Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Acrylates and methacrylates based on bisphenol A (BPA)

Evaluation statement

26 June 2024

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AICIS evaluation statement

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Acrylates and methacrylates based on bisphenol A (BPA)

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Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

Chemicals in this evaluation are structurally related chemicals listed on the Australian Inventory of Industrial Chemicals (the Inventory).

These chemicals all contain the bisphenol A (BPA) moiety and have potential to contain at least one acrylate or methacrylate group.

This evaluation is a human health risk assessment for all identified industrial uses of these chemicals. Chemicals in this evaluation are likely to have similar use patterns.

In this evaluation the chemicals will be referred to as follows:

- CAS No.1565-94-2 – BPA glycidyl dimethacrylate
- CAS No. 4687-94-9 – BPA glycidyl diacrylate
- CAS No. 41637-38-1 – ethoxylated BPA dimethacrylate
- CAS No. 64401-02-1 – ethoxylated BPA diacrylate
- CAS No. 56744-60-6 – BPA bis(methacryloyloxyethoxyethyl ether)
- CAS No. 27689-12-9 – BPA bis(3-methacryloyloxypropyl) ether
- CAS No. 24448-20-2 – BPA bis(methacryloyloxyethyl) ether
- CAS No. 36425-15-7 – Epichlorohydrin-BPA-methacrylic acid polymer
- CAS No. 55818-57-0 – BPA-epichlorohydrin polymer acrylate.

Summary of evaluation

Summary of introduction, use and end use

There is no specific information about the introduction, use and end use of the chemicals in this evaluation in Australia.

Based on international uses, these chemicals are mainly used commercially in a wide range of products such as adhesives, coatings and printing inks and site limited use in manufacturing other chemicals and polymer products. Domestic uses in adhesives and sealants have been identified for three chemicals. Half of these chemicals have reported use in food contact materials in plastics, coatings, paperboard, adhesives, printing inks.

The following chemicals have cosmetic use in nail products:

- BPA glycidyl dimethacrylate (CAS No.1565-94-2)
- BPA glycidyl diacrylate (CAS No. 4687-94-9)
- ethoxylated BPA dimethacrylate (CAS No. 41637-38-1)
- ethoxylated BPA diacrylate (CAS No. 64401-02-1)
- BPA bis(methacryloyloxyethoxyethyl ether) (CAS No. 56744-60-6).

Human health

Summary of health hazards

The identified health hazards are based on available data for the some of the chemicals in the group and data from structurally related UVCBs (unknown or variable composition, complex reaction products or biological materials) that are not on the Australian Inventory.The release of BPA through degradation of ether linkages is not expected under most conditions and the available toxicity and toxicokinetic data do not provide evidence of BPA release. The toxicological properties of these chemicals are expected to mainly result from the pendant (meth)acrylate groups.

Some chemicals in this evaluation may be introduced as polymers. Polymer toxicity can be attributed to the presence of some specific functional groups present. Under the *Industrial Chemicals (IC) (General) Rules 2019* (IC Rules 2019), acrylates and methacrylates are considered high concern reactive functional groups. The hazards of polymers will depend on the number average molecular weight (Mn), functional group equivalent weight (FGEW) and the amount of low molecular weight species present. The available information indicates that the polymers are likely to be introduced and used with significant number of species below a molecular weight of 1000 Da. Where polymers in this group are introduced as high molecular weight polymers with a low content of low molecular weight species, these chemicals are expected to have limited bioavailability and low hazard potential.

Based on the available information these chemicals:

- have low acute and dermal toxicity
- are not skin or eye irritants
- are not considered to have genotoxic potential
- are not expected to cause serious systemic health effects following repeated exposure.

Based on the weight of evidence from available in vivo, in silico and human data, the chemicals have potential to be skin sensitisers. The available data indicate that acrylates are more sensitising than methacrylates in this group. Although mixed results were reported from in vivo studies and data are not available for many of these chemicals, there is considered sufficient evidence to classify all acrylates reported in this Evaluation Statement. Positive reactions in humans have been reported for BPA glycidyl dimethacrylate (CAS No. 1565-94-2), BPA glycidylacrylate (CAS No. 4687-94-9) and BPA bis(methacryloyloxyethyl) ether (CAS No. 24448-20-2). Although reactions may be associated with presence of epoxy impurities or cross reactivity to epoxy resin or other methacrylates this does not explain all reported incidences.

Based on the available data, most of these chemicals are not expected to cause significant adverse effects on reproduction or development. There is no evidence of effects on fertility or development or adverse effects in reproductive organs in a number of animal studies.

No inhalation data are available and no data are available to evaluate carcinogenicity.

For further details of the health hazard information see **Supporting Information**.

Hazard classifications relevant for worker health and safety

Some chemicals in this Evaluation Statement satisfy the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

(UNECE 2017) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical hazards and environmental hazards.

The classification applies to all acrylates (CAS numbers 4687-94-9; 24447-78-7; 37625-93-7; 52985-33-8; 53814-24-7; 55818-57-0; 56361-55-8; 61722-28-9; 64401-02-1; 72004-73-0 and 85865-95-8) and two methacrylates (CAS numbers 1565-94-2 and 24448-20-2). If empirical data become available for a specific chemical, this data may be used to amend the default classification for that chemical. In addition, the classification does not apply if any of the polymers meet the definition of a polymer of low concern in the *IC Rules 2019.*

Health hazards	Hazard category	Hazard statement
Skin sensitisation	Skin Sens. 1	H317: May cause an allergic skin reaction

Summary of health risk

Public

Based on the available use information, the public may be exposed to some of these chemicals by direct application of these chemicals to the nails from using nail enhancement products (such as artificial nails) at concentrations 5–10%. There is sufficient evidence that 2 of these chemicals, BPA glycidyl acrylate and BPA glycidyl methacrylate, are skin sensitisers with positive reactions in animals and humans. Data available for the other chemicals with identified cosmetic use indicate a lower sensitisation potential or less widespread use.

When using nail products containing these chemicals, short term small volume skin contact in the immediate vicinity of the fingernail may occur. Exposure is considered more probable for home use of these chemicals compared to the use in salons by trained personnel. The low volatility of these chemicals limits the potential for exposure through vapour inhalation. The risk is highest when products are in a liquid form as they contain monomers that may be bioavailable. If products are not completely set, dried or ‘UV-cured’, there is an increased risk of absorption of residual monomers through the skin. The risk is lower after the liquid nail product has hardened or set, as the monomers polymerise, which reduces their bioavailability. These chemicals may cause cross reactions in individuals who are sensitised to other acrylates and methacrylates in other products. Overall, there are risks to the public specific to these chemicals that requires management.

Although some of these chemicals may have consumer use in adhesives and sealants, any exposure would be incidental and overall use in these products does not appear to be widespread. The public could come into contact with articles or coated surfaces containing these chemicals. However, it is expected that these chemicals will be bound within articles or coated surfaces and hence will not be bioavailable.

The public may also be exposed to some of these chemicals and any residual BPA through their use in food contact materials such as adhesives, packaging and printing inks. Previous surveys undertaken in Australia have shown that very few foods contain detectable levels of BPA. Therefore, dietary exposure to BPA for Australian consumers is low and likely to have been reduced further since the surveys were conducted because of the phase out of BPA use. Such low levels in the food supply are unlikely to pose a health risk to consumers (FSANZ n.d.).

Workers

During product formulation and packaging, dermal exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

Beauticians and/or nail technicians who frequently apply nail enhancement products to consumers in professional settings are likely to have a higher risk of repeated exposure to these chemicals used in cosmetics via the dermal route. There may be risk of inhalation exposure including from dust particles containing these chemicals when filing, buffing, or removing nails. However, adverse effects arising from this type of exposure would not be due to the intrinsic hazard properties of these chemicals.

Chemicals in this evaluation are potential skin sensitisers. Risks from exposure to the polymers in the group will depend on the Mn and the amount of low molecular weight species present in individual polymers. Polymers with low Mn (<1000 g/mol) and high amount of low molecular weight species present may pose a risk to workers. Control measures to minimise dermal exposure are needed to manage the risk to workers (see **Proposed means for managing risk** section).

Proposed means for managing risk

Public health

Recommendation to Department of Health and Aged Care

It is recommended that the delegate of the Secretary for Poisons Scheduling list the chemicals BPA glycidyl dimethacrylate (CAS No. 1565-94-2) and BPA glycidylacrylate (CAS No. 4687-94-9) in the *Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons)* (SUSMP).

It is recommended that to manage the potential risk associated with the use of these chemicals the entry:

- results in labelling requirements that provide warning statements and safety directions relating to skin sensitisation.

Consideration should also be given to the following:

- the skin sensitisation potential based on animal and human data. The elicitation of skin sensitisation has been observed at low concentrations (<10 ppm)
- the potential use of these chemicals in nail enhancement products that may be available in Australia at concentrations up to 10% (based on overseas exposure data)
- the increasing trend of DIY at home cosmetic nail products used outside of professional settings
- the US Cosmetic Ingredient Review Committee concluded that BPA glycidyl dimethacrylate (CAS No. 1565-94-2) is safe for use in nail enhancement products where skin contact is avoided. The Committee noted that products should be accompanied with directions to avoid skin contact due to the sensitising potential of methacrylates
- the potential use of the chemical in therapeutic products.

Workers

Recommendation to Safe Work Australia

It is recommended that Safe Work Australia (SWA) update the Hazardous Chemical Information System (HCIS) to include classifications relevant to work health and safety.

Some of these chemicals are polymers. Where relevant, the recommended classification and labelling entry should have the following note appended. 'Note 15: The hazards of a polymer may depend on several factors. For more information refer to the assessment report published on the website of the Australian Industrial Chemicals Introduction Scheme'.

Information relating to safe introduction and use

The information in this statement should be used by a person conducting a business or undertaking at a workplace (such as an employer) to determine the appropriate controls under the relevant jurisdiction Work Health and Safety laws.

Control measures that could be implemented to manage the risks arising from dermal exposure to these chemicals include, but are not limited to:

- minimising manual processes and work tasks through automating processes
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Measures required to eliminate or manage risk arising from storing, handling and using these hazardous chemicals depend on the physical form and how these chemicals are used.

These control measures may need to be supplemented with conducting health monitoring for any worker who is at significant risk of exposure to the chemical if valid techniques are available to monitor the effect on the worker's health.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk.

Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

Conclusions

The Executive Director is satisfied that the identified risks to human health from the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under *Section 100* of the *Industrial Chemicals Act 2019* apply.

2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Grouping rationale

Chemicals reported in this evaluation all contain bisphenol A (BPA) groups. All chemicals in the group have potential to contain at least one (meth)acrylate functional group. Acrylates and methacrylates are considered to have high concern reactive functional groups under the *IC Rules 2019*.

For all chemicals in this group, phenols of the BPA group are connected to other groups by an ether linkage. These can be grouped into 3 main subgroups: discrete chemicals, alkoxylated BPA (meth)acrylates and polymers.

Discrete chemicals

Ten chemicals are discrete chemicals that contain 1 or 2 terminal (meth)acrylate groups (see Table 1). The groups linking BPA and the (meth)acrylate are either linear or branched alkyl, alkoxy or hydroxyalkyl. The chemical with CAS No. 85865-95-8 is a UVCB containing 2 BPA groups linked by a phenyl linker.

Table 1. Description of discrete chemicals

CAS Number	(Meth)acrylate functionality	Linking Group
24447-78-7	diacrylate	ethanol
24448-20-2	dimethacrylate	ethanol
72004-73-0	monoacrylate	ethanol
56361-55-8	diacrylate	ethoxyethanol
56744-60-6	dimethacrylate	ethoxyethanol
4687-94-9	diacrylate	glycidyl
1565-94-2	dimethacrylate	glycidyl
24447-72-1	dimethacrylate	isopropanol
27689-12-9	dimethacrylate	propanol
85865-95-8	diacrylate	UVCB containing 2 BPA groups linked by a phenyl linker

Alkoxylated BPA (meth)acrylates

Three chemicals are UVCBs in which 2 terminal (meth)acrylate groups are joined by alkoxylated chains (ethoxylated or propoxylated) (see Table 2).

Table 2. Description of alkoxylated BPA (meth)acrylates

CAS Number	(Meth)acrylate functionality	Alkoxylate chain
41637-38-1	dimethacrylate	ethoxylate
61722-28-9	diacrylate	propoxylate
64401-02-1	diacrylate	ethoxylate

These chemicals may meet the definition of a polymer depending on the number of ethoxylate or propoxylate units. Hazards of the polymers will depend on the number average molecular weight (Mn), Functional Group Equivalent Weight (FGEW) and the amount of low molecular weight species present. The INCI names for ethoxylated BPA dimethacrylate (CAS No. 41637-38-1) and ethoxylated BPA diacrylate (CAS No.64401-02-1) indicate a low degree of ethoxylation (2 and 4, respectively).

Polymers

Seven chemicals are polymers comprised of 2 or 3 monomers including BPA or substituted BPA, an epoxide and (meth)acrylic acid (see Table 3). In 4 of these polymers, it is expected that there are pendant (meth)acrylates as the CAS identity indicates that the (meth)acrylates are appended to a prepolymer of the BPA and (chloromethyl)oxirane monomers. For the remaining 3 polymers, although the CAS identity indicates no prepolymer is formed, the presence of (meth)acrylate functionality cannot be ruled out.

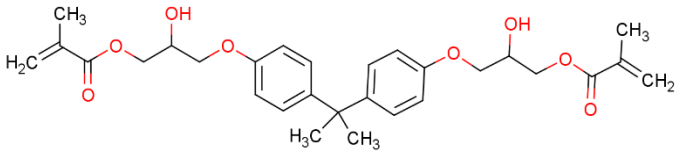
Table 3. Description of polymers

CAS Number	(Meth)acrylate functionality	Comment
36425-15-7	potential methacrylate	CAS identity does not indicate prepolymer but REACH registration describes as oligomeric reaction product of BPA and (chloromethyl)oxirane reaction products with methacrylic acid (REACH n.d.-a)
37625-93-7	potential acrylate	CAS identity does not indicate prepolymer
52985-33-8	potential acrylate	CAS identity does not indicate prepolymer
53814-24-7	diacrylate	CAS identity indicates that the (meth)acrylates are appended to a prepolymer of the BPA and (chloromethyl)oxirane monomers
55818-57-0	acrylate	CAS identity indicates that the (meth)acrylates are appended to a prepolymer of the BPA and (chloromethyl)oxirane monomers
61970-25-0	methacrylate	CAS identity indicates that the (meth)acrylates are appended to a prepolymer of the BPA and (chloromethyl)oxirane monomers
62395-94-2	dimethacrylate	CAS identity indicates that the (meth)acrylates are appended to a prepolymer of the BPA and (chloromethyl)oxirane monomers

Hazards of the polymers will depend on the Mn, FGEW and the amount of LMW species present. Data available from the REACH dossiers indicate that molecular weights are < 1000 (see **Health hazard information** section). The average degree of polymerisation (n) for BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) is reported to be ≤ 0.1 (Government of Canada 2020). There is no information regarding the other polymers in this group.

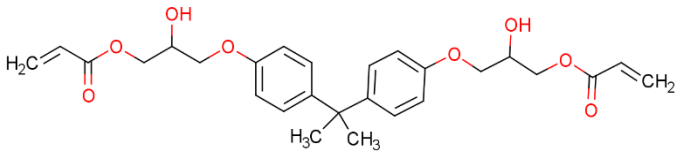
These polymers have been previously assessed under NICNAS (NICNAS 2019a). These are being reassessed together with similar chemicals to consider new information.

Chemical identity

Chemical name	2-Propenoic acid, 2-methyl-, (1-methylethylidene)bis[4,1-phenyleneoxy(2-hydroxy-3,1-propanediyl)] ester
CAS No.	1565-94-2
Synonyms	isopropylidenediphenyl bisoxyhydroxypropyl methacrylate (INCI) bisphenol A glycidyl methacrylate BPA glycidyl dimethacrylate bis-GMA
Molecular formula	C29H36O8
Molecular weight (g/mol)	512.6
SMILES (canonical)	O=C(OCC(O)COC1=CC=C(C=C1)C(C2=CC=C(OCC(O)COC(=O)C(=C)C)C=C2)(C)C)C(=C)C
Chemical description	-
Structural formula:	

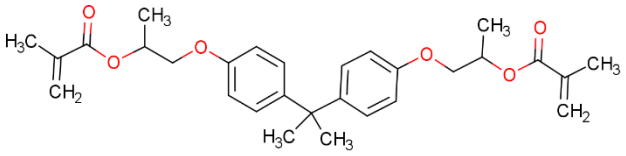
Chemical name	2-Propenoic acid, (1-methylethylidene)bis[4,1-phenyleneoxy(2-hydroxy-3,1-propanediyl)] ester
CAS No.	4687-94-9
Synonyms	bisphenol A diglycidyl etherdiacrylate bisphenol A bis(3-acrylato-2-hydroxypropyl) ether BPA glycidyl diacrylate bis-GA
Molecular formula	C27H32O8
Molecular weight (g/mol)	484.5
SMILES (canonical)	O=C(OCC(O)COC1=CC=C(C=C1)C(C2=CC=C(OCC(O)COC(=O)C=C)C=C2)(C)C)C=C
Chemical description	-

Structural formula:



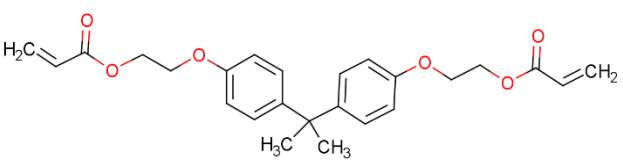
Chemical name	2-Propenoic acid, 2-methyl-, (1-methylethylidene)bis[4,1-phenyleneoxy(1-methyl-2,1-ethanediyl)] ester
CAS No.	24447-72-1
Synonyms	(1-methylethylidene)bis[4,1-phenyleneoxy(1-methyl-2,1-ethanediyl)] bismethacrylate
Molecular formula	C29H36O6
Molecular weight (g/mol)	480.6
SMILES (canonical)	O=C(OC(C)COC1=CC=C(C=C1)C(C2=CC=C(OCC(OC(=O)C(=C)C)C)C=C2)(C)C)C(=C)C
Chemical description	-

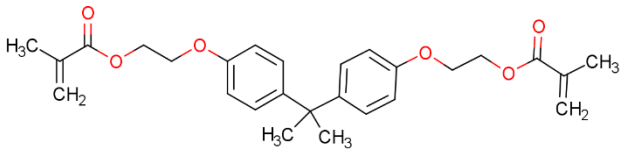
Structural formula:

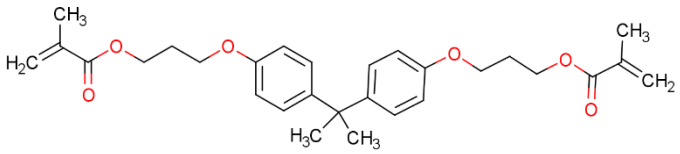


Chemical name	2-Propenoic acid, (1-methylethylidene)bis(4,1-phenyleneoxy-2,1-ethanediyl) ester
CAS No.	24447-78-7
Synonyms	bisphenol A bis(2-hydroxyethyl ether) diacrylate
Molecular formula	C25H28O6
Molecular weight (g/mol)	424.5
SMILES (canonical)	O=C(OCCOC1=CC=C(C=C1)C(C2=CC=C(OCCOC(=O)C=C)C=C2)(C)C)C=C
Chemical description	-

Structural formula:

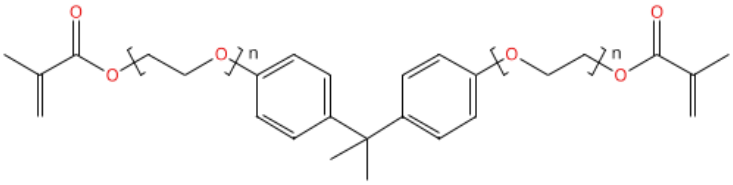


Chemical name	2-Propenoic acid, 2-methyl-, (1-methylethylidene)bis(4,1-phenyleneoxy-2,1-ethanediyl) ester
CAS No.	24448-20-2
Synonyms	2,2-bis[4-(2-methacryloxyethoxy)phenyl]propane bisphenol A bis(2-hydroxyethyl ether) dimethacrylateBPA bis(methacryloyloxyethyl) ether
Molecular formula	C27H32O6
Molecular weight (g/mol)	452.5
SMILES (canonical)	O=C(OCCOC1=CC=C(C=C1)C(C2=CC=C(OCCOC(=O)C(=C)C)C=C2)(C)C)C(=C)C
Chemical description	-
Structural formula:	

Chemical name	2-Propenoic acid, 2-methyl-, (1-methylethylidene)bis(4,1-phenyleneoxy-3,1-propanediyl) ester
CAS No.	27689-12-9
Synonyms	(1-methylethylidene)bis(4,1-phenyleneoxy-3,1-propanediyl) bismethacrylate 2,2-bis[4-(3-methacryloyloxypropoxy)phenyl]propane bisphenol A bis(3-methacryloyloxypropyl) ether
Molecular formula	C29H36O6
Molecular weight (g/mol)	480.6
SMILES (canonical)	O=C(OCCCOC1=CC=C(C=C1)C(C2=CC=C(OCCCOC(=O)C(=C)C)C=C2)(C)C)C(=C)C
Chemical description	-
Structural formula:	

Chemical name	2-Propenoic acid, 2-methyl-, polymer with (chloromethyl)oxirane and 4,4'-(1-methylethylidene)bis[phenol]
CAS No.	36425-15-7
Synonyms	epichlorohydrin, bisphenol A, methacrylic acid polymer epichlorohydrin-BPA-methacrylic acid polymer
Molecular formula	(C15H16O2.C4H6O2.C3H5ClO)x
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	polymer

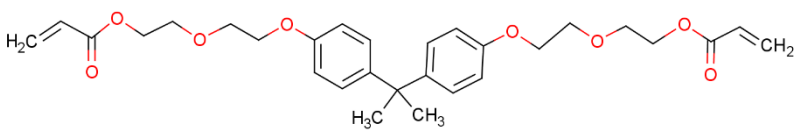
Chemical name	2-Propenoic acid, polymer with (chloromethyl)oxirane and 4,4'-(1-methylethylidene)bis[phenol]
CAS No.	37625-93-7
Synonyms	bisphenol A-epichlorohydrin-acrylic acid polymer phenol, 4,4'-(1-methyethylidene)bis-, polymer with (chloromethyl)oxirane, di-2-propenoate
Molecular formula	(C15H16O2.C3H5ClO.C3H4O2)x
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	polymer

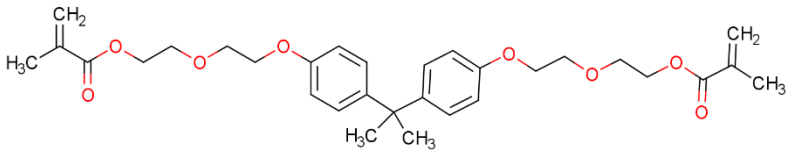
Chemical name	Poly(oxy-1,2-ethanediyl), .alpha.,.alpha.'-[(1-methylethylidene)di-4,1-phenylene]bis[.omega.-[(2-methyl-1-oxo-2-propenyl)oxy]-
CAS No.	41637-38-1
Synonyms	bisphenol A, ethoxylated, dimethacrylate ethoxylated BPA dimethacrylate This CAS number is associated with the INCI name 'isopropylidenediphenol PEG-2 dimethacrylate'. However, the CAS number can cover an unspecified number of ethoxylate units.
Molecular formula	(C2H4O)n(C2H4O)nC23H24O4
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	UVCB/polymer depending on level of ethoxylation
Structural formula:	

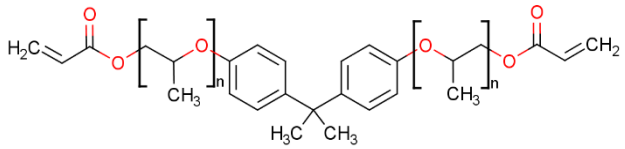
Chemical name	2-Propenoic acid, polymer with 2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bis[oxirane]
CAS No.	52985-33-8
Synonyms	acrylic acid-bisphenol A diglycidyl ether polymer
Molecular formula	(C21H24O4.C3H4O2)x
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	polymer

Chemical name	Phenol, 4,4'-(1-methylethylidene)bis-, polymer with (chloromethyl)oxirane, di-2-propenoate
CAS No.	53814-24-7
Synonyms	bisphenol A-epichlorohydrin polymer diacrylate
Molecular formula	(C15H16O2.C3H5ClO)x.2C3H4O2
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	polymer

Chemical name	Phenol, 4,4'-(1-methylethylidene)bis-, polymer with (chloromethyl)oxirane, 2-propenoate
CAS No.	55818-57-0
Synonyms	This CAS number is associated with the INCI name ‘isopropylidenediphenyl bisoxyhydroxypropyl acrylate’. However, this name represents a discrete chemical and not a polymer. bisphenol A-epichlorohydrin polymer acrylate oxirane, (chloromethyl)-, polymer with 4,4′-(1-methylethylidene)bis[phenol], 2-propenoate
Molecular formula	(C15H16O2.C3H5ClO)x.xC3H4O2
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	polymer

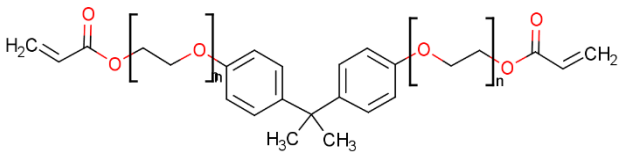
Chemical name	2-Propenoic acid, (1-methylethylidene)bis(4,1-phenyleneoxy-2,1-ethanediyloxy-2,1-ethanediyl) ester
CAS No.	56361-55-8
Synonyms	bisphenol A diethylene glycol diacrylate 2,2-bis(4-acryloxyethoxyethoxyphenyl)propane
Molecular formula	C29H36O8
Molecular weight (g/mol)	512.6
SMILES (canonical)	O=C(OCCOCCOC1=CC=C(C=C1)C(C2=CC=C(OCCOCCOC(=O)C=C)C=C2)(C)C)C=C
Chemical description	-
Structural formula:	

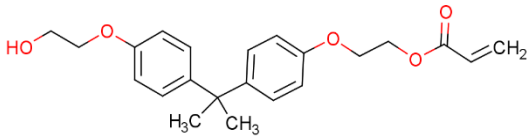
Chemical name	2-Propenoic acid, 2-methyl-, (1-methylethylidene)bis(4,1-phenyleneoxy-2,1-ethanediyloxy-2,1-ethanediyl) ester
CAS No.	56744-60-6
Synonyms	bisphenol A bis(methacryloyloxyethoxyethyl ether) BPA bis(methacryloyloxyethoxyethyl ether) 2,2-bis[4-(methacryloxydiethoxy)phenyl]propane
Molecular formula	C31H40O8
Molecular weight (g/mol)	540.7
SMILES	O=C(OCCOCCOC1=CC=C(C=C1)C(C2=CC=C(OCCOCCOC(=O)C(=C)C)C=C2)(C)C)C(=C)C
Chemical description	-
Structural formula:	

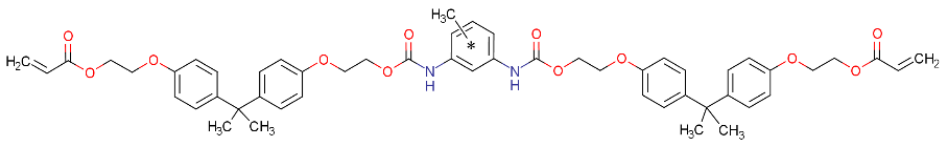
Chemical name	Poly[oxy(methyl-1,2-ethanediyl)], .alpha.,.alpha.'-[(1-methylethylidene)di-4,1-phenylene]bis[.omega.-[(1-oxo-2-propenyl)oxy]-
CAS No.	61722-28-9
Synonyms	bisphenol A, polypropylene glycol ether, diacrylate bisphenol A propoxylate diacrylate
Molecular formula	(C3H6O)n(C3H6O)nC21H20O4
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	UVCB/polymer depending on level of alkoxylation
Structural formula:	

Chemical name	Phenol, 4,4'-(1-methylethylidene)bis-, polymer with (chloromethyl)oxirane, 2-methyl-2-propenoate
CAS No.	61970-25-0
Synonyms	bisphenol A, epichlorohydrin polymer, methacrylate
Molecular formula	(C15H16O2.C3H5ClO)x.xC4H6O2
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	polymer

Chemical name	Phenol, 4,4'-(1-methylethylidene)bis-, polymer with (chloromethyl)oxirane, bis(2-methyl-2-propenoate)
CAS No.	62395-94-2
Synonyms	bisphenol A-epichlorohydrin copolymer dimethacrylate
Molecular formula	(C15H16O2.C3H5ClO)x.2C4H6O2
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	polymer

Chemical name	Poly(oxy-1,2-ethanediyl), .alpha.,.alpha.'-[(1-methylethylidene)di-4,1-phenylene]bis[.omega.-[(1-oxo-2-propenyl)oxy]-
CAS No.	64401-02-1
Synonyms	bisphenol A, ethoxylated, acrylateethoxylated BPA diacrylate ethoxylated BPA diacrylate This CAS number is associated with the INCI name 'isopropylidenediphenol PEG-4 diacrylate'. However, the CAS number can cover an unspecified number of ethoxylate units.
Molecular formula	(C2H4O)n(C2H4O)nC21H20O4
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	UVCB/polymer depending on level of ethoxylation
Structural formula:	

Chemical name	2-Propenoic acid, 2-[4-[1-[4-(2-hydroxyethoxy)phenyl]-1-methylethyl]phenoxy]ethyl ester
CAS No.	72004-73-0
Synonyms	2-propenoic acid, 2-[4-[1-[4-(2-hydroxyethoxy)phenyl]-1-methylethyl]phenoxy]ethyl ester 2,2-bis[4-(2-hydroxyethoxy)phenyl]propyl monoacrylate
Molecular formula	C22H26O5
Molecular weight (g/mol)	370.4
SMILES (canonical)	O=C(OCCOC1=CC=C(C=C1)C(C2=CC=C(OCCO)C=C2)(C)C)C=C
Chemical description	-
Structural formula:	

Chemical name	2-Propenoic acid, (methyl-1,3-phenylene)bis[iminocarbonyloxy-2,1-ethanediyloxy-4,1-phenylene(1-methylethylidene)-4,1-phenyleneoxy-2,1-ethanediyl] ester
CAS No.	85865-95-8
Synonyms	(methyl-1,3-phenylene)bis[iminocarbonyloxy-2,1-ethanediyloxy-4,1-phenylene(1-methylethylidene)-4,1-phenyleneoxy-2,1-ethanediyl] diacrylate
Molecular formula	C53H58N2O12
Molecular weight (g/mol)	unspecified
SMILES (canonical)	-
Chemical description	UVCB
Structural formula:	

Introduction and use

Australia

No specific information is available on the introduction, use and end use of these chemicals in Australia.

International

The following international uses have been identified from the following sources:

- European Union Registration, Evaluation and Authorisation of Chemicals (REACH) dossiers
- European Chemicals Agency (ECHA) Assessment of Regulatory Needs report (ECHA 2021)
- the Substances in Preparations in Nordic Countries (SPIN n.d.) database
- Galleria Chemica (Chemwatch n.d.)
- United States Environmental Protection Agency Chemical Data Reporting (CDR) (US EPA 2016; US EPA 2020)
- Consumer Product Information Database (DeLima Associates n.d.)
- PubChem (NCBI n.d.)
- INCIpedia (Personal Care Products Council n.d).
- the European Commission Cosmetic Ingredients and Substances (CosIng) database (EC n.d.)
- USEPA Chemical and Products Database (USEPA n.d.)
- Food Contact Chemicals database (FCCdb n.d.)
- Cosmetic Ingredient Reviews (CIR 2005; CIR 2023)
- publicly available safety data sheets (SDS).

Based on international use information, the following chemicals have cosmetic uses:

- BPA glycidyl dimethacrylate (CAS No.1565-94-2), used as film formers, single use for nail enhancement products at concentrations up to 4.3–9.5% reported in 2021, frequency of use reported to be 2 (EC n.d., Personal Care Products Council n.d, CIR 2023); two nail products were listed in the Skin Deep database (EWG n.d.)
- ethoxylated BPA dimethacrylate (CAS No. 41637-38-1), used as film formers in nail extenders, polishes and enamels, frequency of use reported to be 15 (EC n.d., Personal Care Products Council n.d)
- BPA glycidyl diacrylate (CAS No. 4687-94-9), nail products 1–10% concentration (SDS)
- ethoxylated BPA diacrylate (CAS No. 64401-02-1), used as film formers (EC n.d.; Personal Care Products Council n.d). No specific reported use was identified.

The chemicals BPA glycidyl dimethacrylate (CAS No.1565-94-2) and BPA bis(methacryloyloxyethoxyethyl ether) (CAS No. 56744-60-6) are reported to be used in personal care products with concentrations ≥1% but <30% by weight (USEPA CDR 2016).

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) is linked with the INCI name ‘isopropylidenediphenyl bisoxyhydroxypropyl acrylate’, which has reported use as film formers (EC n.d.; Personal Care Products Council n.d,) and also has reported cosmetic use in Canada (Government of Canada 2020). However, it is unclear whether identified cosmetic

use is due to the link with INCI name. No consumer uses were reported under REACH of consumer product databases (DeLima Associates n.d.; EWG n.d.; REACH n.d.-b).

Many of these chemicals have reported commercial uses (Chemwatch n.d.; NCBI n.d.; SPIN n.d.; USEPA n.d.).

- paints and coatings
- ink, toner and colourants
- adhesive and sealants
- water treatment products
- lubricant and grease products
- construction products
- solvents
- reprographic agents.

Concentrations up to 90% were reported (USEPA CDR 2016; USEPA CDR 2020). Some of the commercial uses may also be used in domestic applications. However, available information suggests that domestic use of most of these chemicals is not widespread.

Domestic uses were identified for the following chemicals:

- epichlorohydrin-bisphenol A-methacrylic acid polymer (CAS No. 36425-15-7) as sealants (REACH n.d.-a)
- ethoxylated BPA dimethacrylate (CAS No. 41637-38-1) in home maintenance products (USEPA n.d.).

The Consumer Product Information Database lists 2 old products for the chemical BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) in an electronics lubricant and an epoxy adhesive at concentrations up to 2.5% and 85–90% respectively (DeLima Associates n.d). The REACH dossiers for these chemicals BPA propanol dimethacrylate (CAS No. 27689-12-9) and BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) report no identified consumer uses (REACH n.d.-c; REACH n.d.-b).

Half the chemicals have reported use in food contact materials in plastics, coatings, paperboard, adhesives, printing inks (FCCdb n.d.).

Some chemicals also have reported site limited applications as chemical intermediates and in polymer manufacturing (USEPA CDR 2020; Chemwatch n.d.).

No uses were identified for chemicals with CAS numbers 24447-72-1, 52985-33-8 and 61722-28-9.

Existing Australian regulatory controls

Public

No specific controls are currently available for these chemicals.

Workers

These chemicals are not listed on the Hazardous Chemical Information System and no specific exposure standards are available in Australia (SWA n.d.).

International regulatory status

Exposure standards

No specific exposure standards were identified for these chemicals.

European Union

The European Commission is proposing a ban on the use of BPA in food contact materials (FCMs), including plastic and coated packaging.

United States of America

The Cosmetic Ingredient (CIR) Expert Panel concluded that BPA glycidyl dimethacrylate (CAS No. 1565-94-2) is safe for use in nail enhancement products where skin contact is avoided. They noted that products should be accompanied with directions to avoid skin contact due to the sensitising potential of methacrylates (CIR 2005). The panel reconsidered this conclusion in 2021–2022 and decided that this assessment remains valid, as no new toxicity data warrants re-evaluation of these chemicals (CIR 2023).

Exposure

Public

A FSANZ survey of bisphenol A in Australian food was undertaken as part of phase 2 of the 24th Australian Total Diet Study (ATDS). This survey found that dietary exposures of Australian consumers are low and within acceptable safe limits, even using highly conservative methodologies. FSANZ concluded that dietary exposure to bisphenol A for Australian consumers is therefore low, and likely to be reduced further because of consumer-led reductions in bisphenol A use in food contact materials (FSANZ 2016).

Health hazard information

Limited data are available for these chemicals. Given their close structural similarities, data for the following UVCBs are used to support conclusions on endpoints for health hazard assessment:

- esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (no CAS No., EC No. 701-362-9)
- esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (no CAS No., EC No. 935-411-2)
- reaction products of methacrylic acid and 2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bisoxirane (no CAS No., EC No. 701-308-4).

These chemicals are similar to CAS numbers 64401-02-1, 41637-38-1 and 36425-15-7 respectively.

A number of the chemicals in this evaluation are polymers or UVCBs. In the REACH dossiers, the identity of the substance described in industry submitted REACH dossiers is as follows:

- BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) – 4,4'-Isopropylidenediphenol, oligomeric reaction products with 1-chloro-2,3-epoxypropane, esters with acrylic acid' with a molecular weight of 484.6 g/mol
- EC No. 701-362-9 – esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated with a molecular weight of 424.5 g/mol
- EC No. 935-411-2 – esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid with a molecular weight of 452.55 g/mol
- EC No. 701-308-4 – 4,4'-Isopropylidenediphenol, oligomeric reaction products with 1-chloro-2,3-epoxypropane, reaction products with methacrylic acid with a molecular weight of 516.6 g/mol.

The above chemical composition is assumed to be the test material for these chemicals in studies described below unless otherwise stated. Given the similar molecular weights to discrete chemicals and the likelihood that other polymers/UVCBs in this evaluation have a similar molecular weight distribution, it is considered appropriate to read across this data to other members of the group that do not have toxicity data.

Toxicokinetics

No toxicokinetic data are available for this group of chemicals and physicochemical data are limited.

Absorption across biological membranes will depend on the molecular weights and for polymers and UVCBs, the percentage of low molecular weight species. Chemicals with molecular weights below 500 Da are considered more likely to be absorbed, while those with molecular weights above 1000 Da are considered less likely to be absorbed. Available data indicates that the polymers and UVCBs in this evaluation are most likely being introduced and used with significant number of species below a molecular weight of 1000 Da.

(Meth)acrylates are deduced to be metabolised via two pathways: by ester hydrolysis (esterases) in various tissues; and by conjugation with glutathione (GSH), which has been demonstrated for acrylates and methacrylates in vitro and in vivo (formation of mercapturic acid) (Greim et al. 1995). Hydrolysis of (meth)acrylate esters, which is catalysed by carboxylesterases, results in the formation of (meth)acrylic acid and alcohol (McCarthy and Witz 1997; Meyer 2012).

The chemicals in this evaluation are not expected to be metabolised to BPA because the ether bond is resistant to hydrolysis. In a hydrolysis study, BPA glycidyl dimethacrylate (CAS No.1565-94-2), was reacted with phosphoric acid, hydrochloric acid, and sodium hydroxide in methanol or methanol/water mixed media at 37°C. The chemical was partly converted into monomethacrylate by phosphoric acid and into monomethacrylate and 2, 2-bis [4-(2, 3-dihydroxypropoxy) phenyl] propane (BHP) by hydrochloric acid. No BPA was formed by chemical induced hydrolysis (Kadoma and Tanaka 2000).

Acute toxicity

Based on the available data, chemicals in this group have low acute oral and dermal toxicity with median lethal dose (LD50) values reported to be >2000 mg/kg bw in rat studies. No data for acute inhalation toxicity was available.

Oral

4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4)

In a GLP compliant acute oral toxicity study, similar to the Economic Cooperation and Development (OECD) Test Guideline (TG) study TG 423, SPF-Wistar rats (5/sex/dose) were treated with the chemical. Four groups were given a single dose of a test solution, containing 50% test substance and 50% arachidis oil, by gavage. The doses of the undiluted chemical were 10, 12.6, 16, or 20 ml/kg bw (calculated to be 1.17, 14.7, 18.6 and 23.4 g/kg bw based on a density of 1.17 g/mL). Clinical symptoms included lower activity level, mild coordination disturbances, and abnormal posture, piloerection, and diarrhoea. No deaths were recorded in the first 24 hours following treatment. Pathological postmortem examination revealed erythematous gastric and enteric mucosa, but no other observable pathology was found. The chemical is considered to be of low toxicity with LD50 of >23400 mg/kg bw (REACH n.d.-a).

In a GLP compliant, non-guideline fixed dose acute oral toxicity study, Wistar Bor: WISW (SPFTNO) rats (5/sex/dose) were treated with the chemical at 5110 mg/kg bw. There were no signs of toxicity except for salivation in some individuals that lasted up to 20 minutes. No animals died from the exposure. At necroscopy no abnormalities were detected. The LD50 was determined to be >5110 mg/kg bw (REACH n.d.-a).

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0)

In a GLP compliant acute oral toxicity study conducted similarly to OECD TG 401, Sprague Dawley (SD) rats (5/sex/dose) were treated with the chemical at 2000 mg/kg bw. No deaths were observed, and animals appeared normal and expected gain in bodyweight was reported over the study period. No abnormalities were noted at necropsy. The oral LD50 was determined to be >2000 mg/kg bw (REACH n.d.-b).

Esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9)

In a GLP compliant acute oral toxicity study similar to OECD TG 423, SD rats (3 females/group) in the first group were treated with the chemical at 2000 mg/kg bw and then a second group was administered the same dose level. No clinical signs were observed at this dose. The oral LD50 was determined to be >2000 mg/kg bw (REACH n.d.-d).

Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No 935-411-2)

In a GLP compliant acute oral toxicity study similar to OECD TG 423, Wistar Han rats (6 females/dose) were treated with the chemical at 2000 mg/kg bw. The oral LD50 was determined to be >2000 mg/kg bw (REACH n.d.-e).

Dermal

In a GLP compliant acute dermal toxicity test conducted in accordance with OECD TG 402, the chemical BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) was applied to the skin of SD rats (5/sex) at 2000 mg/kg bw. Local effects such as erythema and scabs were observed at the application site. No clinical signs indicative of systemic toxicity were observed in any of the animals. Slight to well defined erythema was observed in the females at the application site. The LD50 was determined to be >2000 mg/kg bw (REACH n.d.-b).

In a GLP compliant acute dermal toxicity test conducted in accordance with OECD TG 402, the chemical, esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9), was applied to the skin of 5 female and 5 male SD rats at the dose level of 2000 mg/kg bw. No unscheduled deaths or clinical signs indicative of systemic toxicity were observed in any of the animals. The LD50 was determined to be >2000 mg/kg bw (REACH n.d.-d).

In a GLP compliant acute dermal toxicity test conducted in accordance with OECD TG 402, the chemical, esterification products of 4,4’-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2), was applied to the skin of 3 female Wistar Han rats at 2000 mg/kg bw. No unexpected changes in body weight gain occurred, no clinical signs were observed, and no abnormalities were seen at necropsy. The LD50 was determined to be >2000 mg/kg bw (REACH n.d.-e).

Inhalation

No data was available.

Corrosion/Irritation

Skin irritation

Chemicals in this group are not irritating based on the available data from GLP compliant skin irritation studies in rabbits and one in vitro assay.

BPA propanol dimethacrylate (CAS No. 27689-12-9)

In a GLP compliant skin irritation study conducted in accordance with OECD TG 404, NZW rabbits (2 female, 1 male) were treated with the chemical for 4 hours under semi-occlusive conditions. Observations were recorded at 24, 48, 72 hours after patch removal. No erythema or oedema was observed in any animal throughout the study (REACH n.d.-c).

4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4)

In a skin irritation study similar to OECD TG 404, 6 albino rabbits (sex not specified) were treated with the chemical for 24 hours under occluded conditions. There were 4 application sites on each rabbit, 2 for treatment with the chemical with and without abrasion and 2 untreated sites with and without abrasion. There were no signs of erythema or oedema on intact skin and mild effects were observed on the abraded skin which resolved within 72 hours of the exposure (REACH n.d.-a).

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0)

In a GLP compliant skin irritation study conducted in accordance with OECD TG 404, 3 male NZW rabbits were treated with the chemical for 4 hours under semi-occlusive conditions and observed for 7 days. There were no signs of irritation at any time (REACH n.d.-b)

In a GLP compliant skin irritation study similar to OECD TG 404, 3 female NZW rabbits were treated with the chemical for 4 hours under semi-occlusive conditions and observed for 3 days. There were no signs of irritation at any time (REACH n.d.-b)

Esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9)

In a GLP compliant skin irritation study conducted in accordance with OECD TG 404, 3 male NZW rabbits were treated with the chemical for 4 hours under semi-occlusive conditions and observed for 7 days. There were no signs of irritation at any time (REACH-n.d.-d)

In a GLP compliant skin irritation study similar to OECD TG 404, 3 NZW rabbits (2 males, 1 female) were treated with the chemical for 4 hours under semiocclusive conditions and observed for 4 days. There were no signs of irritation at any time (REACH n.d.-d).

Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2)

In a GLP compliant in vitro skin irritation study conducted in accordance with OECD TG 439 (in vitro reconstructed human epidermis (RHE) test method for skin irritation), the chemical was applied to RhE, for an exposure period of 15 minutes, followed by a 42-hour recovery period. A mean tissue viability value of 119% was reported for the chemical in this study. It was determined to not be irritating to the skin given that the mean viability was >50% after the MTT reduction (REACH n.d.-e).

Eye irritation

The chemicals are not irritating to eyes based on the available data from GLP compliant eye irritation studies in rabbits and two ex vivo assays.

BPA propanol dimethacrylate (CAS No. 27689-12-9)

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, the chemical was instilled into 1 eye each of 3 NZW rabbits (1 male, 2 females). The eyes were observed at 24, 48, 72 hours after instillation. There was no corneal opacity, iritis or conjunctival chemosis at any time during the study. Conjunctival redness observed in all animals persisted for 48 hours after dosing but resolved in all animals within 72 hours after dosing (REACH n.d.-c).

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0)

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, the chemical was instilled into 1 eye each of 3 male NZW rabbits. The eyes were observed at 1, 24, 48, 72 hours after instillation. Instillation of the test substance resulted in conjunctival redness, chemosis and discharge that completely resolved in all animals within 72

hours. The following mean scores were the same for each animal: corneal opacity 0/4, iritis 0/2, conjunctival redness 0.7/3 and chemosis 0/4 (REACH n.d.-b).

In a GLP compliant eye irritation study conducted similarly to OECD TG 405, the chemical was instilled into 1 eye each of 3 females NZW rabbits. The eyes were observed at 1, 24, 48, 72 hours, 4 days and 7 days after instillation. The following mean scores for all timepoints and rabbits were reported: corneal opacity 0/4, iritis 0/2, conjunctival redness 0.8/3 and chemosis 0.1/4. The conjunctival redness was fully reversible within 7 days and chemosis resolved within 48 hours (REACH n.d.-b).

In a GLP compliant eye irritation study conducted in accordance with EU Method B.5 (similar to OECD TG 405), the chemical was instilled into 1 eye each of 3 NZW rabbits (sex unspecified). The eyes were observed at 1, 2, 3, 4 days and 7 days after instillation. There were no signs of corneal opacity or iritis in any of the animals. The following mean scores for all timepoints and rabbits were reported: corneal opacity 0/4, iritis 0/2, conjunctival redness 1/3 and chemosis 0.45/4. The conjunctival redness and chemosis was fully reversible within 4 days (REACH n.d.-b).

Esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9)

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, the chemical was instilled into 1 eye each of 3 female SPF albino rabbits. The eyes were observed at 24, 48 and 72 hours after instillation. One hour after application of the test article, animals showed conjunctival redness, chemosis and discharge which resolved within one day after instillation. The following mean scores for all timepoints and rabbits were reported: corneal opacity 0/4, iritis 0/2, conjunctival redness 0/3 and chemosis 0/4 (REACH-n.d.-d).

In a GLP compliant eye irritation study conducted in accordance with OECD TG 405, the chemical was instilled into 1 eye each of 3 female NZW rabbits. The eyes were observed at 1, 24, 48 and 72 hours after instillation. No corneal damage or iridial inflammation was observed. Only temporary mild conjunctival reactions were reported that resolved within one day after instillation. The following mean scores for all timepoints and rabbits were reported: corneal opacity 0/4, iritis 0/2, conjunctival redness 0/3 and chemosis 0/4 (REACH n.d.-d).

Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2)

In a GLP compliant ex vivo eye corrosivity/irritation study conducted according to OECD TG 437, the chemical was applied to 3 bovine corneas per experiment. The mean in vitro irritancy score (IVIS) was 0 (IVIS >55 is regarded as serious eye damage and IVIS $\leq$3 is UN GHS No Category). Based on the criteria of the assay, the chemical did not meet the GHS criteria for classification (REACH n.d.-e)

4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4)

In a GLP compliant ex vivo eye corrosivity/irritation study conducted according to OECD TG 437, the chemical was applied to 3 bovine corneas. The mean in vitro irritancy score (IVIS) was 0.2. Based on the prediction model criteria, chemicals with IVIS values of ≤3 are not considered to be corrosive or severely irritating to eyes (REACH n.d.-f).

Sensitisation

Skin sensitisation

Based on the weight of evidence from available in vivo, human observations and in silico data, the chemicals have potential to be skin sensitisers. The available data indicate that the acrylates are more sensitising than the methacrylates. Based on the data for BPA glycidyl diacrylate (CAS No. 4687-94-9), BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) and other polymers with pendant acrylate group, there is sufficient evidence to classify all the acrylates in this evaluation. The available animal and human data are sufficient to classify BPA glycidyl dimethacrylate (CAS No. 1565-94-2) and BPA bis(methacryloyloxyethyl) ether (CAS No. 24448-20-2). Although reactions may be associated with presence of epoxy impurities or cross reactivity to epoxy resins or other methacrylates, this does not explain all reported incidences.

Overall data are not sufficient to sub-categorise. No data are available regarding respiratory sensitisation.

Methacrylates

BPA glycidyl dimethacrylate (CAS No.1565-94-2)

In a guinea pig maximisation test (GPMT), groups of Hartley Dunkin guinea pigs (15 female/group) were pretreated dermally with 10% sodium lauryl sulfate in petrolatum. BPA glycidyl dimethacrylate (CAS No. 1565-94-2, whole product) dissolved in an olive oil vehicle was applied at 10 or 20% for intradermal induction and then 100% for topical induction. Challenge was performed 2 weeks after topical application using the chemical (whole product) at 10% in petrolatum. Thirteen of 15 guinea pigs became sensitised at the first and second challenge with a mean response of 1.17. The chemical could be resolved into three components by high performance liquid chromatography (HPLC). Only fraction 1 (free from linear and branched BPA glycidyl dimethacrylate) caused sensitisation in guinea pigs (8 of 15). The authors concluded the allergenic potential in fraction 1 may have been epoxy resin MW 340 (Bjorkner et al. 1984; CIR 2005).

BPA bis(3-methacryloyloxypropyl) ether (CAS No. 27689-12-9)

In a sensitisation study similar to the GPMT (TG 406), guinea pigs (5/dose, sex unspecified) received intradermal injections on the flanks with 5% dilution of chemical BPA bis(3-methacryloyloxypropyl) ether (CAS No. 28689-12-9) (unspecified vehicle) with Freund's Complete Adjuvant (FCA) on days 1, 5 and 9. 5. Control animals received pre-treatment of FCA only. On day 22, all animals received 0.025 mL of 10, 30 or 100% of the chemical as a topical application on one 2 cm^2 site per treatment per animal. Skin reactions were read at 24, 48, and 72 hours after application of the test material. No erythema was observed on any animals at any time following the challenge treatment including at 100% concentration of the chemical. Based on the results of this study, the chemical was not sensitising (REACH n.d.-c).

In a GPMT, groups of Hartley Dunkin guinea pigs (15 female/group) were pretreated dermally with 10% sodium lauryl sulfate in petrolatum. BPA bis(3-methacryloyloxypropyl) ether (CAS No. 27689-12-9, whole product) in olive oil was applied at 5, 10 or 20% for intradermal induction and then 100% in petrolatum for topical induction. Challenge was performed 2 weeks after topical application using the chemical (whole product) at 10% in petrolatum. The GPM test procedure was repeated twice with each intradermal injection. Challenge reactions (concentration not specified) were all negative (Bjorkner et al. 1984).

BPA bis(methacryloyloxyethyl) ether (CAS No. 24448-20-2)

In a GPMT, groups of Hartley Dunkin guinea pigs (15 female/group) were pretreated dermally with 10% sodium lauryl sulfate in petrolatum. The chemical with CAS No. 24448-20-2 (main fraction) in olive oil/acetone (10:1) and applied at 5% for intradermal induction and then 50% in petrolatum for topical induction. Challenge was performed 2 weeks after topical application using the chemical (main fraction) at 5% in petrolatum. Eight and 11 of 15 guinea pigs became sensitised at the first and second challenge respectively, with a mean response of 0.8 and 1.43 respectively (Bjorkner et al. 1984).

4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4)

In a GLP compliant local lymph node assay (LLNA) conducted in accordance with OECD TG 429, CBA/J- mice (5 female/dose) received topical applications at 0, 10%, 25% or 50% of the chemical in acetone/olive oil (4:1 v/v). The reported stimulation indices (SI) were 1, 0.9, 0.8, 1.7 for concentrations of 0, 10%, 25% and 50% respectively. Slight erythema (score 1) and no oedema (score 0) was observed on both ears of all mice treated with the chemical when examined on day 3 after treatment. SI value for the maximum non-irritating concentration (50%) was 1.7 (REACH n.d.-f). The chemical was not expected to be sensitising.

Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2)

In a GLP compliant local lymph node assay (LLNA) conducted in accordance with OECD TG 429, CBA:J mice (5 female/dose) received topical applications at 0%, 25% 50% or 100% of the chemical in acetone/olive oil (4:1 v/v). The reported SIs were 0.9, 0.9 and 0.8 for concentrations of 25%, 50% and 100% respectively. The chemical is not considered to be a skin sensitiser since there was no indication that it elicited as SI = 3 when tested up to 100% (REACH-n.d.-e).

The same chemical gave a positive response in the KeratinoSen assay. In this GLP compliant keratinocyte activation test (KeratinoSen assay), conducted in accordance with OECD TG 442D, the chemical was tested at concentrations from 0.98 up to 2000 µM in culture medium containing 1% DMSO. At these tested concentrations, statistically significant gene-fold inductions above the threshold of 1.5 were noted at 15.63 µM, with an apparent dose response relationship. Two test runs were conducted, and the evaluation criteria for a positive response (cytotoxicity and production of luciferase as measured by flash luminescence) were met in both runs. Thus, the chemical was considered to activate the Nrf2 transcription factor and induce significant luciferase activity, a positive result indicating keratinocyte activation and skin sensitisation (REACH n.d.-e).

Acrylates

BPA glycidyl diacrylate (CAS No. 4687-94-9)

In a GPMT, groups of Hartley Dunkin guinea pigs (15 female/group) were pretreated dermally with 10% sodium lauryl sulfate in petrolatum. BPA glycidyl diacrylate (CAS No. 4687-94-9, main fraction) in olive oil was applied at 10 or 20% for intradermal induction and then 100% for topical induction. Challenge was performed 2 weeks after topical application using the chemical (main fraction) at 5% in petrolatum. Nine and 14 of 15 guinea pigs became sensitised at the first and second challenge respectively with a mean response of 0.8 and 1.43 respectively (Bjorkner et al. 1984).

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0)

In a GLP compliant LLNA conducted in accordance with OECD TG 429, CBA mice (5 female/dose) received topical applications at 0, 25%, 50% or 100% of the chemical in acetone/olive oil (4:1 v/v). Dermal irritation reactions included slight to well defined erythema in two animals but were not considered to have a toxicologically significant effect on the nodes. The reported SIs were 1, 27, 34 and 9.5 for concentrations of 0, 10%, 25% and 50% respectively. The reported concentration producing a three-fold increase in lymphocyte proliferation (EC3) was not calculated because a clear dose-response was not observed. These results indicate that the chemical could elicit a SI = 3 and has a strong sensitisation potential (REACH-n.d.-b).

In a GLP compliant local lymph node assay (LLNA) conducted in accordance with OECD TG 429, CBA/Ca mice (6 female/dose, 4 groups) received topical applications at 0 (vehicle only or no treatment), 3%, 10% or 30% of the chemical in acetone. Three days after the last application the mice were sacrificed, and the auricular lymph nodes were removed. Lymph node response was evaluated by measuring the cellular content (indicator of cell proliferation) and weight of each animal's pooled lymph nodes. A defined area with a diameter of 0.8 cm was punched out of the apical part of each ear and the weight of the pooled punches was determined in order to evaluate indications of possible skin irritation. A statistically significant increase in lymph node cellularity and in lymph node weights was observed at the test substance concentrations of 3, 10 and 30%. Irritation of the ears was present as shown by statistically significant increased ear weights at concentrations of 10 and 30%. However, lymph node proliferation was noticed also at lower test substance concentration (3%) where no significant increase in ear weight was determined. The reported SIs were 1.61, 2.96 and 2.61 for concentrations of 3, 10 and 30%. The use of lymph node cell counts and weights has undergone validation in Europe using different mouse strains to the one used in this test but has not been validated by the OECD. A “positive” threshold level based on the lymph node cell count index has not been determined for the CBA mouse strain. However, based on SI criteria for other strains (1.4-1,55) (Ehling at al 2005) the chemical is considered to be sensitising (REACH n.d.-b).

Esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9)

In a GLP compliant local lymph node assay (LLNA) conducted in accordance with OECD TG 429, CBA mice (4 female/dose) received topical applications at 0%, 5%, 10%, 25% 50% or 100% of the chemical in acetone/olive oil (4:1 v/v). The reported SIs were 1.05, 0.99, 2.07, 1.53 and 1.81 for concentrations of 5%, 10%, 25%, 50% and 100%, respectively. A three-fold increase in lymphocyte proliferation (EC3) was not reached at 100% so the chemical is not considered to be a sensitiser (REACH n.d.-d).

Other polymers with pendant acrylates

Positive results were obtained from several in vivo skin sensitisation studies and in vitro assays for alkoxylated polyols with pendant acrylates and an oxepanone based polyester with pendant acrylates (AICIS 2023).

Observation in humans

The following observations in humans were reported, with limited information, for the chemical BPA glycidyl dimethacrylate (CAS No. 1565-94-2) (CIR 2005):

- A case of occupational allergic contact dermatitis was reported in a 20 year old dental assistant. After 3 months of working with dental resins, she developed eczema on the fingers of the right hand which spread to the left hand and eyelids. She had been handling materials without gloves. She was given the dental screening series patch test. She had a +2 reaction to the chemical (2%) and had a positive reaction to concentrations as low as 0.0002%. Twenty control people were tested, and none had a positive reaction.
- Seven persons (6 dental nurses and a dentist) had been occupationally sensitised to dental resin products. 4 of the 5 persons patch tested 2% of the chemical in petrolatum were reported to have responses varying from +2 to +4.
- Four women, 31–53 years old had adverse contact reactions from artificial nails. The clinical observations included fingertip dermatitis in 3 patients, nail fold dermatitis in 3 patients, nail dystrophy, paraesthesia, ulnar border hand dermatitis, and eyelid and neck dermatitis each present in one patient. No reactions were reported for the patients following patch testing with the chemical.
- A study reporting the 'use' of a commercial meth(acrylate) series on 24 patients found that 1 dental assistant tested positive to the chemical at 2% in petrolatum.

Limited data in humans are available for the other chemicals. In addition to BPA glycidyl dimethacrylate (CAS No. 1565-94-2), there are reported positive patch test reactions for BPA bis(methacryloyloxyethyl) ether (CAS No. 24448-20-2) and BPA glycidyl diacrylate (CAS No 4687-94-9).

In a study with few details, patch test files were reviewed over the period 1992–2008 for reactions to epoxy (meth)acrylates. The patients' medical records were also examined for exposure to determine whether the allergic reactions were associated with specific exposures. Most of the reports of positive patch test reactions could not be directly associated with specific exposures; and cross reactivity to DGEBA epoxy resin or other methacrylates was considered to be most likely. However, independent reactions to BPA glycidyl diacrylate (CAS No. 4687-94-9) indicated a specific exposure. An advertisement worker was found to have developed occupational allergic contact dermatitis from using a UV-curable primer containing BPA glycidyl diacrylate (CA No. 4687-94-9) in his silk print photo emulsion. A cleaner was reported to have allergic reactions to low levels of epoxy resins (3.2 ppm) in addition to BPA glycidyl dimethacrylate (CAS No. 1565-94-2) at 1ppm and BPA glycidyl diacrylate at (CAS No. 4687-94-9) at 10 ppm. This indicates that positive reactions for BPA glycidyl dimethacrylate (CAS No. 1565-94-2) cannot be solely explained by the presence of impurities. A manicurist strongly reacted to BPA bis(methacryloyloxyethyl) ether (CAS No. 24448-20-2) and it could not be explained by epoxy resin or some other allergy. The chemical was not listed in the product declarations and the patient's artificial nail products were not analysed for this substance (Aalto-Korte et al. 2009; Carmichael et al. 1997).

In silico

All of these chemicals in this group (apart from the polymers and UVCBs which are not suitable for profiling because of their variable structures) were found to have structural alerts for protein binding. This occurred when these chemicals underwent Michael Addition reactions when profiled by the OECD QSAR Toolbox v4.6 (OECD QSAR 2023). The mechanism of skin sensitisation is initiated when proteins in the skin act as nucleophiles that bind to electrophiles such as (meth)acrylates through a Michael Addition reaction.

No structural alerts for sensitisation were observed for the chemicals in the expert rule based system, DEREK (Deductive Estimation of Risk from Existing Knowledge) Nexus (version 6.0.1). The QSAR modelling using OASIS–TIMES (Optimised Approach based on Structural

Indices Set–Tissue MEtabolism Simulator; version 2.28.1.6) predicted positive results (in domain) for skin sensitisation (mechanistic alert: bifunctional alpha, beta-carbonyl containing compounds) for the discrete chemicals in this group.

Repeat dose toxicity

Oral

Based on the data available, these chemicals are not expected to cause serious damage to health from repeated oral exposure. Effects in the liver and kidneys are often seen in repeated dose studies but these are at high doses. A dose response is not seen and changes do not correlate with adverse function and adverse histopathological effects.

4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4)

In a GLP compliant 90 day study conducted in accordance with OECD TG 408, Wistar rats (10/sex/dose) were administered the chemical by oral gavage at 0, 100, 300, or 1000 mg/kg bw/day, 7 days a week for 90 days. Changes were observed in the haematological and blood chemistry parameters and organ weights (liver, thyroid) but were not considered to be adverse effects given that there were no accompanying adverse pathological findings. The histopathological findings (minimal centrilobular hepatocyte hypertrophy) in the liver of one male in the mid-dose group and most of the animals in the high-dose group were considered to be adaptive changes. There was increased post-dosing salivation at all doses. Body weight gains for males in the low and mid-dose groups were lower than the controls but were not observed at the highest dose, so was not considered to be treatment related. There were no treatment related mortality, clinical signs or adverse effects reported for body weights, food consumption, haematology, clinical chemistry, organ weights or gross or histopathology. The NOAEL was determined to be 1000 mg/kg bw/day (REACH n.d.-f).

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0)

In a GLP compliant 90 day study conducted in accordance with OECD TG 408, Wistar rats (10/sex/dose) were administered the chemical by oral gavage at 0, 100, 300, or 1000 mg/kg bw/day 7 days a week for 92/93 days.

The following observations were made for animals in the 1000 mg/kg bw/day group:

- higher mean relative kidney weights (males)
- lower mean absolute thymus weight, mean thymus to body weight ratio and mean thymus to brain weight ratio (females)
- higher relative neutrophil and monocyte counts and lower platelet count (males)
- increased mean absolute neutrophil count, elevated mean relative monocyte counts and reduced platelets (females)
- minimal to slight decreased lymphocyte numbers in the mesenteric lymph nodes (both sexes)
- minimal focal/multifocal hepatocellular necrosis (presence of scattered collections of a few necrotic hepatocytes) were noted in 2/10 males and 1/10 females
- minimal multifocal cell hypertrophy was recorded in 7/9 males in the pituitary gland
- increased cholesterol and phospholipid levels (both sexes)
- aminotransferase activities increased (females).

The following observations were made for animals in the 300 mg/kg bw/day group:

- higher mean relative kidney weights (males)
- reduced locomotor activity (males)
- increased salivation in both sexes
- minimal to slight decreased lymphocyte numbers in the mesenteric lymph nodes (both sexes)
- increased cholesterol and phospholipid levels (both sexes)
- increased liver enzyme activation (both sexes).

The following observations were made for animals in the 100 mg/kg bw/day group:

- reduced locomotor activity (males)
- increased mean cholesterol and mean phospholipid levels (males)
- increased enzyme activation (males).

No gross pathological findings were reported. Test item induced microscopic findings were reported in the liver of a few rats at 1000 mg/kg bw/day which resulted in minimal hepatocellular necrosis (death of liver cells), moderate hepatocellular hypertrophy (enlarged liver cells) or vacuolation (formation of vacuoles or storage vesicles in cells). These effects were considered to be the histological correlates of the increased liver enzymes recorded in clinical biochemistry. The most prominent liver microscopic findings were observed in the female rat no. 72 (1000 mg/kg bw/day) and were associated with changes in kidneys, lymphoid organs and ovaries consistent with stress/altered metabolic status (REACH n.d.-b). The no observed effect level (NOEL) was determined to be below the lowest dose level of 100 mg/kg bw/day and the NOAEL was 1000 mg/kg bw/day.

In a GLP compliant combined repeated dose toxicity and reproduction/developmental toxicity screening study conducted in accordance with OECD TG 422, Crl:CD(SD) rats (5/sex/dose for the toxicity subgroup; 5 males/dose and 10 females/dose for the reproductive subgroup) were administered the chemical by oral gavage at 100, 300, or 900 mg/kg bw/day. Males and females in the toxicity subgroup and males in the reproductive subgroup were treated daily for 5 consecutive weeks. Reproductive subgroup females were treated daily for 2 weeks before pairing, throughout pairing, gestation and lactation until the day prior to termination on day 7 of lactation. A similarly constituted control group received the vehicle, propylene glycol, at the same volume dose. A dose related trend was evident for changes in haematological (slightly prolonged prothrombin time) and biochemical parameters (elevated total bilirubin, bile acid and cholesterol levels). There was no clear evidence of an adverse effect of treatment on mean organ weights among all animals at scheduled termination. There were no macroscopic abnormalities and no test substance related lesions at microscopic examination. The NOAEL for systemic toxicity was determined to be >900 mg/kg bw/day (REACH n.d.-b).

In a non-guideline dose range finding study, NZW rabbits (3 non-pregnant females/dose) were administered the chemical BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) at 300 and 1000 mg/kg bw/day in drinking water for 7 days each dose. Macroscopic post-mortem examination was conducted on the principal thoracic and abdominal organs. Food consumption was moderately reduced in all animals at 1000 mg/kg bw/day, correlated with a slight body weight loss. However, body weight loss did not exceed 4% and one female with increased food consumption stopped losing weight at the end of treatment period. The dose level of 1000 mg/kg bw/day was considered to be close to the Maximum Tolerated Dose (MTD) under the experimental conditions of the study (REACH n.d.-b).

Esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9)

In a GLP compliant 28 day repeated dose toxicity study conducted in accordance with OECD TG 407, SD rats (5/sex/dose) were administered the chemical by oral gavage at 0, 100, 300 or 1000 mg/kg bw/day daily for 4 weeks. Increased salivation was reported for all animals at the highest dose. A dose related higher mean cholesterol level was reported in males at all doses and females at the mid and higher doses. Minor biochemicals changes were observed. Mean liver weights were higher in females treated at 300 mg/kg bw/day, and in males and females treated at 1000 mg/kg bw/day. There were no treatment related macroscopic findings. Microscopic findings were seen in the liver (hepatocellular hypertrophy in males and females treated at 1000 mg/kg bw/day) and kidney (increased vacuolation in proximal tubules in females treated at 300 mg/kg bw/day and in males and females treated at 1000 mg/kg bw/day).The NOEL was determined to be 100 mg/kg bw/day based on the changes in mean blood cholesterol levels which were observed in the presence of non-adverse increased mean liver weight and liver microscopic findings (hepatocellular hypertrophy) (REACH n.d.-d).

In a GLP compliant 90 day repeated dose toxicity study conducted in accordance with OECD TG 408, SD rats (10/sex/dose) were administered the chemical by oral gavage at 0, 50, 250 or 1000 mg/kg bw/day daily for 13 weeks**.** Animals in the high dose group (male only) had reduced mean body weights. One male treated at 1000 mg/kg bw/day was prematurely sacrificed in week 10 for humane reasons (poor health condition). Test item related renal changes (moderate dilatation and vacuolation of cortical tubules) were considered to have contributed to the moribund status of this rat. Therefore, this death was considered to be related to the test item treatment. There were no other premature deaths in the study.

Increased salivation was observed in all animals in the high dose group and a few animals in the mid dose group. The surviving animals (both sexes) in the high dose group had similar kidney effects to those observed in the prematurely dead male: vacuolisation and dilatation of cortical tubules.

Minimal to moderate hepatic centrilobular hypertrophy was reported in both sexes at 1000 mg/kg bw/day and in females at 250 mg/kg bw/day, accompanied by follicular cell hypertrophy in the thyroid. These changes were considered adaptive and probably related to enzyme inducing properties of the test item. Vacuolation of Kupffer cells in the liver was also observed in both sexes at 1000 mg/kg bw/day.

In addition, there were decreased mean thymic weights in all test item treated groups except in 50 mg/kg bw/day females and increased mean adrenal weights in 1000 mg/kg bw/day males and females, which were stress related secondary effects of test item treatment. They were not associated with adverse histological findings. At the high dose levels, in addition to lowered mean body weights in males, elevated levels of mean cholesterol concentrations, kidney effects (increase creatinine and urea levels associated with increase of relative kidney weight and vacuolisation and dilatation of cortical tubules) and higher mean calcium levels were reported.

There were no adverse findings at 50 and 250 mg/kg bw/day. Under the experimental conditions and results of this study, the NOAEL was determined to be 250 mg/kg bw/day based on the weight changes, biochemical and kidney effects reported for 1000 mg/kg bw/day (REACH n.d.-d).

Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2)

In a GLP compliant 90 day repeated dose toxicity study conducted in accordance with OECD TG 408, SD rats (10/sex/dose) were administered the chemical by oral gavage in corn oil at 0, 100, 300 and 1000 mg/kg bw/day for 13 weeks. No unscheduled deaths occurred during the study. The test item was well tolerated with no relevant clinical signs and no effects on body weight, food consumption, ophthalmological, coagulation parameters or thyroid hormones. Minor haematological effects were observed in all animals at all dose levels. Slightly lower white blood cell and lymphocyte counts were observed in females at all dose levels. These small differences were statistically significant but inadequately dose related and comparable to historical control data. Therefore, these observations were considered as not treatment related. Moderately higher total cholesterol levels were noted in groups treated at 300 or 1000 mg/kg bw/day. Higher creatinine levels at 300 mg/kg bw/day and higher urea and creatinine levels were noted in females at 1000 mg/kg bw/day. Test item related increased liver weights were noted in males and females at 300 and 1000 mg/kg bw/day, and increased kidney weights in females at 1000 mg/kg bw/day. Test item related microscopic observations included increased severity and incidence of tubular vacuolation and dilatation in the kidney, and hepatocellular hypertrophy in males and females treated at all dose levels. The NOEL was determined to be 100 mg/kg bw/day (REACH n.d.-e).

In a GLP compliant combined repeated dose toxicity study with the reproduction/developmental toxicity screening test conducted in accordance with OECD TG 422, SD rats (10/sex/dose) were administered the chemical by oral gavage at 0, 100, 300, or 1000 mg/kg bw/day in corn oil. Males were treated for approximately 4 weeks: 2 weeks before mating, during the mating period (up to 2 weeks) until the day before euthanasia. Females were treated for an overall period of 7 to 9 weeks: 2 weeks before mating, through mating (up to 2 weeks) and gestation (3 weeks) until day 13 *post-partum* (*p.p.*) inclusive. Increased salivation was observed in a dose related incidence. Higher cholesterol levels were noted in males at all doses. Decreased adrenal weights were noted in males treated at 300 or 1000 mg/kg bw/day and correlated with microscopic cortical atrophy at 1000 mg/kg bw/day.

There was a trend towards increased liver weights in males treated at 300 mg/kg bw/day and in females treated at 1000 mg/kg bw/day that correlated with microscopic hepatocellular hypertrophy. Microscopic hepatocellular hypertrophy was also observed in males at 1000 mg/kg bw/day. Microscopic examination found non-adverse changes in the kidneys from one male and one female treated at 1000 mg/kg bw/day and in males treated at 100 mg/kg bw/day. Non-adverse effects were reported in the mesenteric lymph node from males treated at 300 mg/kg bw/day and from females treated at 100 mg/kg bw/day. The NOAEL for parental toxicity was determined to be 300 mg/kg bw/day (REACH n.d.-e).

Dermal

No data are available to evaluate dermal repeat dose toxicity.

Inhalation

No data are available to evaluate respiratory repeat dose toxicity.

Genotoxicity

Based on the available data for some chemicals in the group and read across data, the chemicals in this evaluation are not expected to be genotoxic. The results from in vitro genotoxicity assays were negative apart from one positive result in an in vitro cytogenicity/micronucleus study. Results from 2 in vivo studies (a mammalian alkaline comet assay and an erythrocyte micronucleus test) were negative.

In vitro

Negative results were reported for the following in vitro assays:

- for BPA propanol dimethacrylate (CAS No. 27689-12-9) in 2 GLP compliant bacterial reverse mutation assays (OECD TG 471) in *Salmonella (S). typhimurium* TA1535, TA1537, TA98, TA100 and *Escherichia (E) coli* WP2 with and without metabolic activation (S9) at concentrations up to 5000 μg/plate (REACH n.d.-c)
- for 4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4) in a bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA97a, TA98, TA100 and TA102 with and without metabolic activation (S9) at concentrations up to 12500 μg/plate (REACH n.d.-f)
- for BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) in a GLP compliant bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA1535, TA1537, TA98, TA100 and *E. coli* WP2 uvrA with and without metabolic activation (S9) at concentrations up to 6000 µg/plate and 3000 pg/plate in 2 assays (REACH n.d.-b)
- for the chemical esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9) in a GLP compliant bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA98, TA100 and TA102, TA1535, TA1537 with and without metabolic activation (S9) at concentrations up to 5000 mg/plate (REACH n.d.-d)
- for esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2) in a GLP compliant bacterial reverse mutation assay (OECD TG 471) in *S. typhimurium* TA1535, TA1537, TA98, TA100 and TA102 with and without metabolic activation (S9) at concentrations up to 5000 mg/plate (REACH n.d.-e)
- for 4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4) in a GLP compliant mammalian cell gene mutation assay (OECD TG 476) at the thymidine kinase locus in mouse lymphoma L5178Y cells. Negative results were reported in 2 studies with metabolic activation at concentrations up to 100 μg/mL, and without metabolic activation at concentrations up to 200 μg/mL (REACH n.d.-f).
- for BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) in a GLP compliant mammalian cell gene mutation assay (OECD TG 476) at the hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus in mouse lymphoma L5178Y cells at concentrations up to 75 µg/mL with metabolic activation (S9) and up to 125 µg/mL without activation (REACH n.d.-b)
- for the chemical, esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9), in 2 GLP compliant mammalian cell gene mutation assays (OECD TG 476) at the HPRT locus in mouse lymphoma L5178Y cells at concentrations up to 250 μg/mL with S9 activation and up to 40 μg/mL with activation in one study and concentrations up to 210 μg/mL or 45 μg/mL with and without S9 activation, respectively (REACH n.d.-d)
- for esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2) in a GLP compliant mammalian cell gene mutation assay (OECD TG 476) at the HPRT locus in mouse lymphoma L5178Y cells at concentrations up to 500 µg/mL (REACH n.d.-e).

Mixed results were obtained with GLP compliant in vitro micronucleus tests conducted in accordance with OECD TG 487:

- The chemical, esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9), induced chromosome damage or damage to the cell division apparatus using L5178Y mouse lymphoma cells without metabolic activation and did not do so with metabolic activation (REACH n.d.-d).
- Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2) did not induce chromosomal damage or damage to the cell division apparatus using L5178Y TK+/- mouse lymphoma cells either in the presence or absence of metabolic activation at concentrations up to 25 and 50 µg/mL in 2 assays (REACH n.d.-e).

In vivo

In a GLP compliant mammalian erythrocyte micronucleus test conducted in accordance with OECD TG 474, male CD-1 mice (5/dose) were treated with BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0) at dose levels of 500 and 1000 and twice at 2000 mg/kg bw/day. The incidence of micronuclei in bone marrow polychromatic erythrocytes did not increase in any of the treated groups, indicating a lack of clastogenicity (REACH n.d.-b).

The chemical, esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9), in a GLP compliant mammalian alkaline comet assay, conducted similarly to OECD TG 489 in male SD rats (3 animals/dose) were administered 2 single treatments of the chemical by oral gavage at doses of 500, 1000 and 2000 mg/kg bw/day on 2 consecutive days. DNA damage in the liver, stomach and duodenum was not observed (REACH n.d.-d).

In silico

No structural alerts for bacterial in vitro mutagenicity were observed for the chemicals. The polymers and UVCBs were not suitable for profiling because of their variable structures in the expert rule based system, DEREK (Deductive Estimation of Risk from Existing Knowledge) Nexus (version 6.0.1).

Carcinogenicity

No carcinogenicity data are available for these chemicals. Structure/activity modelling did not reveal any alerts for carcinogenicity using OECD QSAR Toolbox (OECD 2020).

Reproductive and development toxicity

Based on the available data, the chemicals are not expected to cause significant adverse effects on reproduction or development. There is no evidence of effects on fertility or development or adverse effects in reproductive organs in a number of studies. This supports that BPA is not released from the chemicals under physiological conditions.

Reproductive Toxicity

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0)

In a GLP compliant extended one generation reproductive toxicity study, conducted similarly to TG 443, including both developmental neurotoxicity and immunotoxicity endpoints, the chemical in polyethylene glycol was administered to Wistar rats (F0 25/sex/dose) by oral gavage. Dosage for F0 animals was 0, 40, 100 and 200 mg/kg bw/day daily, 7 days a week

for 10 weeks before mating and 2 weeks during mating for all animals. Additionally, females were dosed for approximately 3 weeks during resulting pregnancies and for one week through the weaning of their F1 offspring. Dosage for the F1 animals (PND 7-20) was 0, 10, 25 and 50 mg/kg bw/day. Study design and cohort assignment are summarised below:

- (F1) Cohort 1A (reproductive toxicity) 20 animals/sex/dose: 12-13 weeks; direct dosing of pups on PND 7-20 and post-weaning for 10-11 weeks.
- (F1) Cohort 1B (reproductive toxicity) 20 animals/sex/dose: 13-15 weeks; direct dosing of pups on PND 7-20 and post-weaning for 11-13 weeks.
- (F1) Cohort 2A (developmental neurotoxicity) 10 animals/sex/dose: 10-12 weeks; direct dosing of pups on PND 7-20 and post-weaning for 8-10 weeks.
- (F1) Cohort 2B (developmental neurotoxicity) 10 animals/sex/dose: 2 weeks; direct dosing of pups on PND 7-20, except for animals that were necropsied on PND 22 which were also dosed on PND 21 using dose levels for PND 7-20.
- (F1) Cohort 3 (developmental immunotoxicity) 10 males and 9 females: 6-8 weeks; direct dosing of pups on PND 7-20 and post-weaning for 4-6 weeks.
- F1 animals allocated to the positive control group (group 5) were not directly dosed with the test item.

No adverse changes were reported in the F0 animals regarding:

- mortality/moribundity
- clinical signs
- body weight
- food consumption
- oestrous cycle determination
- clinical pathology including measurement of thyroid hormones and urinalysis
- gross necropsy findings
- sperm analysis
- organ weights
- histopathologic examinations.

Five pups of the control group, 17 pups at 40 mg/kg bw/day, 12 pups at 100 mg/kg bw/day, and 29 pups at 200 mg/kg bw/day did not survive the scheduled treatment period. Most mortality cases occurred on a single day, when 34 pups were found dead or missing. This incidence did not show a correlation to the dose administered. The most relevant macroscopic observations for these pups that did not survive until scheduled necropsy were essentially confined to lungs that were not collapsed, and fluid was found in the thoracic and/or abdominal cavity. None of these macroscopic findings were recorded for F1 animals that survived until scheduled necropsy. These findings suggest that the deaths were caused by the gavage dosing procedure.

There were no treatment related effects on antibody levels or pathology findings in the lymphoid organs of F1 animals at any dose levels, indicating that the chemical does not appear to induce immunotoxic effects. Minor effects such as increased grip strength and motor activity were observed. No treatment related adverse effects on neurodevelopment were reported for the F1 group. A NOAEL for general toxicity was determined for F0 animals at 200 mg/kg bw/day, noting that possible adversity of higher TSH and T4 levels in males could not be assessed in this study. A NOAEL for reproductive toxicity in F0 animals was at

least 200 mg/kg bw/day in the absence of adverse effects at this dose on reproduction parameters. A NOAEL was determined for general toxicity of F1 animals ≥ 200 mg/kg bw/day, noting that the possible adversity of higher T4 levels in some of the animals could not be assessed in this study (REACH n.d.-b).

In a GLP compliant combined repeated dose and reproductive/developmental screening study conducted in accordance with TG 422 (see **Repeat dose toxicity**: **oral**), the chemical in propylene glycol was administered to Crl:CD(SD) rats (5 animals/dose for toxicity subgroup and 5 males and 10 females/dose for reproductive subgroup) at 100, 300 and 900 mg/kg bw/day daily, 7 days a week. Oestrous cycle length, pre-coital interval, mating performance and fertility and gestation length of the reproductive subgroup females were unaffected by treatment. There was no evidence of organ weight changes or tissue alterations in the reproductive organs. There were no clinical signs observed for F1 offspring that were considered to be related to parental treatment. Offspring survival and growth from birth to day 7 was unaffected by treatment. There were no macroscopic abnormalities detected among the offspring that died during the early post-natal period, or at scheduled termination on day 7 that were attributable to parental treatment. The NOAEL for systemic toxicity and for reproductive/developmental toxicity was >900 g/kg bw/day (REACH n.d.-b).

In the 90 day oral repeated dose toxicity study (see **Repeat dose toxicity: oral** section), decreased prostate weights at all levels, decreased seminal vesicle weights (dose levels unspecified) and reduced sperm motility were reported following treatment with the chemical. Multifocal cell hypertrophy was also observed in the pars distalis of the pituitary gland of males, but the pathological significance of this finding could not be determined. The study authors considered that the pituitary findings and the decreased prostate weights observed (at all dose levels) and decreased seminal vesicle weights (dose levels not specified) may represent an indicator of mild disruption of testosterone production/levels. There were no microscopic findings in the prostate gland, seminal vesicles or coagulating glands to account for the decreased weights recorded at necropsy Based on these results, the NOAEL for reproductive toxicity was determined to be <100 mg/kg bw/day (REACH n.d.-b).

Esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9)

In a GLP compliant reproductive/developmental screening study conducted in accordance with OECD TG 421, SD rats (10/sex/dose) were administered the chemical in corn oil by oral gavage daily at 0, 50, 250 and 1000 mg/kg bw/day for 2 weeks before mating and during the mating period for all animals (at least 5 weeks in total for males) and for females, during pregnancy and lactation until day 5 post-partum inclusive and until sacrifice for females which had not delivered. At 1000 mg/kg bw/day elevated mean cholesterol levels were reported at the end of the treatment period which were considered to be adverse. There were no adverse findings at 50 and 250 mg/kg bw/day. The microscopic examination and mean organ weights showed test item related changes in liver only. There was no evidence of organ weight changes or tissue alterations in the testes, uterus or ovaries following treatment with the chemical. Administration of the test item in rats at 1000 mg/kg bw/day induced mild centrilobular hypertrophy and vacuolation of Kupffer cells in the liver which correlated with the higher mean liver weight at necropsy. Centrilobular hypertrophy alone was also observed in males at 250 mg/kg bw/day. In the absence of any associated degenerative liver changes, these observations were considered not to be adverse. There were no test item related effects on pairing, mating and fertility data. There were no toxicologically relevant effects on delivery data. In pups, there were no test item related deaths or clinical signs and no test item related effects on mean pup body weights, mean pup body weight gains, on the percentage of male pups at birth and no test item related findings noted at necropsy. The NOAEL for parental toxicity was determined to be 250 mg/kg bw/day and the NOAEL for

reproductive performance (mating and fertility) and for toxic effects on progeny was 1000 mg/kg bw/day (REACH n.d.-d)

In the 90 day oral repeated dose toxicity study (see **Repeat dose toxicity: oral** section), there was no evidence of organ weight changes or tissue alterations in the testes, uterus or ovaries following treatment with the chemical. The absolute epididymides weights were slightly higher in the 1000 mg/kg bw/day group but were not accompanied by changes in the testes (organ weights or histology) and were considered a direct consequence of lower terminal body weights (REACH n.d.-d).

In the 28 day oral repeated dose toxicity study (see **Repeat dose toxicity: oral** section), there was no evidence of organ weight changes or tissue alterations in the reproductive organs following treatment with the chemical (REACH n.d.-d).

Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2)

In a GLP compliant combined repeated dose toxicity study, with reproduction/development toxicity screening (see **Repeat dose toxicity: oral** section) conducted in accordance with OECD TG 422, SD rats (10/sex/dose) were administered the chemical in corn oil by oral gavage daily at 0, 100, 300 and 1000 mg/kg bw/day. Observations of the pups from birth to day 13 p.p. did not report any effects on mortality, viability, clinical signs, sex ratio or anogenital distance. Changes in body weight gain were noted but there was a poor dose relationship. Areolae were observed in 3 and 5 male pups at 300 and 1000 mg/kg bw/day, respectively. The NOAEL for parental toxicity and reproductive performance was considered to be 1000 mg/kg bw/day in males and females based on the absence of adverse findings and absence of effects on mating or fertility at this dose level. The NOEL for toxic effects on progeny was considered to be 100 mg/kg bw/day given the dose related retention of areolae in male pups from 300 mg/kg bw/day (REACH n.d.-e).

In the 90 day oral repeated dose toxicity study (see **Repeat dose toxicity: oral** section), there was no evidence of organ weight changes or tissue alterations in the reproductive organs (not specified) following treatment with the chemical (REACH n.d.-e).

Developmental Toxicity

4,4'-Isopropylidenediphenol, oligomeric reaction products with 1- chloro-2,3-epoxypropane, reaction products with methacrylic acid (EC No. 701-308-4)

In a GLP compliant prenatal developmental toxicity study conducted in accordance with OECD TG 414, pregnant SD rats (24/dose) were administered the chemical in polyethylene glycol by gavage at 0, 100, 300 or 1000 mg/kg bw/day on day 3 (pre-implantation) to gestational day (GD) 19 inclusive. No mortality, clinical signs, gross pathological findings or adverse effects on body weight and weight changes of dams were observed. No changes in pre- and post-implantation loss, total litter loss by resorption, early or late resorptions, foetal mortality were observed. At all dosages the incidence of foetuses with costal cartilage not fused to sternebrae was higher than in controls, with statistical significance being reached at 100 and 1000 mg/kg bw/day. However, no dosage effect relationship was observed. This isolated finding was considered to be incidental and unrelated to maternal treatment. The NOEL was 1000 mg/kg bw/day (REACH n.d.-f).

BPA-epichlorohydrin polymer acrylate (CAS No. 55818-57-0)

In a GLP compliant prenatal developmental toxicity study conducted in accordance with OECD TG 414, Wistar rats (24 mated females/group) were administered the chemical in polyethylene glycol by oral gavage daily at doses of 0, 100, 300 and 1000 mg/kg bw/day for 15 days during the gestation period from day 6–20 post coitum. No test item related clinical symptoms or signs were observed at any dose during the study. One female in the mid-dose group was euthanised for ethical reasons. The animal had symptoms that were not seen in any other animals and therefore were not considered to be test related. Regarding the maternal data, no test item related premature deaths were recorded. No test item related clinical symptoms or signs, changes in food consumption or body weights were observed at any dose. The foetal examinations in the highest dose group found increases in placenta weights on a litter basis by 23 and by 24% on an individual basis. This increase was considered to be test item related. Differences noted in low and mid-dose groups were small and unrelated to dose and; therefore, considered to be incidental. No test findings were observed during external examination of the foetuses. No test item related effects on sex ratio and mean body weights of the foetuses were noted in any group. No test item related abnormalities and variations were noted during external and fresh visceral examinations of foetuses. No findings were noted during skeletal examination of the foetuses. A small number of incomplete or non-ossified bones and/or supernumerary ribs remained within the ranges of the respective historical control values and were therefore considered to be of no toxicological relevance. There were no additional cartilage findings in any of the foetuses that were considered to be related to the treatment with the test item. The NOEL and NOAEL for maternal toxicity was considered to be >1000 mg/kg bw/day. Placenta weight differences seen in the highest dose group were considered to be test item related changes; the NOEL for prenatal development was therefore considered to be 300 mg/kg/day. The NOAEL for prenatal developmental toxicity was defined as 1000 mg/kg bw/day (REACH n.d.-b).

In a GLP compliant prenatal developmental toxicity study conducted in accordance with OECD TG 414, NZW rabbits (24 mated females/group) were administered the chemical in polyethylene glycol by oral gavage daily at doses of 0, 100, 300 and 1000 mg/kg bw/day from day 6 to day 28 inclusive post coitum. There were no test item related external variations and no external and visceral malformations in litters in any groups. Treatment related increased skeletal variations were reported at doses of 300 and 1000 mg/kg bw/day (mainly incomplete ossification of sternebrae, interparietal and metacarpal bones and thickened ribs) but were considered non-adverse. At 300 and 1000 mg/kg/day, a test item treatment effect on slightly increased incidences of split interparietal or parietal were considered to be non-adverse. Since the differences from control incidences were low (no statistical differences), the findings were of low incidences and did not impact the global shape of the skull and are probably due to ossification delay. Minor variations in foetal gall bladders were observed at the highest dose. The maternal and embryo foetal developmental NOAEL was determined to be >1000 mg/kg bw/day, based on: the non-adverse effects on dam body weight change, food consumption, non-adverse increased incidences of foetal gall bladder and skeletal variations at this dose (REACH n.d.-b).

In a prenatal developmental toxicity range finding study conducted similarly to OECD TG 414, Wistar rats (8/group) were administered the chemical in polyethylene glycol by oral gavage daily at doses of 0, 100, 300 and 1000 mg/kg bw/day for 15 days during the gestation period from day 6–20 post coitum. All rats survived the scheduled study period. No clinical signs were observed in the mid-dose group. In all groups no effects of the treatment with the test item on reproduction data were recorded. During external and macroscopic examination no external abnormalities and variations. The NOAEL was >1,000 mg/kg bw/day (REACH n.d.-b).

In a prenatal developmental toxicity range finding study conducted similarly to OECD TG 414, NZW rabbits (6/group) were administered the chemical in 1% methylcellulose by oral gavage daily at doses of 0, 100, 300 and 1000 mg/kg bw/day for 15 days during the

gestation period from day 6–28 post coitum. One animal died and was found to have a coloured deposit in the liver. This was not considered to be treatment related as there were no similar liver effects in the other animals and no premature deaths at the higher doses. At 100 and 300 mg/kg/day, there were no adverse findings on maternal parameters or foetuses. At 1000 mg/kg/day, there were signs of maternal toxicity (body weight loss, low food consumption and low gravid uterus weight) associated with low foetal body weight. There were no test item related findings following external foetal examination. The LOAEL was 300 mg/kg bw/day based on foetal weight changes (REACH n.d.-b)

Esterification products of acrylic acid and 4,4'-isopropylidenediphenol ethoxylated (EC No. 701-362-9)

In a GLP compliant prenatal developmental toxicity study conducted similarly to OECD TG 414, pregnant SD rats (24/group) were administered the chemical in corn oil by oral gavage daily at doses of 0, 50, 250 and 1000 mg/kg bw/day during the gestation period from day 6–20 inclusive post coitum. At 1000 mg/kg/day, lower foetal body weight and increased foetal ossification delays were observed in presence of some signs of limited maternal toxicity (i.e. lower body weight gain and net body weight gain). At 50 and 250 mg/kg/day, there were signs of slight foetal ossification delays compared with controls, but they remained within the range reported for historical control data. Under the experimental conditions and results of this study, the NOAEL for maternal toxicity and for embryo-foetal development was considered to be 1000 mg/kg bw/day (REACH n.d.-d).

Esterification products of 4,4'-isopropylidenediphenol, ethoxylated and 2-methylprop-2-enoic acid (EC No. 935-411-2)

In a GLP compliant prenatal developmental toxicity study conducted similarly to OECD TG 414, time mated female SD rats (24/group) were administered the chemical in corn oil by oral gavage daily at doses of 0, 100, 300 and 1000 mg/kg bw/day during the gestation period from day 5 to day 20 post coitum inclusive. Body weight, body weight change and food consumption were unaffected by the test item treatment. At necropsy of the dams, no test item related macroscopic findings were observed. Gravid uterus weight, carcass weight, net body weight change and gestation parameters were not impacted by the test item treatment. No effects on the foetal body weight, placental weight, sex ratio or anogenital distance were noted at any dose level. At external, soft tissue or skeletal examination of the foetuses, no variations or malformations attributable to the test item treatment were noted. The NOAEL for maternal toxicity was 1000 mg/kg bw/day and the NOEL for embryo foetal development was considered to be 1000 mg/kg bw/day (REACH n.d.-e).

References

Aalto-Korte K, Jungewelter S, Henriks-Eckerman M-L, Kuuliala O and Jolanki R (2009) 'Contact allergy to epoxy (meth)acrylates', *Contact Dermatitis*, 61:19–21.

AICIS (Australian Industrial Chemicals Introduction Scheme) (2023) *Polymers with pendant acrylates*, AICIS, accessed 14 February 2024.

Bonefeld-Jorgensen EC, Long M, Hofmeister MV and Vinggaard AM (2007) 'Endocrine-disrupting potential of bisphenol A, bisphenol A dimethacrylate, 4-n-nonylphenol, and 4-n-octylphenol in vitro: new data and a brief review', *Environ Health Perspect*, 115 Suppl(Suppl1): 69–76.

Borkner B, Niklasson B and Persson K (1984) 'The sensitizing potential of di-(meth)acrylates based on bisphenol A or epoxy resin in the guinea pig', *Contact Dermatitis,* 10:286–304.

Carmichael AJ, Gibson JJ and Walls AWG (1997) 'Allergic contact dermatitis to bisphenol-A-glycidyldimethacrylate (BIS-GMA) dental resin associated with sensitivity to epoxy resin', *British Dental Journal*, 183(8)297–298.

CAS (Chemical Abstracts Service) (n.d.) *CAS SciFinder*^{n}, CAS website, accessed 14 February 2024.

Chemwatch (n.d.) *Galleria Chemica*, Chemwatch website, accessed 9 February 2024.

CIR (Cosmetic Ingredient Review) (2005) *Final Report of the Safety Assessment of Methacrylate Ester Monomers Used in Nail Enhancement Products*, CIR, accessed 9 February 2024.

CIR (Cosmetic Ingredient Review) (2023) *Methacrylate Ester Monomers*, CIR, accessed 9 February 2024.

Darmani H and Al-Hiyasat AS (2004) 'Reproductive toxic effect of bisphenol A dimethacrylate in mice', *J Biomed Mater Res A,*69(4):637–643.

Darmani H and Alkhatib MA (2023) 'Non-monotonic effects of Bisphenol A Dimethacrylate on male mouse reproductive system and fertility leads to impaired conceptive performance', *Toxicology Mechanisms and Methods*, 34(3): 262–270.

DeLima Associates (n.d.) *Consumer Product Information Database*, DeLima Associates website, accessed 9 February 2024.

ECHA (European Chemicals Agency) (2021) *Assessment of regulatory needs – Bisphenols*, ECHA, accessed 9 February 2024.

EC (European Commission) (n.d.) *CosIng*, EC website, accessed 9 February 2024.

EWG (Environmental Working Group) (n.d.) *EWG's Skin Deep*, EWG website, accessed 9 February 2024.

FCCdb (Food Contact Chemicals database) (n.d.) *Food contact chemicals database ver 5.0*, accessed 9 February 2024.

FSANZ (Food Standards Australia New Zealand) (2016) *24th Australian Total Diet Study Phase 2,* FSANZ, accessed 13 March 2024.

Government of Canada (2000) *Draft Screening Assessment Other Polymers Group,* Government of Canada, accessed 14 March 2024.

Kadoma Y and Tanaka M (2000) 'Acid and base-catalyzed hydrolysis of bisphenol A-related Compounds, *Dental Materials Journal,* 19(2): 139–152.

McCarthy TJ and Witz G (1997) 'Structure-activity relationships in the hydrolysis of acrylate and methacrylate esters by carboxyesterase in vitro', *Toxicology, 116:153*–158.

Meyer J-M (2012) 'TEGMA and Bisphenol-A: the same level of risk in dental medicine?' *Materials Science, Medicine* Corpus ID: 32091400. Accessed 9 February 2024 (translated from French by the author).

Personal Care Products Council (n.d.) *Cosmetic Ingredient Identification Database*, Personal Care Products Council website, accessed 9 February 2024.

NCBI (National Centre for Biotechnology Information) (n.d.) *PubChem*, NCBI website, accessed 9 February 2024.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2019a) *IMAP Single Assessment Report -Bisphenol A (BPA)-based miscellaneous polymers: Human health tier II assessment*, NICNAS, accessed 9 February 2024.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme) (2019b) *IMAP Single Assessment Report - Phenol, 4,4'-(1-methylethylidene)bis-: Human health tier II assessment*, NICNAS, accessed 9 February 2024.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-a) *Registered dossier for CAS No. 36425-15-7,* accessed 9 February 2024.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-b) *Registered dossier for CAS No. 55818-57-0,* accessed 9 February 2024.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-c) *Registered dossier for CAS No. 27689-12-9*, accessed 9 February 2024.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-d) *Registered dossier for EC No. 701-362-9*, accessed 9 February 2024.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-e) *Registered dossier for EC No. 935-411-2,* accessed 9 February 2024.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.-f) *Registered dossier for EC No. 701-308-4,* accessed 14 March 2024.

SPIN (Substances in Preparation in Nordic Countries) (n.d.) *SPIN Database*, SPIN website, accessed 9 February 2024.

SWA (Safe Work Australia) (n.d.) *Hazardous Chemical Information System,* SWA website, accessed 9 February 2024.

TGA (Therapeutic Goods Administration) (2024) *Standard for the Uniform Scheduling of Medicines and Poisons (Poisons Standard February 2024)*, TGA, accessed 9 February 2024.

UNECE (United Nations Economic Commission for Europe) (2017) *Globally Harmonized System of Classification and Labelling of Chemicals (GHS)* Seventh Revised Edition, UNECE, accessed 9 February 2024.

US EPA (United States Environmental Protection Agency) (n.d.) *Chemical and Products Database (CPDat)*, US EPA website, accessed 9 February 2024.

US EPA Chemical Data Reporting (CDR) (2016) *2016 CDR Data*, US EPA website, accessed 9 February 2024.

US EPA Chemical Data Reporting (CDR) (2020) *2020 CDR Data*, US EPA website, accessed 9 February 2024.