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

2-Octenenitrile, 3,5,7-trimethyl-

Assessment statement (CA09850)

14 November 2024

Table of contents

AICIS assessment statement (CA9850)

Chemical in this assessment

Name	CAS registry number
2-Octenenitrile, 3,5,7-trimethyl-	947237-95-8

Reason for the assessment

An application for an assessment certificate under section 31 of the *Industrial Chemicals Act 2019* (the Act).

Certificate Application type

AICIS received the application in a Very Low to Low Risk type.

Defined scope of assessment

The chemical has been assessed:

- as a fragrance ingredient imported into Australia at up to 1 tonne/year
- as imported in fragrance formulations at up to 1% concentration for local reformulation into continuous action air fresheners at up to 0.5% concentration, fine fragrances at up to 0.2% concentration, instant action air fresheners at up to 0.1% concentration, and other cosmetic and household products at up to 0.02% concentration
- as imported in continuous action air fresheners at up to 0.5% concentration, in fine fragrances at up to 0.2% concentration, in instant action air fresheners at up to 0.1% concentration, and in other cosmetic and household products at up to 0.02% concentration

Summary of assessment

Summary of introduction, use and end use

The assessed chemical will not be manufactured in Australia. It will be imported either in fragrance formulations at up to 1% concentration for local reformulation into end use cosmetics and household products or in finished end use cosmetic and household products at various concentrations, including in air fresheners (up to 0.5% in continuous action air fresheners and up to 0.1% in instant action air fresheners), fine fragrances at up to 0.2%, and other cosmetic and household products at up to 0.02% concentrations.

The cosmetic and household end use products containing the assessed chemical are proposed to be used by professional workers and members of the general public.

Human health

Summary of health hazards

The submitted toxicological data on the assessed chemical (see **Supporting Information** section) indicate that the assessed chemical is:

- of low acute oral toxicity
- slightly irritating to skin and eyes
- not a skin sensitiser based on a guinea pig maximisation test
- not mutagenic or genotoxic based on a bacterial reverse mutation test and in vitro mammalian cell micronucleus test

No inhalation or repeated dose toxicity data were provided for the assessed chemical.

The assessed chemical contains a nitrile functional group. Nitrile compounds may be able to release cyanide on metabolism and produce typical cyanide toxicity. In rodents, aliphatic nitriles have been shown to cause malformations, foetal death and intrauterine growth retardation (IUGR) when given orally at doses ranging from 30 – 2,000 mg/kg/day during the organogenesis period (days 6-15 of gestation). Malformations vary but tend to be cleft palate or relate to disruptions to the developing neural tube/central nervous system and may also include limb/tail abnormalities. Embryo-foetal toxicity has also been generally observed (Dereck Nexus Version 6.0.1). However, not all nitriles are capable of liberating significant amounts of cyanide. In the case of the assessed chemical, alkyl substituents of more than 4 carbons may less likely release cyanide on metabolism (Dereck Nexus Version 6.0.1).

Hazard classifications relevant for worker health and safety

Based on limited data provided by the applicant, the assessed chemical cannot be classified 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 adopted for industrial chemicals in Australia.

Summary of health risk

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 0.5% concentration using a wide range of cosmetic and household products. The principal route of exposure will be dermal and inhalation, while incidental oral or ocular exposure is also possible. Inhalation exposure occurs particularly from the use of air care products and other products applied by spray.

The assessed chemical is slightly irritating to skin and eyes. However, irritation effects are not expected to occur from use of the assessed chemical at the proposed low end use concentrations (up to 0.5%) in cosmetic and household products. The continuous action air fresheners are not expected to come into direct contact with skin or eyes due to designed nature of the products.

No inhalation toxicity data are provided for the assessed chemical. Due to low concentrations of the assessed chemical in the end use products (up to 0.5%), it is not expected to pose a health risk through inhalation.

No quantitative risk assessment was possible to determine the margin of exposure, due to lack of repeated dose toxicity data. Based on the worst-case exposure scenario, consumers simultaneously using multiple cosmetic and household products may be systemically exposed to the assessed chemical at approximately 77 µg/kg bw/day through repeated or prolonged exposure (see **Supporting information** section). Considering this very low systemic exposure level to the assessed chemical in the worst-case exposure scenario, health risks from repeated exposure to the public are not expected.

This assessment does not identify any risks to public health that require specific risk management measures.

Workers

Reformulation workers may be incidentally exposed to the assessed chemical at up to 1% concentration during reformulation processes mainly via the dermal route, while ocular and inhalation exposures are also possible. To mitigate potential repeated dose exposure risks to reformulation workers, control measures would be required (see **Means for managing risk**) to minimise the exposure. It is anticipated by the applicant that engineering controls such as enclosed and automated processes and local ventilation will be implemented where possible. Use of appropriate personal protective equipment (PPE) such as safety glasses, impervious chemical resistant gloves, protective clothing and respiratory protection will reduce worker exposure.

Professional workers in cleaning or cosmetic businesses may experience exposure via dermal, inhalation and accidental ocular exposure to the assessed chemical during the use of cleaning or cosmetic products containing the assessed chemical at up to 0.2% concentration. The professional workers may wear some PPE (including gloves, coveralls and face masks or safety glasses). If PPE is used, exposure of such workers is expected to be of a similar or lesser extent than that experienced by consumers using the same end use products containing the assessed chemical, requiring no specific risk management measures for these workers.

Environment

Summary of environmental hazard characteristics

According to domestic environmental hazard thresholds and based on the available data the assessed chemical is:

- Persistent (P)
- Not bioaccumulative (Not B)
- Not Toxic (Not T)

Environmental hazard classification

The assessed chemical satisfies the criteria for classification according to the *Globally Harmonized System of Classification and Labelling of Chemicals* (GHS) (UNECE, 2017) as Acute Category 2 (H401) and Chronic Category 2 (H411) based on the toxicity data for invertebrates and algae. Considerations were also made for the low degradation and bioaccumulation potential of the assessed chemical:

Environmental Hazard	Hazard Category	Hazard Statement
Hazardous to the aquatic environment (acute / short-term)	Aquatic Acute 2	H401: Toxic to aquatic life
Hazardous to the aquatic environment (long-term)	Aquatic Chronic 2	H411: Toxic to aquatic life with long lasting effects

Summary of environmental risk

The assessed chemical will be introduced as a fragrance ingredient for use in a variety of cosmetic and household products. These uses may result in the release of the assessed chemical to sewers and to air.

The assessed chemical is not readily degradable and is persistent. The assessed chemical has a low potential for bioaccumulation and is not expected to cause toxic effects in aquatic organisms according to the *Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals* (DCCEEW 2022).

Although the assessed chemical is persistent, it does not meet all three PBT criteria. Hence, it is unlikely to have unpredictable long-term effects and its risk may be estimated by the risk quotient method (RQ = PEC ÷ PNEC). Based on the expected RQ values < 1 for the river and ocean compartments, it is expected that the environmental risk from the introduction of the assessed chemical can be managed.

Means for managing risk

Workers

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

Information relating to safe introduction and use

The following control measures should be implemented to manage the risk arising from exposure to the assessed chemical during reformulation:

- Use of engineering controls such as
  - automated and enclosed systems where possible
  - adequate workplace ventilation to avoid accumulation of vapours, mists, or aerosols
- Use of safe work practices to
  - avoid contact with eyes and skin
  - avoid inhalation of vapours, mists or aerosols
- Use of personal protective equipment (PPE)
  - coveralls
  - gloves
  - safety glasses or goggles
  - respiratory protection if exposure to vapours, mists or aerosols is possible
- A copy of the Safety Data Sheet (SDS) should be easily accessible to workers.

Conclusions

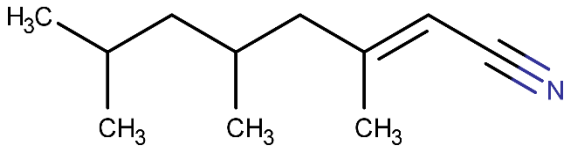
The Executive Director is satisfied that the risks to human health or the environment associated with the introduction and use of the industrial chemical can be managed.

Note:

1. Obligations to report additional information about hazards under s 100 of the *Industrial Chemicals Act 2019* apply.
2. You should be aware of your obligations under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Supporting information

Chemical identity

Chemical name	2-Octenenitrile, 3,5,7-trimethyl-
CAS No.	947237-95-8
Synonyms	3,5,7-Trimethyl-2-octenenitrile
Molecular formula	$C_{11}H_{19}N$
Molecular weight (g/mol)	165.28
SMILES (canonical)	N#CC=C(C)CC(C)CC(C)C
Structural formula	

Chemical description

The assessed chemical is a mixture of E and Z isomers with a combined purity of greater than or equal to 95%.

Relevant physical and chemical properties

Physical form	Colourless or light-yellow translucent liquid
Melting point	-103.5 ± 0.1 °C
Boiling point	237.9 ± 0.5 °C at 101.3 kPa
Relative density (D20/4)	0.837
Vapour pressure	5.47×10^{-3} kPa at 20 °C
Water solubility	22.3 mg/L at 20°C and pH 5
Ionisable in the environment?	No
log K_{ow}	3.89
log K_{oc}	2.83 (calculated)
Flash point	104.8 ± 0.4 °C

Autoignition temperature	381 °C

Human exposure

Public

There will be widespread and repeated exposure of the public to the assessed chemical at up to 0.5% concentration through the use of a range of cosmetic and household products. The principal route of exposure will be dermal, while ocular and inhalation exposures are also possible, particularly if the products are applied by spray.

Dermal exposure

Data on typical use patterns of cosmetic products (SCCS 2012; Cadby et al. 2002; ACI 2010; Loretz et al. 2006) in which the assessed chemical may be used are shown in the following table. A dermal absorption (DA) rate of 100% was used as a worst-case scenario along with a combined average body weight (BW) for males and females of 60 kg for calculation purposes.

Product type	Amount (mg/day)	C (%)	RF	Daily systemic exposure (µg/kg bw/day)
Body lotion	7,820	0.02	1	26
Face cream	1,540	0.02	1	5
Hand cream	2,160	0.02	1	7
Fine fragrances	750	0.2	1	25
Deodorant (non-spray)	1,500	0.02	1	5
Shampoo	10,460	0.02	0.01	0
Conditioner	3,920	0.02	0.01	0
Shower gel	18,670	0.02	0.01	1
Hand wash soap	20,000	0.02	0.01	1
Hair styling products	4,000	0.02	0.1	1
Hair dye products	11,600	0.02	0.1	4
Total				**75**

C = maximum intended concentration of assessed chemical; RF = retention factor
Daily systemic exposure = (Amount × C × RF × DA)/BW

Dermal exposure from using household cleaning products and wearing clothes will result in approximately additional 1 µg/kg bw/day systemic exposure, considering low concentrations and retention factors for these products.

Inhalation exposure

Hairspray was taken as a worst-case scenario example for the inhalation exposure assessment. A 2-zone approach was used (Steiling et al. 2014; Rothe et al. 2011; Earnest Jr. 2009). An adult inhalation rate of 20 m^3/day (enHealth 2012) was used and it was conservatively assumed that the fraction of the assessed chemical inhaled is 50%.

Amount of hairspray applied	9.89	g/day
Maximum intended concentration of the chemical	0.02	%
Inhalation rate of the user	20	m^3/day
Exposure duration zone 1	1	minutes
Exposure duration zone 2	20	minutes
Fraction inhaled by the user	50	%
Volume zone 1	1	m^3
Volume zone 2	10	m^3
Daily systemic exposure	**1**	**µg/kg bw/day**

C = maximum intended concentration of assessed chemical
Total daily systemic exposure = daily systemic exposure zone 1 + daily systemic exposure zone 2

- Daily systemic exposure zone 1 = (amount × C × inhalation rate × exposure duration zone 1 × fraction inhaled)/volume zone 1/body weight
- Daily systemic exposure zone 2 = (amount × C × inhalation rate × exposure duration zone 2 × fraction inhaled)/volume zone 2/body weight

It is acknowledged that inhalation exposure to the assessed chemical from use of other cosmetic and household products may also occur.

Overall, the worst-case scenario estimation is for a person who is a simultaneous user of all products listed in the above tables that contain the assessed chemical at the maximum intended concentrations specified in various product types. This would result in a combined internal dose of 77 µg/kg bw/day (= 0.077 mg/kg bw/day) for the assessed chemical. This very low level of worst-case systemic exposure (below 0.1 mg/kg bw/day) is unlikely to pose a health risk to the public with repeated use of products containing the assessed chemical.

Health hazard information

Acute toxicity

Oral

Acute toxicity potential of the assessed chemical was tested following the OECD TG 423. The assessed chemical was administered by oral gavage to 6 female Sprague Dawley rats at the single dose of 2,000 mg/kg bw. One test animal was found dead 24 hours after the treatment. Treatment related clinical signs were noted, including decrease in spontaneous activity (3/6 animals), associated with bradypnea (1/6 animal), hypothermia (3/6 animals), decrease of

muscle tone (3/6 animals), eyes partially closed (1/6 animal), and absence of righting and Preyer's reflexes (1/6 animal). All survived test animals recovered from the treatment by day 3. A slight decrease (4.4%) in body weight was observed 48 hours after the treatment. Then, the body weight remained normal. Macroscopic examination of the test animal found dead revealed a white thickening at the level of the forestomach and the presence of red foci on the corpus. Macroscopic examination of the rest of the test animals did not reveal any treatment related changes. Based on the results of this study, the median lethal oral dose (LD50) of the chemical was determined to be greater than 2,000 mg/kg bw in female rats. The assessed chemical is of low acute oral toxicity in rats.

Corrosion/Irritation

Skin irritation

Skin irritation potential of the assessed chemical was tested in rabbits following the OECD TG 404. Skin of 3 New Zealand White male rabbits were exposed to 0.5 mL of the undiluted assessed chemical for 4 hours under semi-occlusive conditions. Slight erythema (maximum score of 1) was noted in two test animals 1 hour after the patch removal. Slight to well defined erythema (maximum score of 2) was noted in all test animals 24 hours after the exposure which was reversible in 4 days. Slight oedema (maximum score of 1) was noted in 1 test animal 24 hours after the exposure which was reversible in 72 hours. Dryness of skin at application area was noted in 1 test animal 48 hours after the exposure and in the other 2 animals 72 hours after the exposure. The affected skin recovered to normal between day 4 and day 13 of the test. Based on the results, the assessed chemical is considered as slightly irritating to the skin but does not meet the GHS criteria for classification as adopted by Australia for industrial chemicals.

Eye irritation

Eye irritation potential of the assessed chemical was tested in rabbits following the OECD TG 405. The undiluted chemical (0.1 mL) was instilled in one eye of each of 3 male New Zealand white rabbits. The untreated eyes of the animals served as controls. Mild conjunctival redness (with score of 1) was observed in 2 test animals 24 hours after the exposure. The effects were fully reversed by 48 hours. Based on the results, the assessed chemical is considered as slightly irritating to the eyes but does not meet the GHS criteria for classification as adopted by Australia for industrial chemicals.

Sensitisation

Skin sensitisation

A guinea pig maximisation test (GPMT) following Magnusson and Kligman method (OECD TG 406) was conducted to assess skin sensitisation potential of the assessed chemical. Ten test animals were induced with the assessed chemical through intradermal injection at 25% concentration on day 1 and topical application at 100% concentration on day 7. After 14 days from topical application the test animals were challenged dermally with 50% and 100% concentrations of the assessed chemical and skin reactions were recorded 24 hours after the challenge. No skin reactions attributable to allergy were observed. The assessed chemical was not a skin sensitiser under the test conditions.

Genotoxicity

The mutagenic potential of the assessed chemical was tested in a bacterial reverse mutation assay following the OECD TG 471 using the plate incorporation and pre-incubation methods. *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98 and TA 100 and *Escherichia coli* strain WP2 (pKM101) were used for the test. The chemical was tested at up to 5 µL/plate in the absence or presence of metabolic activation. No test substance mediated increase in the number of revertant colonies were observed under the test conditions and the assessed chemical was not considered as mutagenic.

The aneugenic and clastogenic potential of the assessed chemical was tested in a screening study. The study followed a non-GLP method similar to the OECD TG 487, in vitro mammalian cell micronucleus test. Cultured lymphocytes from human blood were used. The assessed chemical was tested in the absence and presence of metabolic activation for short term exposure (4 hours) with recovery (24 hours) and in the absence of metabolic activation for long term exposure (24 hours). When tested up to the concentration showing moderate cytotoxicity (at 0.88 mM and 1.32 mM in short term exposure without and with metabolic activation respectively, and at 0.26 mM in long term exposure), the test substance did not induce a statistically significant increase in the number of micronucleated binucleated cells when compared to solvent control. Thus, under the test conditions the assessed chemical is considered as not genotoxic.

Environmental exposure

The assessed chemical will be imported into Australia for use as a fragrance in end use cosmetic and household products, or as a component of fragrance formulations for reformulation into end use products. Reformulation and repackaging will occur in both closed and open processes. Significant releases of the assessed chemical to the environment are not expected during reformulation, transport or storage.

The assessed chemical will be included in a wide range of products, resulting in a variety of potential exposure scenarios.

Consumer and professional end use of the assessed chemical in cosmetic and household products is expected to result in the release of the assessed chemical “down the drain” and into the sewers. Consequently, the assessed chemical will be treated at sewage treatment plants (STPs) before release to surface waters.

Use of the assessed chemical in air care products will result in direct release of the assessed chemical into the air compartment.

Environmental fate

Partitioning

The partitioning of the assessed chemical was not determined. The chemical is treated as if it is mobile in the environment as a worst-case scenario.

Degradation

Based on its measured degradation in water, the assessed chemical is categorised as persistent.

The assessed chemical underwent 0% degradation after 28 days and 1% degradation over 60 days in an OECD TG 301D screening test provided by the applicant. The assessed chemical did not meet the pass level for degradation and is not readily biodegradable.

Bioaccumulation

Based on its log K_{OW} value, the assessed chemical does not have the potential to bioaccumulate.

No bioaccumulation information was provided for the assessed chemical. The experimental partition coefficient of the assessed chemical (log K_{OW} = 3.89) is below the domestic bioaccumulation threshold of log K_{OW} = 4.2 (EPHC, 2009).

Predicted environmental concentration (PEC)

A predicted environmental concentration (PEC) for Australian waters was calculated assuming the maximum allowable introduction volume for environmental exposure band 2 (1,000 kg/annum) with a release reduction factor of 1 for down-the-drain style end use scenarios. Correspondingly, 100% of the introduction volume is released into sewage treatment plants (STP) over 365 days per annum. The extent to which the assessed chemical is removed from the effluent in STP processes was not calculated as a worst-case scenario.

This calculated value is conservative as not all uses of the assessed chemical are expected to result in release to STP.

The calculation of the PEC is detailed in the table below:

Total Annual Import Volume	1,000	kg/year
Proportion expected to be released to sewer	100%	
Annual quantity of chemical released to sewer	1,000	kg/year
Days per year where release occurs	365	days/year
Daily chemical release	2.74	kg/day
Water use	200	L/person/day
Population of Australia	25.423	Million
Removal within STP	0%	Mitigation
Daily effluent production	5,085	ML/day
Dilution Factor - River	1	
Dilution Factor - Ocean	10	
PEC - River	0.54	µg/L
PEC - Ocean	0.05	µg/L

Environmental effects

Effects on aquatic Life

Acute toxicity

The following experimental median effective concentration (EC50) values for the assessed chemical in model organisms across two trophic levels were provided by the applicant:

Taxon	Endpoint	Method
Invertebrate	48h EC50 = 1.98 mg/L	*Daphnia magna* (Water flea) Immobility OECD TG 202 Static conditions Measured concentration
Algae	72h EC50 = 3.24 mg/L	*Pseudokirchneriella subcapitata* (Green algae) Growth rate OECD TG 201 Static conditions Measured concentration

Chronic toxicity

The following experimental no observed effect concentration (NOEC) value for the assessed chemical in algae was provided by the applicant:

Taxon	Endpoint	Method
Algae	72h NOEC = 1.05 mg/L	*Pseudokirchneriella subcapitata* (Green algae) Growth rate OECD TG 201 Static conditions Measured concentration

Predicted no-effect concentration (PNEC)

The predicted no-effect concentration is expected to be greater than 0.54 µg/L.

The available standard acute ecotoxicity endpoints for this chemical are greater than 0.54 mg/L. With a conservative assessment factor of 1,000, the lowest calculable PNEC is > 0.54 µg/L.

Categorisation of environmental hazard

The categorisation of the environmental hazards of the assessed chemical according to domestic environmental hazard thresholds is presented below:

Persistence

Persistent (P). Based on a measured degradation study, the assessed chemical is categorised as Persistent.

Bioaccumulation

Not Bioaccumulative (Not B). Based on the low measured log K_{OW} value, the assessed chemical is categorised as Not Bioaccumulative.

Toxicity

Not Toxic (Not T). Based on available ecotoxicity values above 1 mg/L, the assessed chemical is categorised as Not Toxic.

Environmental risk characterisation

Although the assessed chemical is persistent, it does not meet all three PBT criteria. Hence, it is unlikely to have unpredictable long-term effects (EPHC 2009). Therefore, an estimate of risk can be determined using the risk quotient method:

Compartment	PEC	PNEC	RQ
River	< 0.54 µg/L	> 0.54 µg/L	< 1
Ocean	< 0.05 µg/L	> 0.54 µg/L	< 0.1

The risk quotient for the aquatic compartment is expected to be less than 1. This is based on a conservative PEC, assuming 100% release of 1 tonne/annum to STPs and no removal from the aqueous stream during STP processes, and a conservative PNEC based on an assessment factor of 1000 and acute aquatic toxicity endpoints for the chemical that each exceed 0.54 mg/L.

Therefore, based on the RQ < 1 the assessed chemical is not expected to pose a significant risk to the environment. As such, the environmental risks associated with the proposed introduction of the assessed chemical can be managed.

References

ACI (2010) Consumer Product Ingredient Safety, Exposure and risk screening methods for consumer product ingredients, 2nd Edition, American Cleaning Institute, Washington DC.

Cadby PA, Troy WR, Vey MG (2002) Consumer Exposure to Fragrance Ingredients: Providing Estimates for Safety Evaluation. Regulatory Toxicology and Pharmacology, 36:246-252.

DCCEEW (2022) Australian Environmental Criteria for Persistent, Bioaccumulative and/or Toxic Chemicals, DCCEEW, accessed 06 May 2024.

DEREK (Deductive Estimation of Risk from Existing Knowledge) version 6.0.1 (Nexus version 2.2.2). Developed by Lhasa Limited. Available at https://www.lhasalimited.org/.

Earnest CW Jr. (2009) A Two-Zone Model to Predict Inhalation Exposure to Toxic Chemicals in Cleaning Products, MScEng thesis, The University of Texas at Austin.

enHealth (2012) Australian Exposure Factor Guide, companion document to: Environmental Health Risk Assessment: Guidelines for assessing human health risks from environmental hazards, EnHealth, Commonwealth of Australia.

EPHC (2009) Environment Protection and Heritage Council, Environmental Risk Assessment Guidance Manual for industrial chemicals, Prepared by: Chris Lee-Steere Australian Environment Agency Pty Ltd, February 2009. ISBN 978-1-921173-41-7.

Loretz L, Api AM, Barraj L, Burdick J, Davis DA, Dressler W, Gilberti E, Jarrett G, Mann S, Pan YHL, Re T, Renskers K, Scrafford C, Vater S (2006) Exposure data for personal care products: Hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant. Food and Chemical Toxicology, 44:2008-2018.

Rothe H, Fautz R, Gerber E, Neumann L, Rettinger K, Schuh W, Gronewold C (2011) Special aspects of cosmetic spray evaluations: Principles on inhalation risk assessment. Toxicology Letters, 205:97-104.

SCCS (2012) The SCCS's notes of guidance for the testing of cosmetic substances and their safety evaluation (8th revision), European Commission - Scientific Committee on Consumer Safety.

Steiling W, Bascompta M, Carthew P, Catalano G, Corea N, D'Haese A, Jackson P, Kromidas L, Meurice P, Rothe H, Singal M (2014) Principle considerations for the risk assessment of sprayed consumer products. Toxicology Letters, 227:41-49.

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