2-Butenedioic acid, (E)-, dimethyl ester: Human health tier II assessment

24 April 2015

CAS Number: 624-49-7

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

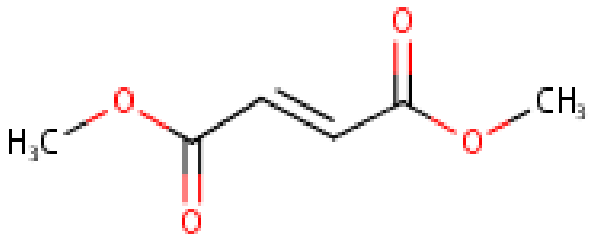
This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

Disclaimer

Acronyms & Abbreviations

Chemical Identity

Synonyms	dimethyl fumarate (DMF) fumaric acid, dimethyl ester fumaderm methyl fumarate
Structural Formula	
Molecular Formula	C6H8O4
Molecular Weight (g/mol)	144.125
Appearance and Odour (where available)	white to off-white crystalline powder
SMILES	C(=O)(C={t}CC(=O)OC)OC

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information:

The chemical has reported domestic use as a biocidal additive (in sachets or directly applied) in consumer products such as:

- leather sofas and couches;
- footwear; and
- textile products (ACCC, 2012)

The chemical has reported non-industrial use as a therapeutic agent in the treatment of multiple sclerosis (TGA, 2013).

International

The chemical has reported domestic use in a range of domestic products including consumer products such as:

- leather sofas and couches;
- footwear articles;
- wooden toys; and
- clothing (ECHA RAC, 2011; HSDB; Lammintausta et al, 2009).

The chemical has reported non-industrial uses in therapeutic products for the treatment of psoriasis and multiple sclerosis (TGA, 2013; ECHA RAC, 2011).

Restrictions

Australian

This chemical is listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedule 4, when used for human therapeutic purposes (SUSMP, 2015).

Schedule 4 chemicals are labelled with 'Prescription Only Medicine, or Prescription Animal Remedy. These are substances, the use or supply of which should be by or on the order of persons permitted by State or Territory legislation to prescribe and should be available from a pharmacist on prescription.' (SUSMP, 2014).

International

The chemical is listed on the following (Galleria Chemica):

- Europe Commission Decision 2009/251/EC—Products containing the chemical are not placed or made available on the market;
- Swedish Chemical Agency, restricted database, 2014—Chemical products (handling, import and export prohibitions) ordinance;
- European Union (EU) Registration, Evaluation, Authorization and Restrictions of Chemicals (REACH) regulation (EC) No. 1907/2006 Annex XVII —'Restrictions on the manufacture, placing on the market and use of certain dangerous substances, mixtures and articles. Dimethyl fumarate (DMF) shall not be used in articles or any parts thereof in concentrations greater than 0.1 mg/kg. Articles or any parts thereof containing DMF in concentrations greater than 0.1 mg/kg shall not be placed on the market';
- United States (US) American Apparel and Footwear Association (AAFA) restricted substance list (RSL): Chemicals prohibited on final product or tested component.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is not listed on the Hazardous Substances Information System (HSIS) (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standard is identified (Galleria Chemica):

- an exposure limit of 2 mg/m^3 time weighted average (TWA) and permissible exposure levels (PELs) of 5–15 mg/m^3 in the United States;
- an occupational exposure limit (OEL) of 10 mg/m^3 in Canada; and
- the US American Conference of Governmental Industrial Hygienists (ACGIH) recommend a threshold limit value (TLV) of 10 mg/m^3.

Health Hazard Information

Toxicokinetics

Dimethyl fumarate (DMF) is completely (100 %) absorbed in animals and in humans, when administered orally. It is metabolised pre-systemically and rapidly converted by esterases to monomethyl fumarate (MMF) before reaching systemic circulation. The bioavailability of the chemical is very high and <1 % is excreted in faeces and urine. The metabolite, MMF is metabolised in mitochondria via the Krebs cycle and is eliminated mainly as carbon dioxide (CO_2) (ECHA RAC, 2011; TGA, 2013).

Acute Toxicity

Oral

The chemical has low to moderate acute oral toxicity in animal tests following oral exposure. The median lethal dose (LD50) in mice and rats was 1200 mg/kg and 3160 mg/kg, respectively. Based on the available animal data, the chemical does not warrant hazard classification for acute oral toxicity.

In an animal study conducted according to good laboratory practice (GLP), the chemical was administered once to Sprague Dawley (SD) rats (three animals/sex/group) at doses of 1470, 2150, 2610, 3160 or 6810 mg/kg. In all groups, mortalities occurred within 24–48 hours following administration and the surviving animals recovered within 24 hours after dosing. The decedents showed reddened gastric mucosa. In animals dosed with 1470 mg/kg, reduced food consumption was observed and at 2150 mg/kg, decreased weight gain was reported. At 2610 mg/kg, female rats showed clinical signs including ataxia, muscular hypotonia, reduced mobility and a reduced respiratory rate. Haemorrhagic erosions in the stomach, engorgement of the mucosa in the forestomach (non-glandular stomach), haemorrhages in the mucosa and epithelial desquamation with oedema in the forestomach were observed in male rats at 3160 mg/kg. At 6810 mg/kg, minimal congestion of the forestomach was noted. The LD50s in female and male SD rats were 2160 mg/kg and 3160 m/kg, respectively (US FDA, 2012).

In another acute toxicity study, Naval Medical Research Institute (NMRI) mice (three/sex/group) were exposed to the chemical at 681, 1000, 1200, 1340 or 1470 mg/kg doses followed by a 14-day observation period. In all groups, mortalities occurred within 90 minutes to 24 hours following administration of the chemical and the surviving animals recovered within two days of dosing. The lowest toxic dose was 681 mg/kg in of both sexes, based on clinical signs such as reduced mobility, ataxia, dyspnoea, muscular hypotonia and cyanosis. Tremor and lying on the abdomen were observed at 1210 mg/kg. Straub's phenomenon (seizure-related behaviour) was observed at 1470 mg/kg and the decedents showed partially pale liver, pale kidneys, a fine-grained structured surface of the kidney, thin-walled stomach with haemorrhagic foci or reddened/severely reddened gastric mucosa, and bloody intestinal contents. Minimal congestion in the stomach was observed at 1470 mg/kg. The LD50 was established as 1200 mg/kg for male mice and 1340 mg/kg for female mice (US FDA, 2012).

Dermal

No data are available for the chemical.

Inhalation

No data are available for the chemical.

Corrosion / Irritation

Skin Irritation

While there are no experimental data available for this chemical, acute dermal effects such as irritation and non-immunological contact urticaria have been reported in humans, in addition to delayed sensitisation effects (ECHA RAC, 2011).

Eye Irritation

No data are available.

Sensitisation

Skin Sensitisation

The chemical is considered to be a skin sensitiser based on the positive results seen in a single guinea pig maximisation test (GPMT) and a local lymph node assay (LLNA).

In a GMPT, 3/9 guinea pigs tested showed sensitisation to the chemical and cross-reaction with monomethyl fumarate and the esters of maleic acid (ECHA RAC, 2011). No further details on the studies were provided.

A standard LLNA was conducted on female CBA/J mice. Random treatment groups of five animals/group were treated with the chemical at concentrations of 3, 1, 0.3, 0.1 or 0.03 % in dimethyl formamide. The test substances were applied daily for three consecutive days to the dorsum of both ears for each mouse. The mice were euthanised five hours later and the auricular lymph nodes were excised. The estimated concentration was determined for the chemical needed to produce a three-fold increase in lymphocyte proliferation (EC3). The chemical caused positive and classifiable skin sensitising reactions at all concentrations. A stimulation index (SI) value of 22.6 was reported for the highest concentration of the chemical tested (3 %) and the EC3 value was determined to be three (Basketter et al, 2013). Based in the EC3 value, the chemical can be considered a strong sensitiser.

There is sufficient information to support a recommendation to classify the chemical with the risk phrase 'May cause sensitisation by skin contact' (Xi; R43) in the HSIS (Work Safe Australia).

Observation in humans

The positive data are supported by the human case reports detailed below.

The chemical is a potent skin sensitiser causing itching, irritation, redness, burns and, in some cases, acute respiratory difficulties (ACCC, 2012). The chemical was also associated with the so called Toxic Sofa Syndrome, which is characterised by persistent dermatitis on the areas of the body in contact with the sofas (i.e. back of thighs, buttocks and back).

Eight studies conducted in humans by patch-testing dimethyl fumarate on already sensitised patients reported that responses are seen at concentrations as low as 0.0001 % (1 mg/kg) (ECHA RAC, 2011).

A case study of furniture-related dermatitis was conducted on 42 patients from Finland and the United Kingdom exposed to a chair textile material containing the chemical. All 42 patients showed sensitisation or dermatitis caused by the chemical (Rantanen, 2008; ECHA RAC, 2011).

In another case study, 15 adults exposed to dimethyl fumarate in shoes and who have suffered severe contact dermatitis showed positive reactions to the chemical during patch testing (Gimenez-Arnau, 2009; ECHA RAC, 2011).

Other studies

A survey was conducted by the Australian Competition & Consumer Commission (ACCC) to determine the DMF concentrations in desiccant sachets as an indicator of the potential presence of DMF in footwear and other leather articles supplied in Australia.

DMF is an anti-fungicide used to stop mould forming in leather and other consumer goods during transport and storage. It can be impregnated into desiccant sachets inside the packaging of leather and fabric covered furniture and shoes, but it can also be applied directly onto the surface of products. In both cases, the DMF can be absorbed into the fabric or leather covering the furniture and remains detectable. DMF is a potent skin sensitiser; however, ACCC reports indicate a low number of alleged injuries associated with the textile, clothing and footwear (TCF) sector. DMF was detected at very low concentrations (0.06 mg/kg to 4.8 mg/kg (parts per million)) in 12 of the 177 desiccant sachets tested. Nine of the 12 had concentration levels below 1 mg/kg. The average concentration found in the desiccant sachets where DMF was present was 0.88 mg/kg. The survey indicated that the levels of DMF in the desiccant sachets were very low and, where DMF is present in the disccant sachets accompanying consumer goods, the concentrations are well below the threshold of 25 mg/kg where additional testing of the article for potential DMF migration may be required. The results also indicate that footwear and bags currently supplied onto the Australian market are unlikely to contain high levels of DMF (ACCC, 2012).

Repeated Dose Toxicity

Oral

In a 13-week oral gavage study in Charles River (CD-1) mice, the chemical was administered to male and female mice at doses of 0, 50, 200 or 400 mg/kg/day. The forestomach and kidney were the primary target organs for toxicity. Forestomach lesions including hyperkeratosis, squamous cell hyperplasia, subacute and chronic inflammation, micro-abscesses and ulceration were reported in both sexes at all doses. Minimal splenic changes (extramedullary haematopoiesis) were also observed at all doses in both sexes (US FDA, 2012).

In a 28-day dose range study in B57BL/6 mice, the chemical was administered at doses of 50, 100, 250 or 400 mg/kg/day by oral gavage. Treatment-related effects at all doses included changes in the forestomach, spleen (increased extramedullary haematopoiesis), testes (tubular degeneration/hypocellularity, tubular giant cells), and epididymis (sperm granuloma) (US FDA, 2012; TGA, 2013).

In a 75-day study, the chemical was administered in male rats at 100 mg/kg by oral gavage. Increased kidney weights, increased incidence and severity of nuclear hypertrophy of the renal tubule, and increased hyaline droplet accumulation were observed (US FDA, 2012). These results are consistent with the male rat-specific a2µ-globulin nephropathy.

In a one-year oral (gavage) study, monkeys were treated with DMF at doses of 0, 5, 25, and 75 mg/kg/day. The kidneys were the only identified target organ. At necropsy, macroscopic findings in the kidney were described as mild bilateral pale discolouration, bilateral increased size, and watery consistency at the highest dose. These changes correlated with renal tubular epithelial regeneration (US FDA, 2012).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the weight of evidence from the available well-conducted in vitro and in vivo genotoxicity studies, the chemical is not considered to be genotoxic. The chemical is negative in bacterial mutation assays, but positive results were obtained from an in vitro clastogenicity assays, with or without metabolic activation. An in vivo micronucleus assay was negative.

In vitro studies

In a bacterial mutation assay, DMF was tested (0–3160 µg/plate) for induction of point mutations using *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 with or without metabolic activation. DMF did not induce increases in revertant colonies (US FDA, 2012).

In a mammalian cell gene mutation assay, DMF was non-mutagenic at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus in Chinese hamster V79 cells (US FDA, 2012).

In a chromosomal aberration study, DMF was investigated in cultured human peripheral lymphocytes at concentrations of 1.56–50 µg/mL without metabolic activation and 6.25–150 µg/mL with metabolic activation. Positive results were noted both in the presence and absence of metabolic activation (US FDA, 2012).

In a chromosomal aberration assay, DMF was investigated in cultured human peripheral blood lymphocytes at concentrations of 30–60 µg/mL with metabolic activation or 0.938–7.5 µg/mL without metabolic activation. The chemical was positive for induction of chromosomal aberrations without metabolic activation (US FDA, 2012).

In vivo studies

In a rat micronucleus assay, DMF did not induce statistically significant increases in micronucleated polychromatic erythrocytes in the bone marrow.

Carcinogenicity

Based on the available data, the chemical induced tumours in the forestomach in mice and rats. Renal tubular adenomas and carcinomas were also reported, and were not limited to male rats.

The chemical was orally administered to rats and mice (75 animals/group in both species) at doses of 100, 150, 400 or 600 mg/kg/day for 104 weeks. Most of the mortalities were related to severe lesions in the heart, forestomach and kidneys. Both mice and rats in both sexes showed DMF-induced tumours in the forestomach (squamous cell papilloma/carcinoma in both species and leiomyosarcoma and fibrosarcoma in mice). Low incidences of kidney tumours in both species, including renal tubular adenomas in both sexes and renal tubular carcinomas in male mice and female rats, were also reported (US FDA, 2012).

In another study, the chemical was administered to CD-1 mice by oral gavage at doses of 0, 25, 75, 200 or 600/400 mg/kg/day for two years. The highest dose of 600 mg/kg/day was reduced to 400 mg/kg/day on day nine due to mortalities in both sexes. All surviving animals were euthanised prematurely in week 101. Renal tubule adenomas and carcinomas were observed in males at 200 and 400 mg/kg/day and in females at 400 mg/kg/day. Squamous cell carcinomas and papillomas of the forestomach in both sexes were observed from 200 mg/kg/day. Leiomyosarcomas of the forestomach were also observed in both sexes at 400 mg/kg/day (US FDA, 2012).

The chemical was orally administered in SD rats at doses of 0, 25, 50, 100 or 150 mg/kg/day by gavage. The study was terminated prematurely at weeks 86 and 88 due to mortalities in the highest two groups, respectively. Treatment-related squamous cell carcinomas and papillomas of the forestomach in both sexes were observed at all doses tested. At 150 mg/kg/day, renal tubule adenomas and carcinomas were observed in males and females, respectively. Testicular interstitial cell adenomas were also reported in males at the 100 and 150 mg/kg/day doses (US FDA, 2012).

Reproductive and Developmental Toxicity

Reproductive and developmental toxicity effects were not observed with this chemical.

Male SD rats were exposed to the chemical at oral doses of 0, 75, 250 or 375 mg/kg/day before and throughout the mating period. There were no treatment-related effects on fertility, but an increase in non-motile sperm was observed at doses of 250 and 375 mg/kg/day. The chemical was administered in female SD rats at doses of 0, 20, 100 or 250 mg/kg/day before mating, during mating and continuing to gestation day (GD) seven. An increase in embryo lethality and disruption of the oestrus cycle was observed at 250 mg/kg/day. The no observed adverse effect level (NOAEL) was determined to be 75 mg/kg/day in male rats and 100 mg/kg/day in female rats (US FDA, 2012).

In an embryo-foetal development study in SD rats, the chemical was administered throughout organogenesis at oral doses of 0, 25, 100 or 250 mg/kg/day. Treatment-related effects such as reduced foetal body weight and delayed ossification were observed at 250 mg/kg/day (US FDA, 2012).

In a developmental study in SD rats, the chemical was administered orally at doses of 0, 25, 100 or 250 mg/kg/day throughout organogenesis and lactation. All offspring showed neuro-behavioural impairment at all treatment doses. Treatment-related effects such as increased mortality, persistent reductions in body weight, delayed sexual maturation in male and female pups and reduced testicular weight were observed in the offspring at 250 mg/kg/day. No NOAEL was identified (US FDA, 2012).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include local effects (skin sensitisation). The chemical can also cause systemic effects including carcinogenicity following repeated exposure (forestomach and kidneys) in rodents.

Public Risk Characterisation

Considering the range of domestic products that could contain DMF, the main route of public exposure is expected through dermal contact with products and/or articles treated with the chemical.

In the EU, the use of DMF in articles is considered to pose an unacceptable risk of sensitisation to consumers at concentrations higher than 0.1 mg/kg (ECHA, 2011). However, the results from a survey conducted by the ACCC indicated that footwear and leather goods currently supplied onto the Australian market contain extremely low levels of DMF (see ***Other Studies*** section), which are well below levels where adverse health effects would occur. Therefore, the risk to public health is not considered to be unreasonable. However, if information becomes available identifying DMF in articles above 0.1 mg/kg in Australia, further risk management may be warranted to ensure public safety.

Occupational Risk Characterisation

Given the critical health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal and inhalation exposure are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

NICNAS Recommendation

While currently it does not appear that DMF is present in consumer articles at harmful levels, should evidence emerge to the contrary, it is recommended that the Australian Competition & Consumer Commission (ACCC) consider mechanisms to control the supply of textile and leather articles that come into direct and prolonged contact with the human skin and that are treated with sufficiently high levels of the chemical to plausibly result in human exposure at unacceptable levels.

The other current risk management measures are considered adequate to protect public and workers' health and safety, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

Work Health and Safety

The chemical is recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from dermal and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which could minimise the risk include, but are not limited to:

- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

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.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

Australian Competition & Consumer Commission (ACCC), 2012. Survey of levels of Dimethyl Fumarate (DMF) concentrations in desiccant sachets as an indicator of the potential presence of DMF in footwear and bag articles supplies in Australia. Accessed January 2015 at https://www.productsafety.gov.au/content/item.phtml?itemId=999216&nodeId=92baed472481aac1752e20284b444c16&fn=Dimethyl%20Fumarate%20(DMF)%20in%20consumer%20products%20survey.pdf

Basketter DA, White IR, Burleson FG, Burleson GR and Kimber I (2013) Dimethyl fumarate: potency prediction and clinical experience. Contact Dermatitis, May; 68(5): 269-72.

European Chemical Agency Committee for Risk Assessment (ECHA RAC) 2011. Background document to the opinions on the Annex XV dossier proposing restrictions on Dimethyl fumarate (DMFu) (Document Number ECHA/RAC/RES-O-0000001305-83-04/S1). Accessed January 2015 at http://echa.europa.eu/documents/10162/13641/background_doc_seac_rac_dmfu_en.pdf

Galleria Chemica. Accessed January 2015 at http://jr.chemwatch.net/galleria/

Gimenez-Arnau A., Silvestre JF, Mercader P, De la Cuadra J, Ballester I, Gallardo F, Pujol R M, Zimerson E and Bruze M (2009) Shoe contact dermatitis from dimethyl fumarate: clinical manifestations, patch test results, chemical analysis, and source of exposure. Contact Dermatitis, 61: 249–260.

Hazardous Substances Data Bank (HSDB). National Library of Medicine. Accessed January 2015 at http://toxnet.nlm.nih.gov.

Jimenez AS, Kuijpers E and Galea K (2012). Integrated Exposure for Risk Assessment in Indoor Environment (INTERA) WHO. Dimethyl fumarate (DMF) case study.

Lammintausta K, Zimmerson E, Hasan T el al. (2009) An epidemic of furniture-related dermatitis: searching for a cause. British Journal of Dermatology; 162 (1): 108-116.

Rantanen, T. (2008), The cause of the Chinese sofa/chair dermatitis epidemic is likely to be contact allergy to dimethylfumarate, a novel potent contact sensitizer. British Journal of Dermatology, 159: 218–221.

The Poisons Standard (the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP)) 2014. Accessed January 2015 at http://www.comlaw.gov.au/Details/F2014L01343

Therapeutic Goods Administration (TGA). Australian Public Assessment report on Dimethyl Fumarate. Accessed January 2015 at https://www.tga.gov.au/auspar/auspar-dimethyl-fumarate

US Food and Drug Administration (FDA). Pharmacology reviews on Dimethyl Fumarate (DMF) for the treatment of patients with relapsing forms of multiple sclerosis (MS). Accessed January 2015 at http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/204063Orig1s000PharmR.pdf

Last update 24 April 2015

Share this page