Australian Government
Department of Health
Australian Industrial Chemicals Introduction Scheme

1-Propanone, 2-methyl-1-[4-(methylthio)phenyl]-2-(4-morpholinyl)-

Evaluation statement

14 September 2021

Table of contents

Contents

AICIS evaluation statement

Subject of the evaluation

1-Propanone, 2-methyl-1-[4-(methylthio)phenyl]-2-(4-morpholinyl)-

Chemical(s) in this evaluation

Name	CAS Registry Number
1-Propanone, 2-methyl-1-[4-(methylthio)phenyl]-2-(4-morpholinyl)-	71868-10-5

Reason for the Evaluation

An evaluation is required to provide information on the risks to human health.

Parameters of evaluation

A human health risk evaluation assessment for all identified industrial uses of the chemical.

Summary of evaluation

Summary of introduction, use and end use

There is very limited information about the chemical's uses and use volumes in Australia.

Based on international information, the chemical is used in a wide range of commercial applications including a photosensitive substance (e.g. use as a photo-initiator), an intermediate in the synthesis of chemicals and in the manufacture of other products (refer to the supporting information).

International data suggested that the chemical may be used as a binder in cosmetic products, but no additional details on this use was found and no evidence of the chemicals used in cosmetics was found. As the chemical is unstable towards UV light, any cosmetic use would be very limited, for example as an initiator in UV-cured fingernail adhesives.

Although there is some possible domestic use of the chemical, this is not expected to be widespread.

Human health

Summary of health hazards

The critical health effects for risk characterisation include:

- systemic acute effects from oral exposure
- systemic effects following repeated oral exposure.

The chemical may be expected to be absorbed across biological membranes due to its relatively low molecular weight. The chemical may be excreted via the urine after metabolic transformation.

The chemical has moderate acute oral toxicity, with a lowest reported median lethal dose (LD50) of 1984 mg/kg body weight (bw) in rats. The chemical has low acute dermal toxicity. There was no information on acute inhalation toxicity.

The chemical is not a skin irritant. The chemical is not a skin sensitiser based on the negative results seen in a guinea pig maximisation test (GPMT). It is slightly irritating to the eyes. The chemical has a low vapour pressure.

In a 90 day oral repeated dose toxicity study in rats, the chemical was reported to have a no observed adverse effect level (NOAEL) of 75 mg/kg bw/day. Cataracts of the eye lens, histopathological changes in the spleen and effects to the peripheral nervous system were observed at the highest dose (220 mg/kg bw/day).

Based on the available data, the chemical is not considered to be genotoxic in vitro or in vivo. Negative results were reported in an in vitro (bacterial reverse mutation assay and a mammalian chromosome aberration test) and in vivo tests (genome mutation micronucleus assay).

The chemical may cause reproductive and developmental toxicity based on the results of a one-generation reproductive toxicity study. The NOAEL for reproductive toxicity in rats was determined to be 40 mg/kg bw/day based on number of implantations, litter size, and number of stillbirths under the conditions of the test. The developmental toxicity NOAEL of the chemical in rats was determined to be 40 mg/kg bw/day, based on an increased number in pre-birth loss and various external and visceral malformations in individual litters noted for middle and highest dose animals.

Health hazard classification

The chemical satisfies the criteria for the 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. This is the current classification in the Hazardous Chemicals Information System (HCIS).

Health Hazards	Hazard Category	Hazard Statement
Acute toxicity – oral	Category 4	H302 (Harmful if swallowed)
Reproductive toxicity – oral	Category 1B	H360FD (May damage fertility or the unborn child)

Summary of health risk

Public

Based on the available information, no cosmetic or domestic uses were identified in Australia. The only known use of the chemical in Australia is in UV curable ink. Based on its

international use patterns, the chemical is not expected to have frequent uses in products that could expose the public directly to the chemical. Therefore, there are no identified risks to the public that require management. However, if information becomes available indicating the chemical does have consumer use, further risk management may be required.

Workers

During product formulation, dermal, ocular and inhalation 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 chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term effects, the chemical could pose a risk to workers unless adequate control measures to minimise dermal, ocular and inhalation exposure are implemented (see Recommendation section).

Once the product is UV-cured, the chemical will be fully reacted with other components and bound to the matrix of the substrates. Therefore, it is not expected to be available for exposure to the users of products.

Conclusions

The conclusions of this evaluation are based on the information described in the statement. Obligations to report additional information about hazards under Section 100 of the Industrial Chemicals Act 2019 apply.

The Executive Director is satisfied that the identified human health risks can be managed within existing risk management frameworks provided all requirements are met under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

The proposed means of managing the risks identified during this evaluation are set out in the Recommendations section.

Recommendations

Advice to industry

The information in this report should be used by persons conducting a business or undertaking at the workplace (such as an employer) to determine the appropriate controls.

Recommended control measures that could be implemented to manage the risk arising from occupational exposure to the chemical include, but are not limited to:

- using closed systems or isolating operations
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker
- 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.

Measures required to eliminate, or manage risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. These control measures should 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. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

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.

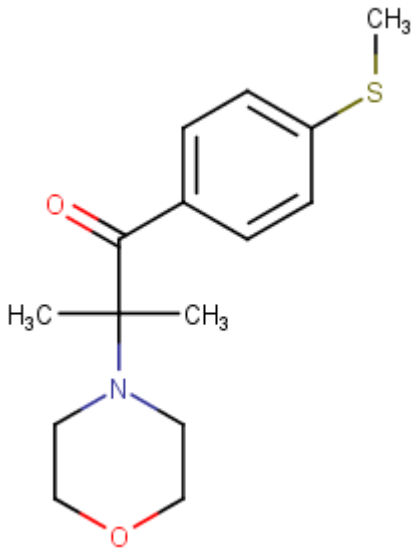
Supporting information

Rationale

The chemical has functional groups (includes heterocyclic, ketone and thio groups) known to have concern for human health safety. It is a substituted cathinone and has widespread industrial uses in formulation, repackaging and manufacturing.

Chemical identity

CAS number	71868-10-5
Synonyms	2-methyl-1-(4-methylsulfanylphenyl)-2-morpholin-4-ylpropan-1-one (IUPAC name) 2-methyl-4'-(methylthio)-2-morpholinopropiophenone methylthiophenyl morpholino isobutanone (INCI name) Igacure 907 UV 907
Structural Formula	

	
Molecular Formula	$C_{15}H_{21}NO_2S$
Molecular Weight (g/mol)	279.40
SMILES	CSc1ccc(cc1)C(=O)C(C)(C)N2CCOCC2 CSC1=CC=C(C=C1)C(=O)C(C)(C)N1CCOCC1 CC(C)(N1CCOCC1)C(=O)c2ccc(SC)cc2 O=C(C(C)(C)N1CCOCC1)C2=CC=C(SC)C=C2
Chemical Description	Highly efficient photoinitiator can be used in UV curing systems

Relevant physical and chemical properties

Physical Form	White to light beige solid powder in ambient conditions (20 °C and 101.3 kPa).
Melting Point	74.6 °C
Particle Size	9.6–40.9 µm (MMD= <22.1 µm)
Boiling Point	Decomposes at >190 °C before boiling
Vapour Pressure	Extrapolated to be 0.0002 Pa at 25 °C
Water Solubility	18 mg/L at 20 °C

log K_{ow}	N/A (No ionic structure)

Introduction and use

Australia

The chemical is used in UV curable inks in Australia.

There are no other available use information for this chemical in Australia.

International

The following international uses have been identified through the European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers, Galleria Chemica, Substances in Preparations in Nordic countries (SPIN) database, United States (US) Personal Care Products Council International Nomenclature Cosmetic Ingredients (INCI) directory, and other data sources via eChemPortal including the US Environmental Protection Agency (EPA).

The chemical has cosmetic uses, including as a binding agent. However, the Compilation of Ingredients used in Cosmetics in the United States of America does not report any occurrences of the chemical (Personal Care Products Council, 2011).

The chemical has potential domestic uses, including in:

- cleaning products
- surface coatings
- surface-active agents
- paints
- pigments, dyes and printing inks
- textile products
- adhesives and sealants
- cleaning and washing agents
- corrosion inhibitors
- fillers
- insulating materials.

Overall information indicates that the chemical is not likely to be widely available for domestic use. The REACH dossiers did not identify any consumer uses of the chemical. Consumer uses in inks toner and colourants were identified by up to two companies in USA and Canada reporting information (Government of Canada, US EPA, 2012). Consumer uses were identified in the SPIN database. However, it should be noted that SPIN does not distinguish between direct use of the chemical, or use of the materials that are produced from chemical reactions involving the chemical. There is no evidence from available consumer product databases for use of this chemical in consumer industrial products.

The chemical has commercial uses, including:

- as a photosensitive agent, fluorescent agent, brightener and UV absorber
- in electrical or electronic products
- in leather tanning
- as a photographic and photocopier agent
- in plastics
- as a solvent and carrier.

The chemical has site-limited industrial uses, including:

- as a metallurgical agent
- in the production of polymers
- in pulp and paper manufacturing
- in textile manufacture.

The chemical is used as a photoinitiator in polymer production. The chemical generates free radicals using the energy of UV-light for the formation of polymeric materials. The main applications of the substance are in high speed inks such as flexo, offset litho and UV ink jet (ECHA, 2019).

Existing Australian regulatory controls

AICIS

No specific restrictions currently apply to the chemical.

Public

No specific restrictions currently apply to the chemical.

Workers

The chemical is classified as hazardous, with the following risk phrases for human health in the Hazardous Chemicals Information System (HCIS) (Safe Work Australia):

- Acute toxicity – Category 4; H302 (Harmful if swallowed)
- Reproductive toxicity – Category 1B; H360FD (May damage fertility. May damage the unborn child)

No exposure standards are available for this chemical in Australia (Safe Work Australia).

International regulatory status

Exposure standards

No exposure standards are available for this chemical.

European Union

The chemical is listed on the candidate list of Substances of Very High Concern (SVHC) for eventual inclusion in Annex XIV (ECHA, 2020). The reason for inclusion is 'Endocrine disrupting properties (Toxic for reproduction (Article 57c)'. In the EU, companies could have legal obligations if the chemical that they produce, supply, or use is included on the candidate list whether on its own, in mixtures, or present in articles.

Health hazard information

Toxicokinetics

The chemical has a relatively low molecular weight of 279 g/mol and a water solubility of 18 mg/L. Absorption across biological membranes is expected.

Absorption
The chemical's particle size typically falls within the 9.6–40.9 µm range. Particles of this size are inhalable, and are likely to reach the smaller bronchioles and or alveoli. Particles deposited in the airways may be transported to the pharynx and the digestive tract by means of the mucociliary clearing mechanism of the respiratory tract and, in some cases, may be subsequently absorbed into the body.

Distribution
The chemical is non-ionic and cannot undergo pH-dependent hydrolysis in the stomach. However, in a combined one-generation repeated dose/developmental toxicity study foetal toxicity and adverse effects in newborn rats revealed that the chemical and/or its metabolites crossed the placental barrier (REACH).

Metabolism
The chemical is photolabile meaning it can degrade to form radicals under light exposure. It can be assumed that the intact chemical circulates in the blood. At locations that are easily penetrated by light (eyes, legs of rats) photo-cleavage resulting in radical formation may occur. These radicals are expected to be responsible for toxicity to eyes and the acanthosis (an increased number of specialised squamous cells in the skin). The absorbed parent compound is most likely subject to hepatic metabolic degradation such as S-demethylation, keto-hydroxylation and morpholine ring cleavage. In addition, metabolic transformation may include ring opening of the morpholine moiety catalysed by cytochrome-P450-dependent monooxygenases (REACH).

The absorption, distribution, metabolism and excretion properties of the chemical in the in silico prediction of blood-brain partitioning (REACH guidance on QSARs R.7c) (Health Impact Assessment model) indicates that the chemical has a good human intestinal absorption. The model of plasma protein binding and another blood-brain barrier model indicate that the chemical has a lower volume of distribution in the human body (with the plasma protein binding more than 95%), indicating reduced capacity for widespread distribution in body tissue. The chemical is expected to cross the blood-brain barrier. The chemical is also unlikely to cause dose-dependent liver injuries and may not be metabolised in liver as a result of the hepatotoxicity model and CYP2D6 inhibitor model. Due to its lower molecular weight (279 g/mol) and relatively good water solubility (18 mg/L), the chemical is likely to be excreted in urine (REACH).

The chemical's structural analogue (moclobemide; CAS No. 71320-77-9, solid, with

MW = 268.7 g/mol, slightly soluble in water and oral LD50 in rats of 707 mg/kg) is expected to be excreted in urine after extensive metabolic transformation. The metabolic pathways consist of mainly oxidative attack of the morpholine moiety. The metabolites are then excreted as conjugates of glucuronic and/or sulfuric acid (Fitzpatrick et al, 2004). Therefore, accumulation in the body is not expected. The chemical in this evaluation is expected to be metabolised and excreted via a similar pathway.

Acute toxicity

Oral

Based on the available data, the chemical has low to moderate acute oral toxicity. In a GLP compliant acute toxicity study conducted in accordance with OECD Test Guideline (TG) 401, the chemical was administered orally (by gavage) at 1000, 2000, or 4000 mg/kg bw to rats of both sexes. At 1000 mg/kg bw 0/5 males and 2/5 females died, at 2000 mg/kg bw 1/5 males and 3/5 females died, at 4000 mg/kg bw 4/5 males and 5/5 females died. Animals showed some clinical signs such as:

- dyspnoea
- exophthalmos (abnormal protrusion of the eyeball or eyeballs)
- ruffled fur
- curved body position
- sedation
- lateral and ventral body position
- chromodacryorrhea (red lacrimal secretion called "bloody tears")
- diarrhoea
- clonic convulsions
- bilateral paresis of the hind limbs (a condition of muscular weakness caused by nerve damage or disease; partial paralysis).

The surviving animals recovered within 28 days. Body weights were in the normal range. The acute oral median lethal dose (LD50) of the chemical was determined to be 1984 mg/kg bw.

Dermal

Based on the available data, the chemical has low acute dermal toxicity. In a GLP compliant acute toxicity study conducted in accordance with OECD TG 402, the chemical was applied at 2000 mg/kg bw to the skin of rats for 24 hours (occlusive exposure). Animals showed some clinical effects such as dyspnoea, exophthalmos, ruffled fur and curved and ventral body positions. The surviving animals recovered within 8 days. No mortalities or abnormalities were observed and no gross lesions were found at necropsy in any male or female animals. The dermal LD50 was determined to be >2000 mg/kg bw, indicating the chemical has low acute dermal toxicity (REACH).

Inhalation

No data are available for the chemical.

Corrosion/irritation

Skin irritation

Based on the available data, the chemical was not a skin irritant or corrosive. In a semi-occlusive skin irritation/corrosion test conducted according to OECD TG 404, 0.5 g were applied on the shaved skin of New Zealand White (NZW) female rabbits (4 hours semi-occlusive exposure). The mean erythema or oedema scores were 0 with a maximum score of 0. The chemical did not induce a dermal irritation response in rabbits under the conditions of the test (REACH).

Eye irritation

Based on the available data, the chemical does not warrant hazard classification for ocular irritation. In an in vivo eye irritation study in New Zealand White rabbits conducted according to OECD TG 405, the mean conjunctivae score was 0.89 (irritation was observed after one hour in 2/3 animals; however, effects were fully reversible within 7 days). The mean chemosis score was 0.22 (slight swelling was observed after one hour; however, effects were fully reversible within 48 hours). The mean corneal opacity score was 0 (slightly irritative reactions after one hour in one animal). The mean iris score of 0 (irritative effects were observed after one hour in one animal). The chemical is slightly irritating to the eye but does not warrant hazard classification (REACH).

Sensitisation

Skin sensitisation

In a GLP compliant in vivo skin sensitisation study conducted in accordance with OECD TG 406 (guinea pig maximisation test (GPMT), Pirbright White guinea pigs (20/group, sex unspecified) were treated with the chemical by intradermal injection (10% in petroleum jelly) and topical administration (10% in petroleum jelly). Following challenge at up to 10% in petroleum jelly, no positive skin reactions were observed in the test group, compared with the negative control. As the chemical did not induce any dermal reactions in test animals, the chemical is considered to be non-sensitising (REACH).

Repeat dose toxicity

Oral

In a repeated dose 90-day oral toxicity study in Sprague Dawley (SD) rats conducted according to OECD TG 408, animals (10/sex/dose) were administered the chemical at 0, 10, 25, 75 or 220 mg/kg bw/day (5 times per week), via oral gavage. No treatment-related mortalities occurred. Treatment-related ophthalmological effects were observed in animals in the 220 mg/kg bw/day group, including eye opacity, and uni- or bilateral absence of pupillary light reflex. Two males, one each in the 25 and 75 mg/kg bw/day dose groups, showed paleness of eye fundus. Paresis of the hind legs was observed in males and females in the highest dose group, beginning on day 7 of treatment. Locomotor impairment improved at week 4 of treatment to the degree that the animals were later able to walk; however, with unsteady gait until week 10 of treatment. Absolute and relative mean liver weight was increased in the highest dose females, and kidney and brain to body weight increased. Histopathological findings included increased occurrences (8/10) of haemosiderosis (a term used for excessive accumulation of iron deposits called hemosiderin in the tissues) in the

spleen of females at the highest dose, segmental demyelination of the peripheral nerve fibres in males (9/10) and females (9/10) at the highest dose. Cataracts of the eye lens in males (1/10) and females (6/10) in the 220 mg/kg bw/day group were observed. A NOAEL of 75 mg/kg bw/day was established based on ophthalmic and body and organ weight changes, as well as histopathology findings observed in the highest group (REACH).

In an oral repeated dose 28-day toxicity study in SD rats conducted according to OECD TG 407, animals of both sexes were dosed by oral gavage, daily at 0, 30, 100 or 300 mg/kg bw/day. One male and 2 female rats died in the highest dose group (300 mg/kg bw/day) as result of treatment and one male died due to misapplication of the test substance. Animals in the highest dose group showed signs of systemic intoxication such as diarrhoea, lameness of the hind legs, altered locomotion, pale or opaque eyes, ruffled fur, hairlessness, increased salivation and emaciation.

The mean food consumption of males in the 100 and 300 mg/kg bw/day groups was depressed in a dose-dependent manner. The mean body weight of treated animals in these groups was significantly depressed in a dose-dependent manner (up to 33%). The mean body weight of females in the 30 mg/kg bw/day group was only slightly and not significantly decreased. Animals in the middle and highest dose groups showed slightly higher alanine aminotransferase (ALT) blood levels in week 5 (up to 2 fold) and animals in the highest dose group showed slightly increased aspartate aminotransferase (AST) blood levels. A significant increase in haemoglobin concentration and haematocrit in males of the 300 mg/kg bw/day group, and a moderate increase in white blood cell numbers in females at the same dose level were reported. A slight decrease in lymphocyte numbers and a slight increase in numbers of segmented neutrophils was observed in both males and females of the 300 mg/kg bw group.

Animals in the highest dose group also showed histopathological effects, including slight hypertrophy of hepatocytes in 4 of 5 males and 2 of 5 females. Treatment-related gross pathological effects in highest dose animals were also observed, including acute congestion with haemorrhage observed in various parenchymatous organs. A NOAEL of 100 mg/kg bw/day was established based on the biochemical changes and histopathological findings (REACH).

Dermal

No data are available for the chemical.

Inhalation

No data are available for the chemical.

Genotoxicity

In vitro

The chemical was negative in a bacterial reverse mutation assay conducted according to OECD TG 471 using *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98, and TA 100, and *Escherichia coli* strain WP2 uvrA at concentrations up to 5000 µg/plate, with and without metabolic activation.

The chemical was negative in an in vitro mammalian chromosome aberration test conducted according to OECD TG 473 (in Chinese hamster lung fibroblasts (V79)) at concentrations up

to 200 µg/mL for up to a 28 hour exposure period, with and without metabolic activation (REACH).

In vivo

The chemical was reported to test negative in a genome mutation micronucleus assay (comparable to OECD TG 487, with acceptable restrictions) in a Chinese hamster random outbred strain at concentrations up to 3000 mg/kg bw/day (REACH).

Carcinogenicity

No data are available for the chemical.

Reproductive and development toxicity

In a one-generation reproductive toxicity study conducted according to OECD TG 415, Sprague Dawley (SD) rats (n=48 females, 24 males/dose/group) were exposed to the chemical via oral gavage at concentrations of 0, 40, 80 or 120 mg/kg bw/day. Animals were administered the chemical once daily, 7 days a week. Males were treated for 10 consecutive weeks prior to mating and thereafter. Females were treated for 2 consecutive weeks prior to mating and thereafter. General, developmental and reproductive toxicity parameters were assessed.

P0 (Parental) effects

During the gestation period, females in the highest dose group were reported to experience hair loss and swollen abdomens. The middle and highest dose females were reported to show staining on the body during both gestation and post-partum phase. Observed treatment-related reproductive effects included reduced fertility in all treated female groups which was statistically significant in the highest dose group. The percentage of post-implantation loss observed in all female treated groups was increased compared to the control groups. Male fertility parameters were not affected, testes and epididymides weights were also not affected. Repeated-dose studies did not show adverse effects on male reproductive organs.

F1 (First Generation) effects

Stillbirths or total litter loss was observed on parturition day or the day after parturition (14.63%) in all females in the highest dose group. A statistically significant decrease in mean foetal weight in the highest dose animals was also observed. A significant increase in pup loss on day 1 post-partum, and a cumulative loss on days 4 and 14 post-partum (17.23%), with a significant decrease in litter weight were observed in the female middle dose group. Statistically significant decreases in the number of viable males or percentage of males and litter weight were also observed in the middle and highest dose groups.

Treatment-related developmental effects were observed in the F1 animals. External malformations, including micrognathia (undersized lower jaw), cleft palate, anasarca (generalised swelling), bent tail (short or swollen), short body, kyphosis (an exaggerated, forward rounding of the spine), malrotated fore and hindlimbs and domed-shape head were observed in the highest dose foetus group. Bent tails were observed in the middle dose foetus group. Pups weaned from the lowest and middle dose groups were reported to have dilated lateral brain ventricles or third ventricle dilated and abnormal urinary bladder sizes. Anasarca

(generalised systemic inflammation) was observed in the lowest dose group. In some cases, there was no evidence of the innominate artery.

Treatment-related skeletal and visceral malformations were also observed, including retardation or no ossification of the sternal elements, sometimes with asymmetrical ossification and rudimentary 14th rib, impaired metacarpal development (incomplete ossification or unossified). An increased incidence of kidney dilatation with enlarged and/or kinked ureters at all dose levels was reported. The following clinical signs were also observed in the highest dose group, compared to controls:

- incomplete ossification of the skull bones
- alteration of ossification in the vertebral column
- displaced ribs
- impaired metatarsal ossification and incomplete ossification of the pubis bone
- anencephaly (absence of significant portions of the skull and brain)
- anophthalmia (absence of one or both eyes)
- microphthalmia (abnormally small eye or eyes)
- displaced testes and kidneys
- cryptorchidism (the absence of at least one testicle from the scrotum)
- kyphosis and short body
- cleft palate
- abnormal shape of the fore and hind limbs, as well as short digits.

On the basis of this study, NOAELs of 40 mg/kg bw/day were determined for general toxicity, reproductive toxicity and developmental toxicity. The data support the existing hazard classification (REACH).

References

ECHA (European Chemicals Agency) (2019) proposal for identification of a substance of very high concern on the basis of the criteria set out in reach article 57. Substance Name: 2-benzyl-2-dimethylamino-4'-morpholinobutyrophenone Accessed May 2021 at https://echa.europa.eu/

ECHA (European Chemicals Agency) (2020) Inclusion of substances of very high concern in the Candidate List for eventual inclusion in Annex XIV. Accessed May 2021 at https://echa.europa.eu/documents/10162/ba42270a-93fe-7cde-6d41-7f7af4e00e66

EU (2008). Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packing of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. Official Journal of the European Union, L353: 1-1355.

D, Fitzpatrick, J, Corish, & B, Hayes 2004. Modelling skin permeability in risk assessment—the future. Chemosphere, 55(10), pp. 1309-1314. Accessed May 2021 at http://jr.chemwatch.net/galleria/

Government of Canada. Inventory updates conducted under Canada's Chemicals Management Plan (CMP). Government of Canada. Available at: https://www.canada.ca/en/health-canada/services/chemical-substances/inventory-updates.html

M, Takai, Y, Kawasaki, S, Arimoto, Y, Tanimoto, Y, Kitamura, & T, Sendo 2018. UV-irradiated 2-methyl-4'-(methylthio)-2-morpholinopropiophenone-containing injection solution produced frameshift mutations in the Ames mutagenicity assay. PMID: 29488202, DOI: 10.1007/s11356-018-1539-8, Environ Sci Pollut Res Int, 25(10).

Personal Care Product Council, 2011. Compilation of Ingredients Used in Cosmetics in the United States, 1st Edition. Accessed May 2021 at http://gov.personalcarecouncil.org/jsp/gov/GovHomePage.jsp

REACH, Chemical 2-methyl-1-(4-methylthiophenyl)-2-morpholinopropan-1-one (CAS No. 71868-10-5, EC No. 400-600-6) Accessed May 2021 at https://echa.europa.eu/fr/registration-dossier/-/registered-dossier/7071/11

Safe Work Australia. Hazardous Chemical Information System (HCIS). Accessed May 2021 at http://hcis.safeworkaustralia.gov.au/HazardousChemical

Substances in Preparations in Nordic Countries (SPIN). Accessed December 2021 at http://www.spin2000.net/spinmyphp/

UNECE (2017). Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Seventh Revised Edition. United Nations Economic Commission for Europe (UNECE), Geneva, Switzerland. Accessed May 2021 at http://www.unece.org/trans/danger/publi/ghs/ghs_rev07/07files_e0.html

US EPA 2012. United States Environment Protection Agency Chemical Data Reporting (CDR) 2012 data, Accessed May 2021 at https://www.epa.gov/chemical-data-reporting/access-cdr-data

Y, Kawasaki, K, Yagi, C, Tsuboi, M, Morizane, Y, Kitamura, & T, Sendo 2013. The polymerization agent, 2-methyl-4'-(methylthio)-2-morpholinopropiophenone induces caspases-3/7 in human blood mononuclear cells in vitro. PMID: 24088257, DOI: 10.1248/bpb.b12-01032, Biol Pharm Bull, 36(10) pp.1640-5.