Australian Government
Department of Health, Disability and Ageing
Australian Industrial Chemicals Introduction Scheme

Bisphenol A dimethacrylate

Evaluation statement (EVA00179)

16 December 2025

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AICIS evaluation statement (EVA00179)

Subject of the evaluation

2-Propenoic acid, 2-methyl-, 1,1′-[(1-methylethylidene)di-4,1-phenylene] ester (Bisphenol A dimethacrylate)

Chemical in this evaluation

CAS name	CAS number
2-Propenoic acid, 2-methyl-, 1,1′-[(1-methylethylidene)di-4,1-phenylene] ester	3253-39-2

Reason for the evaluation

Evaluation Selection Analysis indicated a potential human health risk.

Parameters of evaluation

The chemical is listed on the Australian Inventory of Industrial Chemicals (the Inventory).

This evaluation is a human health risk assessment for all identified industrial uses of the chemical 2-propenoic acid, 2-methyl-, 1,1′-[(1-methylethylidene)di-4,1-phenylene] ester, referred to as bisphenol A dimethacrylate (Bis-DMA). The evaluation primarily focuses on endpoints for which data are available, including skin sensitisation and reproductive toxicity.

Summary of evaluation

Summary of introduction, use and end use

There is currently no specific information about the introduction, use and end use of the chemical in Australia.

Based on international information, the chemical has functional end use as a chemical intermediate. The predominant end use of the chemical is in the production of plastic and polymer products. There is limited evidence suggesting that this may include applications in the production of articles intended for food contact. Currently, the chemical has no identified uses in cosmetic, domestic or commercial products. Historical consumer applications, identified prior to 1990, included dental adhesive products supplied to consumers, and surface coatings.

The chemical also has reported non-industrial applications in clinical dental materials.

Human health

Summary of health hazards

This evaluation primarily reviews endpoints for which data are available for Bis-DMA, including skin sensitisation and reproductive toxicity.

The chemical is expected to be readily metabolised to bisphenol A (BPA) (CAS No. 80-05-7). Therefore, conclusions on systemic toxicity were further supported by BPA data.

Based on the available data the chemical is a skin sensitiser and may cause adverse effects on fertility.

In a reliable Guinea Pig Maximisation Test (GPMT), the majority of animals that were exposed to the chemical were reported to have developed allergic skin reactions.

Collective findings from the 2 available non-guideline studies (14 week drinking water and 28 day intragastric studies) provide consistent evidence that Bis-DMA has the potential to impair fertility following repeated exposure, even at low doses. Adverse effects were observed across multiple reproductive endpoints in both male and female mice, including reduced pregnancy rates, reduced number of implantations, increased embryonic resorptions and disrupted sperm production and quality. Although these were non-guideline studies, similar effects have been observed with the metabolite BPA.

Currently, no toxicological data are available for Bis-DMA across other hazard endpoints. However, its metabolite BPA has been associated with systemic effects following repeated exposure, including liver and kidney effects. BPA is not likely to be genotoxic or carcinogenic.

Hazard classifications relevant for worker health and safety

The chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for worker health and safety as follows. This evaluation does not consider classification of physical hazards and environmental hazards.

Health hazards	Hazard category	Hazard statement
Skin sensitisation	Skin Sens. 1	H317: May cause an allergic skin reaction
Reproductive toxicity	Repro. 1B	H360F: May damage fertility

Summary of health risk

Public

Based on the available use and end use information, the public exposure to the chemical is expected to be minimal.

The public could potentially be exposed to the chemical through migration from food contact materials into food. Based on the available data, extensive use in food packaging is not anticipated, and therefore, concentrations in food are expected to be considerably lower than

those of BPA. Previous surveys conducted by FSANZ in Australia have shown that only a small number of foods contain detectable levels of BPA. Consequently, dietary exposure to BPA among Australian consumers was concluded to be low and considered unlikely to pose a health risk to consumers (FSANZ 2018).

The public could also be exposed to the chemical if it is contained in dental adhesive products supplied directly to consumers (which is an industrial use as it is an excluded therapeutic good). However, this use has not been identified in Australia and reported uses overseas appear to be historical.

Therefore, there are currently no identified risks to the public from industrial uses that require management.

Workers

During product formulation and packaging, dermal, inhalation, and ocular 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. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical long term reproductive effects and sensitisation, the chemical may pose a risk to workers. Control measures to minimise dermal and inhalation exposure are needed to manage the risk to workers (see **Proposed means for managing risk**). These controls related to the classification for reproductive toxicity and sensitisation should minimise risks associated with other toxicity endpoints.

Proposed means for managing risk

Inventory Listing

To manage the potential risks to public health from the introduction and use of the chemical, the Inventory listing should be varied to add a new term of listing under *section 86* of the *Industrial Chemicals (IC) Act 2019*.

Term of listing	Details
Specific requirements to provide information to the Executive Director under *section 101* of the *IC Act*	A person who introduces this chemical must tell the Executive Director the volume of introduction and end use of the chemical within 20 working days if the chemical is being introduced for consumer end use, except end use of articles.

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 (see **Summary of health hazards**).

Information relating to safe introduction and use

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

Recommended control measures that could be implemented to manage the risks arising from dermal, inhalation and ocular exposure to the chemical includes, but are not limited to:

- using closed systems or isolating operations
- 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 chemical.

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.

Measures required to eliminate or manage risk arising from storing, handling and using a hazardous chemical depends on the physical form and the manner in which the chemical is used.

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.

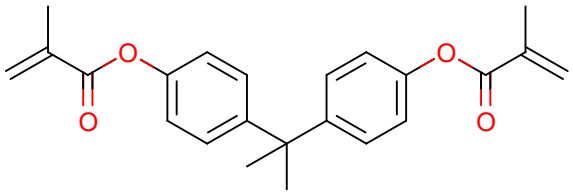
The risk conclusions for the public are driven by the evaluation finding that the chemical is not currently expected to be used in consumer products, aside from articles. Given its potential to cause adverse fertility effects and sensitisation, identification of an introduction for any new consumer end use of the chemical in Australia is considered necessary to ensure appropriate risk management. Therefore, a variation to the listing for the chemical – to add a specific information requirement – is proposed to manage the risks to human health from the introduction or use of the industrial chemical (see **Proposed means of managing risk**).

Note:

1. Obligations to report additional information about hazards under *section 100* of the *Industrial Chemicals Act 2019* apply.
2. A person introducing this chemical should be aware of their obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

CAS number	3253-39-2
CAS name	2-Propenoic acid, 2-methyl-, 1,1′-[(1-methylethylidene)di-4,1-phenylene] ester
Molecular formula	$C_{23}H_{24}O_4$
Associated names	Bisphenol A dimethacrylate (Bis-DMA) 4,4'-Isopropylidenediphenyl dimethacrylate 2,2-Bis(4-methacryloxyphenyl)propane [4-[2-[4-(2-Methylprop-2-enoyloxy)phenyl]propan-2-yl]phenyl] 2-methylprop-2-enoate
Molecular weight (g/mol)	364.44
SMILES (canonical)	O=C(OC1=CC=C(C=C1)C(C2=CC=C(OC(=O)C(=C)C)C=C2)(C)C)C(=C)C
Structural formula	

Relevant physical and chemical properties

Physical form	White to slightly yellow crystalline powder
log K_{ow}	5.35 at 25 °C (predicted)

Introduction and use

Australia

There is currently no information about the introduction, use and end use of the chemical in Australia.

International

The following international uses have been identified through the:

- Galleria Chemica (Chemwatch n.d.)
- Chemical Data Reporting (CDR) Data (US EPA 2020)
- Chemicals and Products Database (CPDat v4.1) (US EPA 2025)
- Literature and publicly available safety data sheets (SDS).

The chemical has reported site limited use as an intermediate in the synthesis of plastic polymers and resins. While limited evidence suggests potential use in the manufacture of plastic food contact materials (see **Public exposure**), the chemical does not appear on publicly available lists of food contact substances (Food Packing Forum 2025). Currently, the chemical has no identified uses in cosmetic, domestic or commercial products. Historical consumer applications were identified, including use in dental adhesive products supplied directly to consumers and in surface coatings. Reports of these uses were prior to 1990.

Industrial use of the chemical overseas does not appear to be widespread. In the United States of America (USA), the last reported production volume was approximately 90 tonnes in 2016, while no production has been recorded in Sweden since 2000 (SPIN n.d.). Furthermore, the chemical is not currently registered under REACH (n.d.).

The chemical has reported non-industrial uses in clinical dental materials.

Existing Australian regulatory controls

Public

No restrictions are identified for the chemical.

Workers

The chemical is not listed in the SWA's HCIS and there are no exposure standards available for the chemical in Australia (SWA n.d.).

International regulatory status

Exposure Standards

No specific exposure standards were identified.

European Union

Bis-DMA is not subject to any specific restriction. However, Commission Regulation (EU) 2024/3190 prohibits the use of BPA and other bisphenols and bisphenol derivatives with harmonised classification for specific hazardous properties in the manufacture of certain food contact materials and articles. This includes classification as Category 1A or 1B 'mutagenic', 'carcinogenic', 'toxic to reproduction', or Category 1 'endocrine disrupting' for human health. Food contact materials and articles that have been manufactured using another bisphenol or bisphenol derivative must not contain any residual BPA (EU 2024).

Human exposure

Public

If the chemical is used in the manufacture of plastics intended for food contact, there is potential for public exposure through migration into food. Use in food contact materials was not identified in Australia. Internationally, limited data are available regarding its use in food contact materials. In a study conducted in Mexico, the chemical was detected in a small number of plastic food contact items (n=5/22), including infant feeding bottles, yoghurt containers, and microwaveable containers. Concentrations ranged from below 0.03 µg/kg in 4 samples to 0.147 µg/kg in one sample. The chemical was not detected in metal food cans (Gonzalez-Castro et al. 2011). Additionally, the chemical was identified in a separate study investigating migration from Mexican meat packaging, with a mean concentration of 420 µg/kg (n=13) (Ceballos-Luna et al. 2022).

In 2018, FSANZ published a statement on BPA which concluded:

FSANZ will continue to monitor the emerging situation with respect to BPA, but notes that previous surveys undertaken in Australia have shown that very few foods contain detectable levels of BPA. Dietary exposure to BPA for Australian consumers is therefore low and likely to have 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 2018).

The chemical has potential use in dental materials supplied to consumers (which is an industrial use as it is an excluded therapeutic good), although this is not expected to be widespread (see **Introduction and use**). Multiple studies on dental materials have shown that Bis-DMA releases BPA more readily through hydrolysis than other BPA-derived monomers, such as bisphenol A diglycidyl dimethacrylate (Bis-GMA), which require ether bond degradation (Atkinson et al. 2002; Schmalz et al. 1999). Hydrolysis and enzymatic degradation by saliva esterases, combined with mechanical forces, can accelerate the breakdown of Bis-DMA-containing resins. This resulted in over 80% conversion to BPA within the first 24 hours following application (Schmalz et al. 1999; Tichy et al. 2025).

Health hazard information

This evaluation primarily reviews endpoints for which data are available for Bis-DMA, including skin sensitisation and reproductive toxicity.

The chemical is expected to be readily metabolised to BPA (see **toxicokinetics**). Therefore, conclusions on systemic toxicity were further supported by data on BPA. AICIS has evaluated and published the human health risks of BPA (CAS No. 80-05-7) (AICIS 2024; NICNAS 2016).

Toxicokinetics

No data are available for Bis-DMA.

Based on the observed skin sensitisation and reproductive effects, the chemical is expected to be sufficiently absorbed following oral and dermal exposure, despite its relatively high log Kow of 5.35. Bis-DMA is a member of the acrylate/methacrylate family.

These compounds are metabolised primarily via 2 pathways: (1) enzymatic hydrolysis by esterases present in various tissues; and (2) conjugation with glutathione (GSH). The latter pathway, which results in the formation of mercapturic acids, has been demonstrated for both acrylates and methacrylates *in vitro* and *in vivo* (Greim et al. 1995). Hydrolysis of methacrylate esters, catalysed by carboxylesterases, produces methacrylic acid and the corresponding alcohol (McCarthy and Witz 1997). Ester hydrolysis of Bis-DMA is predicted to produce the metabolites methacrylic acid (CAS No. 79-41-4) and BPA (CAS No. 80-05-7) (OECD 2021).

Bis-DMA is an ester derivative of BPA, in which 2 methacrylate groups are attached to the hydroxyl groups of BPA via ester bonds (see **Chemical Identity**). When exposed to saliva esterases, these ester bonds may be susceptible to hydrolysis, leading to the release of free BPA (Atkinson et al. 2002; Schmalz et al. 1999).

Acute toxicity

No data are available.

Corrosion/Irritation

No data are available.

Sensitisation

Skin sensitisation

Based on the available data, the chemical is a skin sensitiser, warranting GHS classification.

As a response rate, > 30% was reported in a guinea pig maximisation test (GPMT), the chemical satisfies the criteria for GHS classification (UNECE 2017). In the single available GPMT study, the high response rates observed after intradermal induction at > 1% could not confidently differentiate between Category 1A or 1B, and therefore, sub-categorisation is not proposed. Overall, the available data support classification as skin sensitisation Category 1.

In vivo

The chemical was evaluated for skin sensitisation using a GPMT (similar to OECD TG 406). No information on GLP compliance was available. The study involved parallel testing of a commercial product and a purified fraction of the chemical in female Dunkin Hartley guinea pigs (15/group). Induction was performed intradermally with 10% of either test material in olive oil/acetone vehicle, followed by (non-occlusive) topical applications of 50% (commercial product) or 25% (purified fraction) in petrolatum. Animals were subsequently challenged topically with the chemical at 10% (commercial product) or 5% (purified fraction) in petrolatum. Animals sensitised with the commercial product underwent 3 challenges, with response rates of 53%, 67%, and 80%, respectively. Animals sensitised with the purified fraction were challenged twice, with response rates of 80% and 100%. Positive controls were omitted in the study while negative controls responded as expected (Bjorkner et al. 1984).

In silico

Mechanistic alerts for sensitisation potential, such as acylation, Michael addition, nucleophilic addition, and Schiff base formation, are present across multiple profilers within the OECD QSAR Toolbox v4.5, including OECD and OASIS protein binding profilers and microbial metabolism simulators (OECD 2021).

Observation in humans

Controlled patch testing found no evidence of sensitisation to Bis-DMA in:

- 250 occupational cases in the United Kingdom and 241 patients in Finland with a history of exposure to (meth)acrylates
- 41 patients with known epoxy-resin allergy in the USA.

However, isolated cases of allergic contact dermatitis attributed to Bis-DMA have been reported among dental workers from South Korea, the USA, Sweden, Poland, and Belgium (Aalto-Korte et al. 2009).

These findings indicate that although Bis-DMA has a low prevalence of sensitisation, it may still pose a sensitisation risk, particularly in individuals with frequent and direct exposure.

Repeat dose toxicity

No data are available for the chemical.

Profiling by the OECD QSAR Toolbox v4.5 identified multiple structural alerts for Bis-DMA associated with liver and kidney toxicity. These alerts, which are linked to chemicals such as methyldopa, methylclofenapate, oxyphenisatin, maleic acid, nitrilotriacetic acid, were repeatedly flagged across various simulation or observation models (OECD 2021).

The metabolite BPA is not classified under the GHS for specific target organ toxicity following repeated exposure. In animal studies the chemical has reported health effects in the liver and kidney (NICNAS 2016). The chemical has also been linked to effects on the immune system and metabolism (EFSA 2023).

Genotoxicity

No data are available for the chemical.

In vitro (Ames test) and *in vivo* (micronucleus test) mutagenicity alerts for α,β-unsaturated carbonyls have been identified for Bis-DMA, as profiled by the OECD QSAR Toolbox v4.5.

The metabolite BPA is not considered genotoxic (EFSA 2023; NICNAS 2016).

Carcinogenicity

No data are available for the chemical.

Although BPA produced proliferative changes in the mammary gland in animal studies, including a non-human primate study, these were insufficient to conclude a link to cancer development (NICNAS 2016).

Reproductive and development toxicity

Based on the available data, Bis-DMA is expected to cause adverse effects on fertility and sexual function, warranting GHS classification.

Adverse effects on both male and female fertility were reported in available studies on Bis-DMA in the absence of marked general toxicity. This includes reduced pregnancy rates, reduced number of implantations and adverse effects on sperm parameters. Bis-DMA exposure also caused testicular abnormalities with atrophic seminiferous tubules. Although these were non-guideline studies, similar effects have been observed with BPA. Overall, the findings represent clear evidence of an adverse effect on sexual function and fertility, which is not considered to be a secondary non-specific consequence of other toxic effects. Therefore, the available data support classification of Bis-DMA as a reproductive toxicant, Category 1B (Repr. 1B; H360F).

No data are available to determine developmental effects.

Bis-DMA

In a non-guideline study, male BALB/c mice (10/dose) were given Bis-DMA in drinking water at 0, 0.1, 1.0 or 10 mg/L (corresponding to approximately 0, 0.01, 0.1 and 1.0 mg/kg bw/day) for 14 weeks (Darmani & Alkhatib 2023). Each exposed male was then paired with 2 untreated females for a 10 day mating period. The number of pregnant females, viable foetuses, implantation sites, resorptions, and females with resorptions was recorded 9 days following the end of the mating period.

Effects on male mouse fertility and reproductive function were reported, including:

- decrease in pregnancy rates at all doses (59%, 67%, 47%) vs controls (80%) – not statistically significant
- increase in proportion of female mice with resorptions with increasing doses (10%, 33%, 44%) vs controls (6%) – not statistically significant
- significant reduction in number of implantations (70%) and viable foetuses (51%) vs controls (100%) at high dose
- significant increase in number of resorptions per total implantations at mid and high doses (33% and 30%) vs controls (5%)
- histological abnormalities in testicular tissue at all doses with dose related increase in the severity of effects; no change in relative testes weight.
- reduction in total and relative sperm counts, daily sperm production, and efficiency of sperm production (i.e. sperm/mg testis/day) – statistically significant at low and mid doses, but not at high doses
- elevation in follicle stimulating hormone (FSH), luteinising hormone (LH), and testosterone at all doses – statistically significant increases in LH and testosterone at low dose only.

In a non-guideline study, Swiss mice (10/sex/dose) were exposed to intragastric Bis-DMA at 0, 0.005, 0.025 or 0.1 mg/kg bw/day for 28 days (Darmani & Al-Hiyasat 2004). For reproductive assessment, following the 28-day exposure period, one male mouse was co-housed with 2 female mice for a 10 day mating period. In each pairing, either only the

male or the female received the chemical treatment, enabling evaluation of sex specific reproductive outcomes. Reproductive parameters, including the number of pregnant females, viable foetuses, implantation sites, resorptions, and female with resorptions, were recorded either 7 or 10 days after the mating period, depending on whether the females were exposed to bis-DMA or not. Additionally, for body and organ weight assessment, 5 extra female mice per dose group were included in the study and examined at the end of the 28 day exposure period (i.e. these animals were not mated).

The following effects on fertility and reproductive organs were reported for exposed male mice mated with unexposed female mice:

- no statistically significant effects on number of implantations or viable foetuses
- significant increase in number of resorptions per total implantations at low and mid doses (11% and 13%) vs controls (2%)
- significant decrease in pregnancy rates at all doses (70%, 60%, 17%) vs controls (95%)
- increase in proportion of female mice with resorptions at all doses (64%, 58%, 67%) vs controls (11%) – statistically significant at mid and high dose
- significant increase in relative weights of seminal vesicles and preputial glands at mid and high doses
- significant decrease in total and relative sperm counts, daily sperm production, and efficiency of sperm production at mid and high doses.

A significant reduction in body weight at the end of the mating period was reported at all doses for male mice but no information on body weight gain was available.

The following effects on fertility and reproductive organs were reported for exposed female mice mated with unexposed male mice:

- significant reduction in number of implantations at high dose (67%) and viable foetuses at mid and high doses (83% and 56%) vs controls (100%)
- significant increase in number of resorptions per total implantations at mid and high doses (8% and 17%) vs controls (1%)
- decrease in pregnancy rates at all doses (78%, 80%, 38%) vs controls (100%) – statistically significant at high dose
- increase in proportion of female mice with resorptions at all doses (22%, 63%, 67%) vs controls (10%) – statistically significant at mid dose
- significant increase in relative weights of ovary at mid and high doses and uterus at low dose before mating.

A significant reduction in body weight at the end of the exposure period was reported at all doses for female mice but no information of body weight gain was available.

BPA metabolite

The metabolite BPA is classified for reproductive toxicity (Category 1B; H360F) (AICIS 2024).

Multi-generational studies in rats and mice have reported adverse reproductive effects at high doses of BPA (600 mg/kg bw/day), including reduced litter size, fewer live pups, and effects on reproductive organs (such as decreased ovarian weight, reduced sperm production, and decreased testes/epididymides weight). These findings were supported by non-guideline animal studies. BPA exposure also led to increased resorptions and reduced

pregnancies and implantations. The effects occurred in the absence of marked systemic toxicity. Therefore, the observed effects are not likely to be secondary to general, non-specific toxicity (AICIS 2024; ECHA 2014).

Endocrine effects

Limited data, particularly from *in vivo* studies, are available on the endocrine effects of Bis-DMA. Although some endocrine activity has been observed *in vitro*, the potency of responses was lower than BPA. Overall, the current available data does not provide sufficient evidence of an adverse effect of Bis-DMA as consequence of endocrine activity.

Regarding the metabolite BPA, mechanisms of action underlying its reproductive toxicity have been investigated, though not always systematically. They mainly include interactions with oestrogen and androgen receptors through adult and germline exposures, as well as epigenetic modifications that may influence gene expression and reproductive outcomes (EFSA 2023). The ECHA Risk Assessment Committee concluded that BPA's mode of action for disruption of the reproductive tract may involve both direct and indirect disruption of the hypothalamic–pituitary–gonadal (HPG) axis, or by direct organ specific toxicity (AICIS 2024; ECHA 2014).

In vitro

Bis-DMA has been demonstrated to exhibit oestrogenic activity in several cell systems, albeit with lower potency than BPA.

- In a human breast cancer MCF-7 vitellogenin-luciferase nuclear cell line, Bis-DMA and BPA elicited oestrogen receptor ER-luciferase transactivation, with half-maximal effective concentration (EC50) of 4.8 μM and 3.9 μM, respectively. Both reached approximately 75% of the maximal response induced by oestradiol (Bonefeld-Jørgensen et al. 2007).
- Bis-DMA exhibited clear oestrogenic activity (EC50 = 0.41 μM), though generally weaker than BPA in an ERα-chemically activated luciferase gene expression assay (Boonen et al. 2021).
- In MCF-7 cells (BUS subline), both Bis-DMA and BPA significantly increased cell proliferation at 5 μM and 1 μM, respectively, comparable to the increase seen with 0.001 μM of oestradiol. In ZR-75-1 cells, which have lower oestrogen receptor content, BPA and oestradiol stimulated proliferation while Bis-DMA did not (Schafer et al. 1999).
- Both chemicals also significantly increased proliferation of MCF-7 cells (Bis-DMA at 10 μM vs BPA 0.1 μM) in an E-screen test. However, Bis-DMA did not show oestrogenic activity in yeast 2-hybrid or fluorescence polarisation systems, unlike BPA (Hashimoto & Nakamura 2000).
- Bis-DMA had binding affinity values above 200 μM (i.e. nonspecific binding) using recombinant hER, compared to BPA at 11 μM. Using rabbit uterine oestrogen receptor, Bis-DMA showed a binding affinity of 4.3 μM compared to BPA at 1.6 μM (Andersen et al. 1999).

Additionally, both Bis-DMA and BPA inhibited aromatase activity, an enzyme critical for oestrogen biosynthesis, in JEG-3 cells (40% vs 59% inhibition at 100 μM). Bis-DMA also acted as an aryl hydrocarbon receptor agonist and an androgen receptor antagonist, with lower potency than BPA (Bonefeld-Jørgensen et al. 2007).

In vivo

In juvenile rainbow trouts (6/dose), Bis-DMA at 50 mg/kg induced a weak increase in vitellogenin production, a biomarker of oestrogen exposure, while BPA showed a strong effect at the same dose (Andersen et al. 1999).

Changes in reproductive organ weights and hormone levels were reported in non-guideline studies investigating reproductive toxicity. These differed from those observed with the endocrine effects of BPA (see **Reproductive and developmental toxicity**). Therefore, the relevance of these findings related to endocrine disruption remains uncertain.

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