

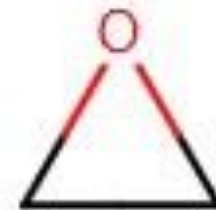
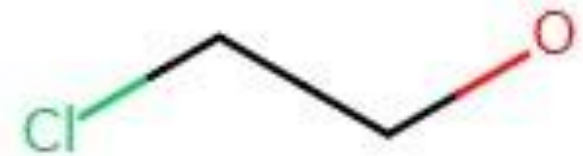
2-Chloroethanol:

Re-assessment of mutagenic potential and provisional dietary reference values

09.10.2025, 97th EFSA Advisory Forum

Carsten Kneuer

Toxicology of Active Substances and Their Metabolites
Pesticide Safety



Ethylene oxide and 2-Chloroethanol: Use and Regulation

- Use of Ethylene oxide (EO) as fumigant for food preservation leads to residues of 2-Chloroethanol (2CE)
- Ethylene oxide no longer authorised for use as a pesticide in the EU under Reg. (EC) 1107/2009 due to CMR properties
- EU Maximum residue levels (MRLs) established at the LOQ
- Current residue definition is the sum of ethylene oxide and 2-chloroethanol

Status under <u>Reg. (EC) No 1107/2009</u>  (repealing <u>Directive 91/414/EEC</u> )		Not approved
Legislation	Old legislation	
Date of approval	Expiration of approval	
Type		
Remarks	Banned - Not assessment has been carried out under Reg. (EU) 1107/2009	

Ethylene oxide and 2-Chloroethanol: Residues in imported goods and Risk Assessment

- From 2020, numerous findings / MRL exceedances in sesame, other commodities and food additives -> Rapid Alert System for Food and Feed (RASFF) notifications
- Initial risk assessments (if conducted) based on MoE approach for EO
- Advanced analytical methods -> residues of 2CE dominating, EO mostly absent
- No health-based guidance values for 2CE derived due to inconsistent and insufficient data -> [Recommendations for action by BfR \(2021\) and EFSA \(2022\)](#)

www.bfr.bund.de


Bundesinstitut für Risikobewertung

DOI 10.17590/20210428-072544

Health risk assessment of ethylene oxide residues in sesame seeds

Updated BfR Opinion No 024/2021 issued 01 September, 2021*


EFSA Journal

STATEMENT

ADOPTED: 28 January 2022
doi: 10.2903/j.efsa.2022.7147

Statement on the BfR opinion regarding the toxicity of 2-chloroethanol

EFSA (European Food Safety Authority),
Jorge Borroto, Anna Federica Castoldi, Arianna Chiusolo, Angelo Colagiorgi, Mathilde Colas,
Federica Crivellente, Chloe De Lentdecker, Frederique Istace, Dimitra Kardassi, Iris Mangas,
Tunde Molnar, Juan Manuel Parra Morte, Andrea Terron and Manuela Tiramani

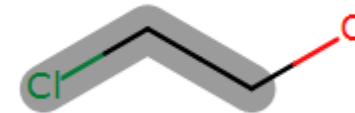
2-Chloroethanol: New data and assessment (1/3)

- Generated and submitted by Food Federation Germany
 - Assessed by BfR
- i) Optimisation of the *in vitro* metabolic activation system, including a feasibility study and PBK modelling to support IVIVE of exposure conditions

- ICCR Roßdorf (2023) Report 2-Chloroethanol: Feasibility Study aiming to demonstrate the transformation of 2-chloroethanol to 2-chloroacetic acid, dated 18.7.2023.
- Lebensmittelverband (2023) 2-Chloroethanol Project on Genotoxicity Tests Overview. Lebensmittelverband Deutschland, dated 12.10.2023
- Procter & Gamble (2023) 2-Chloroethanol In Vitro Metabolism and In-Vitro-to-In-Vivo Extrapolation, dated 27.10.2023
- Procter & Gamble, (2023b) 2-Chloroacetic Acid Formation: Review of In Vitro Data and use of In-Vitro-to-In Vivo Extrapolation, dated 27.10.2023

Toxicity concerns related to

- Alkyl halide – direct DNA reactivity, independent of metabolic activation



- 2-Chloroacetaldehyde – adduct formation following metabolic activation of 2CE



2-Chloroethanol: New data and assessment (2/3)

ii) Full *in vitro* Genotoxicity test battery

- bacterial reverse mutation test (OECD TG 471)
- mammalian cell gene mutation test (OECD TG 476)
- mammalian cell micronucleus test (OECD TG 487)
- ✓ GLP and OECD TG compliant, optimized conditions
- ✓ Negative, applying the formal evaluation criteria

- ASB2024-10963: Chang (2024) ICCR Study Number 4008111
- ASB2024-2781: Sokolowski (2024) ICCR Study Number 4008112
- ASB2024-5121: Naumann (2024) ICCR Study Number 4008113

Table 2 Benchmark dose modelling (BMD) calculations with BMDL-benchmark dose lower limit and BMDU-benchmark dose upper limit

BMR=50 %	BMDL (µg/plate)	BMD	BMDU (µg/plate)	Ratio BMDU/BMDL
TA1535 Exp.1	542	1953	7306	13,5
TA1535 Exp.2	980	1593	2555	2,6
TA100 Exp.1	3812	4395	4939	1,3
TA100 Exp.2	2316	3509	5513	2,4
E.coli Exp.1	3769	5088	6769	1,8
E.coli Exp.2	2806	3528	4398	1,6

Remaining concerns related to

- Dose dependent increases in revertant frequencies just missing the 2-fold / 3-fold threshold at high dose
- Consistent between repeat experiments
- For all three strains detecting base-pair exchange mutations
- ✓ Strictly **dependent on metabolic activation -> potentially related to aldehyde formation**
- ✓ Considered **unlikely to be relevant at dietary exposure levels**
- ✓ Confirmatory mechanistic studies suggested

2-Chloroethanol: New data and assessment (3/3)

iii) Review of the general mammalian toxicity

- Position paper submitted by Food Federation Germany
 - Targeted literature review by BfR
 - including human data (occupational, accidental, suicidal)
 - US-EPA assessments 2012, 2020
- Limited quality of the dataset (no GLP, OECD TG compliant study), reflected in additional uncertainty factor for ADI
 - Instability of 2CE in formulations, data from studies w/o dose verification excluded unless doses freshly prepared
 - Lack of full text access for some studies
 - Proposed values comparable to US-EPA 2012

Reference value	Point of departure (PoD)	Uncertainty / Extrapolation factor (UF)	Reference value (numerical)
ARfD	90-day dog study, dietary NOAEL: 13.3 mg/kg bw/d LOAEL: 18.4 mg/kg bw/d based on vomiting supported by human case reports	<u>Intra- and Interspecies:</u> UF = 100	0.13 mg/kg bw
ADI	90-day dog study, dietary NOAEL: 13.3 mg/kg bw/d LOAEL: 18.4 mg/kg bw/d based on reduced body weight	<u>Intra- and Interspecies:</u> UF = 100 <u>Extrapolation sub- chronic to chronic:</u> UF = 2 <u>quality of dataset:</u> UF = 3	0.02 mg/kg bw/d

2-Chloroethanol: Conclusions and Outlook

- ✓ Relevant **genotoxic potential of 2CE unlikely**, but confirmatory mechanistic study suggested
- ✓ Provisional **ARfD / ADI derived**, call for data to obtain missing full-text reports and systematic literature review recommended

Further activities for discussion

- Harmonisation of the risk assessment / TRVs for 2CE in the EU
- Collection of residue data as basis for proposing separate MRLs
- Validation and Implementation of improved analytical methods measuring EO and 2CE separately

Carsten KNEUER
T +49 30 18412-0
63@bfr.bund.de

German Federal Institute for Risk Assessment
bfr.bund.de/en



valid for texts produced by the BfR
images/photos/graphics are excluded unless otherwise indicated

BfR | Identifying Risks –
Protecting Health

Consumer health protection to go
BfR2GO – the BfR Science Magazine

bfr.bund.de/en/publications/bfr2go/

Follow us

-  @bfrde | @bfren | @Bf3R_centre
-  @bfrde
-  youtube.com/@bfr_bund
-  social.bund.de/@bfr
-  linkedin.com/company/bundesinstitut-f-r-risikobewertung
-  podcast.bfr.bund.de
-  threads.net/@bfrde
-  bsky.app/profile/bfrde.bsky.social