxicological concern (TTC) of 0.0025 µg/kg body weight (bw) per day for genotoxic carcinogens (EFSA Scientific Committee, 2012). Hence, no (geno)toxicity data need to be provided, as the risk posed by genotoxic substances is considered negligible below 0.15 µg/kg food.

3.2.1.2 DHPTAC

In NICNAS (2010), three in vitro genotoxicity studies with the diol DHPTAC are reported. DHPTAC was not mutagenic to Salmonella typhimurium strains TA 1535, TA 1537, TA98, TA100 and TA102 at concentrations up to 5000 µg/plate in the absence and in the presence of metabolic activation (study according to OECD test guideline (TG) 471). DHPTAC did not induce structural and numerical chromosome aberrations in human peripheral blood lymphocytes (OECD TG 473) or mutations in mouse lymphoma cells (OECD TG 476) when tested up to 5000 µg/mL in the presence and absence of metabolic activation. Based on these negative results, DHPTAC is considered to be not genotoxic.

3.2.1.3 HPTAC

The safety of the olefin HPTAC is addressed by read across from DHPTAC. *In silico* analyses were performed using ToxTree (v. 3.1.0) and the OECD QSAR Toolbox (v.4.4.1) for both HPTAC and DHPTAC.
Both HPTAC and DHPTAC are Cramer Class III compounds, and neither contain structural alerts for genotoxic or non-genotoxic carcinogenicity, Ames test mutagenicity, protein binding, or DNA binding. HPTAC contains no structural alerts for the in vivo micronucleus test in contrast to DHPTAC, which contains an H-acceptor alert (H-acceptor-path3-H-acceptor) that is however of low predictive value (Pradeep et al., 2021; Aljallal et al., 2024). All functional groups identified for HPTAC were also identified for DHPTAC. Based on the above, the two substances present sufficient structural similarity to support a read-across. As DHPTAC is evaluated as being not genotoxic (see 3.1.2.1), by read-across the structurally related HPTAC is also considered not to raise concern for genotoxicity.

The OECD Toolbox metabolism simulator profiler was used to identify potential HPTAC and DHPTAC metabolites. All metabolites were classified as Cramer Class III substances and contained either no structural alerts for genotoxicity or only the low predictive value H-acceptor alert.

3.2.1.4 DHPTAC-related oligomers

In silico analyses were performed using OECD QSAR Toolbox (v. 4.4.1) for fifteen representative oligomer structures, which were selected to contain various combinations of cationized and non-cationized glucose units. It is stated that only four of these

[6] In vitro and in vivo genotoxicity tests with EPTAC reported positive results in the REACH registration dossier 2,3-epoxypropyltrimethylammonium chloride 100.019.293 | 82b7250c-73d5-4a88-9d76-d0555e2abd3e - ECHA CHEM

[7] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

[8] In vitro genotoxicity tests with CHPTAC reported positive results in the REACH registration dossier (3-chloro-2-hydroxypropyl)trimethylammonium chloride 100.020.045 | a56161c9-b434-4827-9113-22b6d10d4fdc - ECHA CHEM

structures (all DHPTAC-related oligomers) represent the predominant oligomers present in the cationic GT glucan products, the remaining structures have not been observed. The oligomers were classified as Cramer Class III substances and contained no alerts for carcinogenicity, Ames test mutagenicity, protein binding, or DNA binding. All contained an H-acceptor alert in the in vivo micronucleus module, but this alert is of low predictive value (see 3.2.1.3).

Additionally, the Toolbox metabolism simulator profiler was used to identify potential oligomer metabolites. Most metabolites were classified as Cramer Class III substances and contained only the low predictive value H-acceptor alert. One predicted metabolite also contains a simple aldehyde alert, but as this is also a predicted metabolite of glucose there is no concern for its safety.

Based on the in silico assessment, the DHPTAC-related oligomers do not raise a concern for genotoxicity.

3.2.2 General toxicity

3.2.2.1 DHPTAC

In NICNAS (2010), a sub-chronic 90 day oral study in rats (OECD TG 408) with a no observed adverse effect level (NOAEL) of 300 mg/kg bw/day is reported. Rats (12/sex/group) were given DHPTAC by gavage at doses of 0, 100, 300 or 1000 mg/kg bw/day for 90 days. The study included a 4-week recovery period for an additional 6 animals/group in the control and high dose groups. Changes in the locomotor activity indicative of some neurotoxic effects were considered the only treatment-related effect. These were seen in mid and high dose animals, but had mostly resolved in recovery animals.

3.2.2.2 DHPTAC-related oligomers

In the *in silico* analyses described in 3.2.1.4 no reproductive or developmental toxicity or repeat-dose toxicity were identified, and none of the structures bind with estrogen receptors.

3.2.3 Accumulation potential

For DHPTAC a log Po/w of 1.15 is reported (NICNAS, 2010). Modelled log Po/w values for the DHPTAC-related oligomers range from -8.93 to -2.64. Because these values are all below 3, per the ‘EFSA Note for Guidance’ (EFSA, 2008) there is “evidence for lack of accumulative potential in the mammalian body”. DHPTAC and related oligomers are thus not expected to accumulate in man.

3.2.4 Concluding remarks on toxicity

Given that EPTAC is genotoxic and CHPTAC is potentially genotoxic, the specific migration of these cationizing agents should be limited to 0.15 µg/kg food. In practice this comes down to ‘not detectable’.

HPTAC is considered not to raise concern for genotoxicity, which allows for migration of HPTAC up to 0.05 mg/kg food.

For DHPTAC and DHPTAC-related oligomers (mainly dimers and trimers), the provided data allow for a migration up to 5 mg/kg food.

4 Conclusions

Based on the data submitted, the CBVV concluded that the substance alpha-D-glucan, (1,3),(1,6)-, modified with 2,3-epoxypropyl trimethylammonium chloride or 3-chloro-2-hydroxypropyl trimethylammonium chloride ("Cationic GT glucan") does not raise a safety concern for the consumer under the intended and tested conditions of use as a dewatering agent in paper and paperboard manufacture. To CBVV's opinion, the substance can be included in part A of the Annex to the Commodities Act Regulation on packaging and consumer articles, together with restrictions for relevant impurities. The proposal is as follows.

For use as dewatering agent, a new entry in:

Chapter	**Section**	**Subsections**
II. Paper and cardboard	1.2.2	b. precipitation, fixation, retention and drainage agents m. agents for improving wet strength

for

- Alpha-D-glucan, (1,3),(1,6)-, modified with 2,3-epoxypropyl trimethylammonium chloride or 3-chloro-2-hydroxypropyl trimethylammonium chloride (CAS 1803472-20-9, containing max. 1 mg/kg epichlorohydrin and max. 3% nitrogen), no more than 0,3%

For impurities, requirements on the maximum migration need to be set in:

Chapter	**Section**	**Subparagraph**
II. Paper and board	1.3 Requirements for the final product	1.3.3

for

substance / group of substances	**SML** **mg / kg**
2,3-dihydroxypropyl trimethylammonium chloride	5
3-hydroxypropenyl-trimethylammonium chloride	0.05
2,3-epoxypropyl trimethylammonium chloride	N.D. (<0.002)
3-chloro-2-hydroxypropyl trimethylammonium chloride *	N.D. (<0.002)

* This substance (CHPTAC) is currently in subparagraph 1.3.3 of Part A of the Annex to the Commodities Act Regulation on packaging and consumer articles listed as ‘chlorohydroxypropyl trimethyl ammonium chloride’ with an SML of 0.05 mg/kg

To be noted: the substances 3-MCPD and 1,3-DCP are already regulated in subparagraph 1.3.3 by requirement of an SML of 0.01 mg/kg and ND (not demonstrable), respectively, whereby for practical application ND means a general detection limit of no more than 0.05 mg/kg. This detection limit is however outdated and should be lowered.

In Dutch:

Voor gebruik als ontwateringsmiddel, opname in:

Hoofdstuk	**Paragraaf**	**Subparagrafen**
II. Papier en karton	1.2.2	b. precipitatie-, fixatie-, retentie- en ontwaterings-middelen m. middelen ter verbetering van de natsterkte

van

- Alfa-D-glucaan, (1,3)(1,6)-, gemodificeerd met 2,3-epoxypropyltrimethylammoniumchloride of 3-chloor-2-hydroxypropyltrimethylammoniumchloride (CAS 1803472-20-9, max. 1 mg/kg epichloorhydrine en max. 3% stikstof bevattend), ten hoogste 0,3%

Daarbij moeten de volgende restricties aan onzuiverheden worden opgenomen in:

Hoofdstuk	**Paragraaf**	**Subparagraaf**
II. Papier en karton	1.3 Eisen aan het eindproduct	1.3.3

voor

stof / groep stoffen	**SML** **mg / kg**
2,3-dihydroxypropyltrimethylammoniumchloride	5
3-hydroxypropenyltrimethylammoniumchloride	0,05
2,3-epoxypropyltrimethylammoniumchloride	N.A. (<0,002)
3-chloor-2-hydroxypropyltrimethylammoniumchloride *	N.A. (<0,002)

* Deze stof (CHPTAC) is op dit moment opgenomen in subparagraaf 1.3.3 van Deel A van de Warenwetregeling verpakkingen en gebruiksartikelen als ‘chloorhydroxypropyltrimethylammoniumchloride’ met een SML van 0.05 mg/kg

Opgemerkt dient te worden dat de stoffen 3-MCPD en 1,3-DCP reeds gereguleerd zijn in subparagraaf 1.3.3 middels een SML van respectievelijk 0,01 mg/kg en NA (niet aantoonbaar), waarbij voor NA voor praktische toepassing een generieke aantoonbaarheidslimiet van ten hoogste 0.05 mg/kg bedoeld wordt. Deze aantoonbaarheidslimiet is echter verouderd en dient naar beneden bijgesteld te worden.

Documentation provided to CBVV

Dossier. October 2025. Submitted by Keller and Heckman LLP.

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Abbreviations

bw	body weight
CAS	chemical abstracts service
EFSA	European Food Safety Authority
FCM	food contact materials
mw	molecular weight
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
Po/w	n-octanol/water partition coefficient
SCF	Scientific Committee on Food
SML	specific migration limit
TG	test guideline