CLH report

Proposal for Harmonised Classification and Labelling

**Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2**

International Chemical Identification: Geraniol; (2*E*)-3,7-dimethylocta-2,6-dien-1-ol

EC Number: **203-377-1**

CAS Number: **106-24-1**

Index Number: **-**

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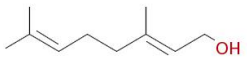
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Geraniol; (2*E*)-3,7-dimethylocta-2,6-dien-1-ol
Other names (usual name, trade name, abbreviation)	(*E*)-3,7-Dimethyl-2,6-octadien-1-ol 3,7-Dimethyl-trans-2,6-octadien-1-ol; Trans-3,7-Dimethyl-2,6-octadien-1-ol; Trans-Geraniol; β-Geraniol; (*E*)-Geraniol; (*E*)-Nerol; Geraniol, Geranyl alcohol; Lemonol; MosquitoSafe; NSC 9279 (SCCS 2012)
ISO common name (if available and appropriate)	
EC number (if available and appropriate)	203-377-1
EC name (if available and appropriate)	Geraniol
CAS number (if available)	106-24-1
Other identity code (if available)	
Molecular formula	$C_{10}H_{18}O$
Structural formula	
SMILES notation (if available)	CC(=CCC/C(=C/CO)/C)C
Molecular weight or molecular weight range	154.2493 Da
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable
Degree of purity (%) (if relevant for the entry in Annex VI)	≥ 98.0 (commercially available geraniol)

Geraniol; (2*E*)-3,7-dimethylocta-2,6-dien-1-ol, hereafter referred to as “geraniol”, is a component of palmarosa oil, geranium oil, citronella oil, rose oil, lavender oil and jasmine oil (SCCS 2012).

Geraniol forms oxidation products with increased sensitizing capacity both via spontaneous autoxidization at air exposure and via metabolic oxidation. Geranial and neral together with hydroperoxide have been identified as oxidation products when geraniol autoxidizes. Geranial and neral were also identified as metabolites of geraniol (SCCS 2012).

Geranial and neral constitute the two cis-trans stereo-isomers of the substance citral (CAS 5392-40-5), for which a separate CLH proposal is submitted by the DK EPA (simultaneously with the current CLH proposal for geraniol).

Geraniol is commonly used as a fragrance, mainly in cosmetics but also in various cleaning and maintenance products.

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
(2*E*)-3,7-dimethylocta-2,6-dien-1-ol CAS No: 106-24-1	≥ 98.0	None	Skin sens. 1 or 1B; H317 Skin irrit. 2; H315 Eye dam. 1; H318 or eye irrit. 2; H319 STOT SE 3; H335(RT1) Aquatic Acute 2 Aquatic Chronic 2; H411

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The impurity contributes to the classification and labelling
Not applicable	-	-	-	-

Table 4: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The additive contributes to the classification and labelling
Not applicable					

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 5:

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry											
Dossier submitters proposal		Geraniol	203-377-1	106-24-1	**Skin Sens. 1A**	H317	GHS07 Wng	H317			
Resulting Annex VI entry if agreed by RAC and COM		Geraniol	203-377-1	106-24-1	**Skin Sens. 1A**	H317	GHS07 Wng	H317			

Table 6: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	hazard class not assessed in this dossier	No
Flammable gases (including chemically unstable gases)	hazard class not assessed in this dossier	No
Oxidising gases	hazard class not assessed in this dossier	No
Gases under pressure	hazard class not assessed in this dossier	No
Flammable liquids	hazard class not assessed in this dossier	No
Flammable solids	hazard class not assessed in this dossier	No
Self-reactive substances	hazard class not assessed in this dossier	No
Pyrophoric liquids	hazard class not assessed in this dossier	No
Pyrophoric solids	hazard class not assessed in this dossier	No
Self-heating substances	hazard class not assessed in this dossier	No
Substances which in contact with water emit flammable gases	hazard class not assessed in this dossier	No
Oxidising liquids	hazard class not assessed in this dossier	No
Oxidising solids	hazard class not assessed in this dossier	No
Organic peroxides	hazard class not assessed in this dossier	No
Corrosive to metals	hazard class not assessed in this dossier	No
Acute toxicity via oral route	hazard class not assessed in this dossier	No
Acute toxicity via dermal route	hazard class not assessed in this dossier	No
Acute toxicity via inhalation route	hazard class not assessed in this dossier	No
Skin corrosion/irritation	hazard class not assessed in this dossier	No
Serious eye damage/eye irritation	hazard class not assessed in this dossier	No
Respiratory sensitisation	hazard class not assessed in this dossier	No
Skin sensitisation	**new harmonised classification proposed**	**Yes**
Germ cell mutagenicity	hazard class not assessed in this dossier	No
Carcinogenicity	hazard class not assessed in this dossier	No
Reproductive toxicity	hazard class not assessed in this dossier	No
Specific target organ toxicity-single exposure	hazard class not assessed in this dossier	No
Specific target organ toxicity-repeated exposure	hazard class not assessed in this dossier	No
Aspiration hazard	hazard class not assessed in this dossier	No
Hazardous to the aquatic environment	hazard class not assessed in this dossier	No
Hazardous to the ozone layer	hazard class not assessed in this dossier	No

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

Geraniol has no classification and labelling history under Directive 67/548/EEC or Regulation (EC) No 1272/2008.

Geraniol is one of the 26 fragrance substances for which individual labelling is required under the Cosmetics Regulation (EC no. 1223/2009) and the Detergents Regulation (EC no 648/2004). Geraniol is also among the 13 allergenic fragrance substances listed in the SCCS opinion which have been frequently reported as well-recognised contact allergens in consumers and thus of most concern (SCCS 2012).

In 2012 the Scientific Committee on Consumer Safety (SCCS) published an opinion on fragrance allergens in cosmetic products. In this opinion geraniol has been categorised as an established contact allergen in humans which has given rise to a significant number (>100-1000) of published cases on contact allergy (SCCS 2012).

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Justification that action is needed at Community level is required.

Reason for a need for action at Community level:

Differences in self-classification
Disagreement by DS with current self-classification

Further detail on need of action at Community level

New classification criteria and difference in self-classification
With the 2nd ATP to CLP new classification criteria were introduced for skin sensitisation allowing sub-categorisation of skin sensitisers into Category 1A (strong sensitisers) and Category 1B (other sensitisers, corresponding to the existing Category 1). A classification in Cat. 1A will lead to more stringent labelling requirements for mixtures containing the substance and is currently regarded as the most important risk management measure for such substances. Correct identification of Category 1A skin sensitisers is thus expected to increase the human protection level for strong sensitisers due to the requirement of labelling of mixtures containing Cat 1A sensitisers ≥0.01% with EUH208: “Contains [name of sensitising substance]. May produce an allergic reaction”.

In the REACH registration dossier the registrants have selfclassified geraniol as a Category 1 skin sensitiser. The same is true for 91.8% (1506 of 1641) of the notifiers in the C&L Inventory (May 2017). Of the remaining notifiers 4.0% (66 of 1641) has notified geraniol as a skin sensitiser in Category 1B, 1.6% (26 of 1641) have not stated the hazard class for sensitisation but have indicated H317 as a labelling hazard statement, and 2.6% (43 of 1641) have not notified a classification for skin sensitisation.

Widespread use in low concentrations
Geraniol is a fragrance that is manufactured in or imported to the EU in amounts of 1000-10.000 tonnes/year and is widely used in products on the EU market. The registered categories of use for consumers are mainly cosmetics, a variety of household products for cleaning and maintenance and biocidal products. The registered uses for professionals are cleaning agents and polishes and wax blends (see section 5 below on identified uses). As geraniol is widely used in a range of frequently used consumer products the general population can be exposed from many different sources.

Geraniol is generally present in low concentrations in individual consumer products. The International Fragrance Association (IFRA) has established maximum recommended limits of geraniol in specific product categories based on a quantitative risk assessment approach. The maximum limits of geraniol in leave-on cosmetic products are between 0.3-5.3% depending on the specific product category. The recommended limits for rinse-off cosmetic products are between 5.0-8.6% and the recommended

maximum limit for non-cosmetic products with direct skin contact is 2.5% (see Table 10 in section 10.8.3 on human exposure) (IFRA 2007).

The SCCS opinion refers to a number of surveys on the presence and content of various allergenic fragrances in various consumer products. Geraniol has been found to be present in 12-49% of the products investigated in different surveys of consumer products. It was concluded by SCCS that taking the total exposure into account, exposure to all 26 allergenic fragrances is foreseeable in daily life (SCCS 2012). The Danish EPA has conducted surveys and assessments of a broad range of consumer products over the last decades. Geraniol has been identified in different types of products, such as cosmetic products (adults and children), household products, and in toys for small children. Generally geraniol is found in low concentrations (>0 - <0.15%) in the investigated products with some exceptions (see also section 10.8.3 on human exposure) (DK EPA database, search February 2017). Data from the Danish Product Register further show that geraniol is present in various products for professional use (mainly cleaning products) and mostly in low concentrations <0.1% (The Danish Product Register, 2016).

Human exposure to geraniol seems to be low based on the IFRA recommendations and reported contents in various consumer products. However, the exposure is assessed to be frequent due to the widespread uses and the high tonnage level of geraniol. It is thus difficult for consumers to avoid exposure.

Human data confirm strong potency of geraniol

Positive patch test frequencies from 92 human patch tests range from 0.1-30% and frequencies equal to or exceeding 2% for selected dermatitis patients and 1% for consecutive (unselected) dermatitis patients are reported in a number of studies. The total number of positive reactions in published cases is > 100 (more than 900). Overall the human data confirm the potency of geraniol.

5 IDENTIFIED USES

Geraniol is used as a fragrance mainly in cosmetics but also in cleaning and maintenance products. Registered uses for consumers include: cosmetics, personal care products, perfumes, fragrances, washing and cleaning products, water softeners, polishes and waxes, air care products, biocidal products, coatings and paints, thinners and paint removers, fillers, plasters, putties and modelling clay, finger paints, inks and toners. Registered uses for professionals include: washing and cleaning products and polishes and waxes.

6 DATA SOURCES

One of the primary sources of information for this CLH report is the SCCS opinion on fragrance allergens from 2012 which contains the most recent and comprehensive assessment of available information on geraniol as well as other fragrance allergens up to year 2011 (SCCS 2012). References on the data cited in this opinion for geraniol have been retrieved when possible.

A supplementary search in the open literature has been done for the period from January 2009 and until November 2016 in order to ensure that potentially relevant studies published after the SCCS opinion are taken into account. The searches have included literature databases such as SciFinder, PubMed and Scopus as well as searches in sources such as OECD SIDS, IPCS INCHEM.

Data in the publicly available part of the REACH registration dossier for geraniol have been assessed as well.

7 PHYSICOCHEMICAL PROPERTIES

Table 7: Summary of physicochemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 1013 hPa	Colourless to pale yellow, oily liquid with a pleasant floral odour	REACH registration dossier	Measured
Melting/freezing point	-15 °C	REACH registration dossier	Measured
Boiling point	>204 °C at 2013 hPa (decomposition)	REACH registration dossier	Measured
Relative density	0.89 g/cm³ at 20 °C	REACH registration dossier	Measured
Vapour pressure	0.266 hPa at 20 °C	REACH registration dossier	Measured
Surface tension	No data	REACH registration dossier	-
Water solubility	100 mg/L at 25 °C	REACH registration dossier	Measured
Partition coefficient n-octanol/water	2.6 at 25 °C	REACH registration dossier	Measured
Flash point	>100 °C at 1013 hPa	REACH registration dossier	Measured
Flammability	No data	REACH registration dossier	-
Explosive properties	No data	REACH registration dossier	-
Self-ignition temperature	250 °C at >1002 - <1018 hPa	REACH registration dossier	Measured
Oxidising properties	No data	REACH registration dossier	-
Granulometry	No data/not applicable	REACH registration dossier	-
Stability in organic solvents and identity of relevant degradation products	No data	REACH registration dossier	-
Dissociation constant	No data	REACH registration dossier	-
Viscosity (dynamic)	8.4 mPa*s (dynamic) at 17 °C	REACH registration dossier	Measured

8 EVALUATION OF PHYSICAL HAZARDS

Physical hazards have not been assessed in this dossier.

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

No relevant non-human or human information has been located.

10 EVALUATION OF HEALTH HAZARDS

Acute toxicity

10.1 Acute toxicity - oral route

Hazard class not assessed in this dossier.

10.2 Acute toxicity - dermal route

Hazard class not assessed in this dossier.

10.3 Acute toxicity - inhalation route

Hazard class not assessed in this dossier.

10.4 Skin corrosion/irritation

Hazard class not assessed in this dossier.

10.5 Serious eye damage/eye irritation

Hazard class not assessed in this dossier.

10.6 Respiratory sensitisation

Hazard class not assessed in this dossier.

10.7 Skin sensitisation

Table 8 summarises relevant animal studies with geraniol which include a total of 16 studies: 9 LLNAs, 1 *ex vivo* LLNA-BrdU ELISA, 5 GPMTs, and 1 Buehler test. Seven of the below reported studies are included in the REACH Registration dossier.

Table 8: Summary table of animal studies on skin sensitisation (chronological order)

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Results	Reference
LLNA					
LLNA TG/GLP: no information	Mice (CBA/Ca), female n = 3/group	Geraniol (in AOO 4:1) Purity 99%	0, 5, 10, 15, 20 and 30% Exp: 3 days	EC3: 22.4%, sensitising	Hagvall et al., 2007
LLNA TG/GLP: no information	Mice (CBA/Ca), female n = 3/group	Geraniol **air-exposed for 10 weeks** (in AOO 4:1) Purity 99%	0, 1, 3, 6, 10 and 20% Exp: 3 days	EC3: 4.4%, sensitising	Hagvall et al., 2007

Method, guideline, deviations if any	**Species, strain, sex, no/group**	**Test substance,**	**Dose levels duration of exposure**	**Results**	**Reference**
		at start, 80% after 10 weeks			
LLNA TG/GLP: no information	Mice (CBA/Ca), female n = 3/group	Geraniol **air-exposed for 45 weeks** (in AOO 4:1) Purity 99% at start, 20% after 45 weeks	0, 0.5, 1, 3, 6 and 10% Exp: 3 days	EC3: 5.8%, sensitising	Hagvall et al., 2007
LLNA OECD TG 429	Mice (CBA/Ca), female n = 4/dose	Geraniol (in 1:3 EtOH:DEP) Purity 98.5%	0, 2.5, 5, 10, 25 and 50%	EC3: 11.4%, sensitising	Lalko & Api, 2006 (also cited in REACH reg.)
LLNA	Mice (no further info) n = 4/dose	Geraniol (in 3:1 EtOH:DEP)	2.5, 5, 10, 25 and 50%	EC3: 11.4%, sensitising *NB: The EC3 value, test concentrations and no. of animals tested are identical to the study above but the vehicles are reported differently. From the references cited it is not possible to identify whether the identical results may actually refer to the same study (but with a mistake reported for the use of vehicle).*	Unpublished summary report RIFM 2009 (RIFM 2003t), as cited in SCCS 2012
LLNA (no reported deviations from OECD TG 429)	Mice (CBA/Ca), male n = 4/dose	Geraniol (in EtOH) Purity 98.5%	0, 1, 3, 10, 30 and 50%	EC3: 5.6%, sensitising	Unpublished summary report RIFM 2009 (RIFM 2001j), as cited in SCCS 2012; Lalko et al., 2004 (also cited in REACH reg.)
LLNA (no reported deviations from OECD TG 429)	Mice (CBA/Ca), male n = 4/dose	Geraniol (in DEP) Purity 98.5%	0, 1, 3, 10, 30 and 50%	EC3: 11.8%, sensitising	Unpublished summary report RIFM 2009 (RIFM 2001k), as cited in SCCS 2012; Lalko et al., 2004 (also cited in REACH reg.)
LLNA (no reported deviations from OECD TG 429)	Mice (CBA/Ca), male n = 4/dose	Geraniol (EtOH:DEP 1:3)	0, 1, 3, 10, 30 and 50%	EC3: 20.4%, sensitising	Unpublished summary report RIFM 2009 (RIFM

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Results	Reference
		Purity 98.5%			2001l), as cited in SCCS 2012; Lalko et al., 2004 (also cited in REACH reg.)
LLNA (no reported deviations from OECD TG 429)	Mice (CBA/Ca), male n = 4/dose	Geraniol (EtOH:DEP 3:1) Purity 98.5%	0, 1, 3, 10, 30 and 50%	EC3: 25.8%, sensitising	Unpublished summary report RIFM 2009 (RIFM 2001m), as cited in SCCS 2012; Lalko et al., 2004 (also cited in REACH reg.)
Ex vivo LLNA-BrdU ELISA TG/GLP: no information	Mice (Balb/c), female n = 4/dose	Geraniol (in AOO 4:1)	0, 2.5, 10, 20 and 50% Exp: 3 days, duration 5 days	EC3: 13.1%, sensitising	Ulker et al., 2014
GPMT					
GPMT (acc. to Magnusson and Kligman 1969)	Guinea pig (Dunkin Hartley) 10 animals	Geraniol (in Dobs/saline for intradermal induction; in 70/30 acetone/PEG 400 for topical induction and challenge)	Intradermal ind.: 0.1% Topical ind.: 50% Chall. conc.: 10%	No sensitisation observed	Unpublished report RIFM 1989, as cited in Lapczynski et al., 2008
GPMT (acc. to Magnusson and Kligman 1969)	Guinea pig (Dunkin Hartley) 10 animals	Geraniol (in Dobs/saline for intradermal induction; in acetone for topical induction and challenge)	Intradermal ind.: 0.1% Topical ind.: 50% Chall. conc.: 10%	Sensitisation observed	Unpublished report RIFM 1989, as cited in Lapczynski et al., 2008
GPMT (acc. to Magnusson and Kligman 1969)	Guinea pig (Dunkin Hartley) 6 animals	Geraniol (in petrolatum)	Intradermal ind.: 5% Topical ind.: 30% Chall. conc.: 10%	Sensitisation observed, positive reactions seen in 3/6 animals	Unpublished report RIFM 1977, as cited in Lapczynski et al., 2008
GPMT	Guinea pig (Himalayan	Geraniol (in	Intradermal ind.:	Sensitisation observed	Klecak et al., 1977 (also

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance,	Dose levels duration of exposure	Results	Reference
(acc. to Magnusson and Kligman 1969)	white-spotted) male/female	petrolatum)	5% Topical ind.: 25% Chall. conc.: subirritant		cited in REACH reg.)
GPMT (acc. to Magnusson and Kligman 1969)	Guinea pig	Geraniol (vehicle not reported)	Intradermal ind.: 10% Topical ind.: 10% Chall. conc.: 10%	Sensitisation observed	Ishihara et al., 1986, as cited in Lapczynski et al., 2008 (also cited in REACH reg.)
Buehler test					
Buehler delayed contact hypersensitivity test	Guinea pig 20 animals in total	Geraniol (in DEP)	Induction: 25% Chall. conc.: 2.5, 7.5, 25%	No sensitisation observed	Unpublished report RIFM 1992, as cited in Lapczynski et al., 2008

Table 9 summarises relevant human tests with geraniol which include 92 patch test studies, 7 HRIPTs, 5 HMTs and 4 case studies. The studies involve thousands of dermatitis patients from different EU countries, North America, and Asia. The majority of the references cited below are not included in the REACH registration dossier.

Table 9: Summary table of human data on skin sensitisation (chronological order)

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
Patch tests, selected patients				
Patch test data, selected patients	Geraniol, 1% (in pet.)	Study of 2798 selected Fragrance mix (FM) I positive patients patch tested with geraniol. Data from IVDK multicentre project (IVDK: Information Network of Departments of Dermatology in Germany, Austria and Switzerland). Data obtained 1998-2013.	**5.5%** were tested positive (n = 2798)	Geier et al., 2015
Patch test data, selected patients	Geraniol, 1% (in pet.)	Study of 940 selected patients with positive reactions to FM I patch tested with geraniol. Data from Department of Dermatology, University Hospital St Rafaël, Belgium. Data obtained 1990-2011.	**5.5%** were tested positive (52/940)	Nardelli et al., 2013
Patch test data, selected patients	Geraniol, 5% (in pet.)	Study of 157 selected patients positive to fragrance mix patch tested with geraniol. Data from	**20.4%** were tested positive (32/157)	Turcic et al., 2011

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		the Allergy Clinic of the Department of Dermatology and Venereology, Zagreb University Hospital Center and School of Medicine, Zagreb, Croatia. Data obtained 2001-2005.		
Patch test data, selected patients	Geraniol, 2% (in pet.)	Study of 86 selected patients patch tested with geraniol. Data from the Cutaneous Allergy Unit of a tertiary referral hospital, Spain. Data obtained 2004-2008.	**19.7%** were tested positive (17/86)	Cuesta et al., 2010
Patch test data, selected patients	Geraniol, 1% (in pet.)	Study of 5695 selected patients patch tested with geraniol. Data from IVDK multicentre project (IVDK: Information Network of Departments of Dermatology in Germany, Austria and Switzerland). Data obtained 2005-2008.	0.9% (95% CI: 0.63-1.1%) were tested positive (50/5695)	Uter et al., 2010
Patch test data, selected patients	Geraniol, 1% (in pet.)	Study of 29 selected patients tested positive to their own deodorant patch tested with geraniol. Data from IVDK multicentre project (IVDK: Information Network of Departments of Dermatology in Germany, Austria and Switzerland). Data obtained 1998-2002.	**6.9%** were tested positive (2/29)	Uter et al., 2007
Patch test data, selected patients	Geraniol, 1% (in pet.)	Study of 141 selected patients tested negative to their own deodorant patch tested with geraniol. Data from IVDK multicentre project (IVDK: Information Network of Departments of Dermatology in Germany, Austria and Switzerland). Data obtained 1998-2002.	0% were tested positive (0/141)	Uter et al., 2007
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Study of 30 selected patients allergic to their own perfumed product, 19 of these patch tested with geraniol.	**21.1%** were tested positive (4/19)	Vocanson et al., 2006
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Multicentre study, a total of 3604 patients tested with FM, sub-group of 160 patients hypersensitive to FM patch tested with geraniol. Data from members of the Hungarian Contact Dermatitis Research Group. Data obtained 1998-1999.	**7.5%** were tested positive (12/160)	Temesvari al., 2002
Patch test data, selected patients	Geraniol, 1% (in pet. and 1% SSO)	A total of 2660 patients patch tested with a standard patch test series, 747 patients suspected of	0.9% were tested positive (7/747)	Wohrl et al., 2001

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		fragrance allergy tested further with a special fragrance series including geraniol. Data from FAZ-Floridsdorf Allergy Centre, Austria. Data obtained 1997-2000.		
Patch test data, selected patients	Geraniol, 1% (in pet.)	A total of 2600 patients patch tested with FM, 226 selected FM-reactive patients patch tested with geraniol. Data from Department of Dermatology, University Hospital, 3000–075 Coimbra, Portugal. Data obtained 1989-1999.	**8.4%** were tested positive (19/226)	Brites et al., 2000
Patch test data, selected patients	Geraniol, 1% (in pet.)	A total of 23660 patients patch tested with FM, a sub-group of 1112 patients patch tested with geraniol. Data from St John's Institute of Dermatology, St Thomas's Hospital, London SEI 7EH, UK. Data obtained 1984-1998.	**6.0%** were tested positive (67/1112)	Buckley et al., 2000
Patch test data, selected patients	Geraniol, 2% (vehicle not reported)	A total of 223 nurses with suspected occupational skin disease patch tested with geraniol. Data from the Department of Occupational Diseases, The Nofer Institute of Occupational Medicine, Lódz, Poland. Data obtained 1995-1999.	0.4% were tested positive (1/223)	Kiec-Swierczynska & Krecisz 2000
Patch test data, selected patients	Geraniol, 5% (in pet.)	A total of 1483 patients with suspected cosmetic contact dermatitis patch tested with geraniol. Data from Nagoya, Japan. Data obtained 1990-1998.	0.3% were tested positive (4/1483)	Sugiura et al., 2000
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Study of 542 selected patients positive to FM patch tested with geraniol. Data from Portugal. Data obtained 1990-1997.	**10.7%** were tested positive (58/542)	Bordalo et al., 1999
Patch test data, selected patients	Geraniol, 2% (in 1% sorbitan sesquioleate)	Study of 50 patients positive to FM patch tested with geraniol. Data from University Hospital Utrecht, The Netherlands. Data obtained 1994-1998.	**6.0%** were tested positive (3/50)	Hendriks & van Ginkel 1999
Patch test data, selected patients	Geraniol, concentration not reported (in pet.)	Study of 40 patients positive to FM patch tested with geraniol. Data from Department of Dermatology, Royal Hallamshire Hospital, Sheffield, UK. Data obtained 1994-1995.	0% were tested positive (0/40)	Katsarma & Gawkrodger 1999
Patch test data, selected patients	Geraniol, 1% (in pet.)	Study of 38 patients positive to FM patch tested with geraniol. Data from the Skin Test	**13.2%** were tested positive (5/38)	Katsarou et al., 1999

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		Laboratory, Department of Dermatology, University of Athens, "A. Sygros" Hospital, Athens, Greece. Data obtained 1985-1996.		
Patch test data, selected patients	Geraniol, 1% (in pet.)	Study of 41 patients sensitive to UV absorbers patch tested with geraniol. Data from the Photobiology unit, Department of Dermatology, University of Gottingen, Germany. Data obtained 1981-1996.	**2.4%** were tested positive (1/41)	Schauder & Ippen 1997 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, 5% (in pet.)	Study of 167 fragrance sensitive volunteer patients patch tested with geraniol. Data from seven centers located in Japan, Northern Ireland, United States, England, Switzerland and Sweden.	**3.0%** were tested positive (5/167)	Larsen et al., 1996
Patch test data, selected patients	Geraniol, 1-2% (in pet.)	Study of 367 patients reacting to FM patch tested with geraniol. Data from Department of Dermatology, Gentofte Hospital, Denmark. Data obtained 1979-1992.	**4.1%** were tested positive (15/367)	Johansen & Menne 1995
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Study of 50 selected patients sensitive to FM patch tested with geraniol. Data from Department of Dermatology and Venereology, Hungary.	**6.0%** were tested positive (3/50)	Becker et al., 1994
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 61 selected patients sensitive to FM patch tested with geraniol. Data from University of Amsterdam and University of Leiden, The Netherlands. Data obtained in 1991.	**13.1%** were tested positive (8/61)	De Groot et al., 1993
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 64 selected patients with cosmetic dermatitis patch tested with geraniol. Data from Department of Dermatology, Toho University School of Medicine, Tokyo, Japan. Data obtained 1990-1991.	**4.7%** were tested positive (3/64)	Haba et al., 1993
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 7 selected patients with facial melanosis patch tested with geraniol. Data from Department of Dermatology, Toho University School of Medicine, Tokyo, Japan. Data obtained 1990-1991.	0% were tested positive (0/7)	Haba et al., 1993
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 32 selected patients with non-cosmetic dermatitis and eczema patch tested with geraniol. Data from Department of Dermatology, Toho University	**3.1%** were tested positive (1/32)	Haba et al., 1993

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		School of Medicine, Tokyo, Japan. Data obtained 1990-1991.		
Patch test data, selected patients	Geraniol, 1% (pet.)	Study of 16 selected children with atopic dermatitis patch tested with geraniol.	0% were tested positive (0/16)	Abifadel et al., 1992 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, 1% (pet.)	Study of 4 selected children with a suspicion of contact dermatitis patch tested with geraniol.	0% were tested positive (0/4)	Abifadel et al., 1992 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 111 selected patients with contact dermatitis patch tested with geraniol. Data from Department of Dermatology, Osaka City University Medical School, Osaka, Japan. Data obtained 1990-1991.	0.9% were tested positive (1/111)	Nagareda et al., 1992
Patch test data, selected patients	Geraniol, 5% (vaselin)	Study of 115 selected patients positive to cosmetics or cosmetic ingredients patch tested with geraniol. Data from Department of Dermatology, Ullevaal Hospital, Oslo, Norway. Data obtained 1987-1988.	0% were tested positive (0/115)	Remaut 1992
Patch test data, selected patients	Geraniol, 1% (pet.)	Study of 17 selected patients sensitive to FM patch tested with geraniol. Data from the Netherlands.	**11.8%** were tested positive (2/17)	Roesyanto-Mahadi et al., 1990
Patch test data, selected patients	Geraniol, 2% (pet.)	Study of 20 selected patients sensitive to FM patch tested with geraniol.	**10.0%** were tested positive (2/20)	Safford et al., 1990
Patch test data, selected patients	Geraniol, 1% (vehicle not reported)	Study of 162 selected patients sensitive to FM patch tested with geraniol. Data from Dermatologische Klinik und Poliklinik, Germany. Data obtained 1987.	**2.5%** were tested positive (4/162)	Enders et al., 1989 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, 2% (pet.)	Study of 19 selected patients with eyelid dermatitis patch tested with geraniol. Data from Contact Dermatitis Clinic of St. Michael's Hospital, Toronto, Canada. Data obtained 1980-1987.	0% were tested positive (0/19)	Nethercott et al., 1989
Patch test data, selected patients	Geraniol, 2% (pet.)	Study of 70 selected patients with dermatitis patch tested with geraniol. Data from Contact Dermatitis Clinic of St. Michael's Hospital, Toronto, Canada. Data obtained 1980-1987.	1.4% were tested positive (1/70)	Nethercott et al., 1989
Patch test data, selected patients	Geraniol, 1% (pet.)	Study of 78 selected patients sensitive to FM patch tested with geraniol. Data from multicenter study involving 6 countries. Data	**5.1%** were tested positive (4/78)	Wilkinson et al., 1989, as cited in SCCNFP 1999

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		obtained 1989.		
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 119 selected patients suffering from cosmetic-relaed contact dermatitis patch tested with geraniol. Data from a multicentre study performed in the Netherlands. Data obtained 1986-1987.	1.7% were tested positive (2/119)	De Groot et al., 1988
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Study of 31 selected patients sensitive to oak moss patch tested with geraniol. Data from Clinica de Dermatologia e Venereologia dos Hospitals da Universidade de Coimbra, Portugal. Data obtained 1980-1986.	**16.1%** were tested positive (5/31)	Goncalo et al., 1988
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Study of 156 selected patients with pure contact allergy to cosmetic products patch tested with geraniol.	1.3% were tested positive (2/156)	Broeckx et al., 1987 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, 20% (pet.)	Study of 574 selected patients with cosmetic contact dermatitis or another eczema patch tested with geraniol. Data obtained 1984-1986.	0.9% were tested positive (5/574)	Hirose et al., 1987
Patch test data, selected patients	Geraniol, 3**%** (pet.)	Study of 63 selected dermatitis patients positive to perfume mixture patch tested with geraniol. Data from Istituto Dermatologico Santa Maria e San Gallicano, Italy. Data obtained 1983-1984.	**6.3%** were tested positive (4/63)	Santucci et al., 1987
Patch test data, selected patients	Geraniol, 1**%** (pet.)	Study of 54 selected dermatitis patients positive to perfume mixture patch tested with geraniol. Data from Istituto Dermatologico Santa Maria e San Gallicano, Italy. Data obtained 1984-1985.	**7.4%** were tested positive (4/54)	Santucci et al., 1987
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Study of 42 selected patients sensitive to perfume mixture patch tested with geraniol.	**24.0%** were tested positive (10/42)	Rudzki & Grzywa 1986 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Study of 403 selected patients with cutaneous reactions to cosmetic products patch tested with geraniol. Data from the North American Contact Dermatitis Group, a task force of the American Academy of Dermatology. Data obtained 1977-1983.	**2.0%** were tested positive (8/403)	Adams & Maibach 1985
Patch test data, selected	Geraniol, 1%	Study of 144 selected patients	**6.9%** were tested	Angelini et al.,

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
patients	(pet.)	sensitive to FM patch tested with geraniol.	positive (10/144)	1985
Patch test data, selected patients	Geraniol, 10% (pet.)	Study of 179 selected patients suspected of cosmetic allergy patch tested with geraniol. Data from the Netherlands.	**6.1%** were tested positive (11/179)	De Groot et al., 1985
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 16 selected patients with cosmetic sensitivity patch tested with geraniol.	0% were tested positive (0/16)	Emmons and Marks 1985 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 15 selected patients with eczematous dermatitis patch tested with geraniol.	**6.7%** were tested positive (1/15)	Emmons and Marks 1985 (also cited in REACH reg.)
Patch test data, selected patients	Geraniol, 1% (pet.)	Study of 182 selected patients suspected of contact allergy to cosmetics patch tested with geraniol. Data from the Netherlands. Data obtained 1977.	1.6% were tested positive (3/182)	Malten et al., 1984
Patch test data, selected patients	Geraniol, 20% (pet.)	Study of 181 selected patients with melanosis faciei feminae patch tested with geraniol. Data obtained 1977-1982	**3.9%** were tested positive (7/181)	Hayakawa et al., 1983
Patch test data, selected patients	Geraniol, (concentration vehicle not reported)	Study of 23 selected fragrance sensitive patients patch tested with geraniol.	**13.0%** were tested positive (3/23)	Sugai 1983
Patch test data, selected patients	Geraniol, (concentration and vehicle not reported)	Multicentre study of 487 patients allergic to cosmetic patch tested with geraniol. Data from US. Data obtained 1977-1980	1.0% were tested positive (5/487)	Eiermann et al., 1982
Patch test data, selected patients	Geraniol, 5% (pet.)	Study of 155 selected cosmetic dermatitis patients patch tested with geraniol.	0.6% were tested positive (1/155)	Itoh 1982
Patch test data, selected patients	Geraniol, 2% (pet.)	Study of 1277 selected patients with contact dermatitis due to household products patch tested with geraniol.	**2.2%** were tested positive (28/1277)	Sugai 1982, as cited in Lapczynski et al., 2008
Patch test data, selected patients	Geraniol, 5% (white petrolatum)	Study of 20 selected perfume sensitive patients patch tested with geraniol.	**30.0%** were tested positive (6/20)	Larsen et al., 1977
Patch test data, selected patients	Geraniol, 10% (pet.)	Study of 15 selected eczema patients allergic to Balsam of Peru patch tested with geraniol.	**13.3%** were tested positive (2/15)	Hjorth 1961, as cited in Hostynek & Maibach 2004 (also cited in REACH reg.)
Patch tests, consecutive (unselected) patients				
Patch test data, consecutive patients	Geraniol, 2% (in pet.)	Study of patch test data by reviewing records of 1951	0.5% (95% CI: 0.2-0.8%) were tested	Mann et al., 2014

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		eczema unselected patients patch tested with geraniol. Data from St Johns Institute of Dermatology at St Thomas Hospital, UK. Data obtained 2011-2012.	positive (9/1951)	
Patch test data, consecutive patients	Geraniol, 4% (in pet.)	Study of 655 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2010-2011.	0.2% were tested positive (1/655)	Hagvall et al., 2013
Patch test data, consecutive patients	Geraniol, 6% (in pet.)	Study of 649 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2010-2011.	0.5% were tested positive (3/649)	Hagvall et al., 2013
Patch test data, consecutive patients	Geraniol, 11% (in pet.)	Study of 655 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2010-2011.	**1.1%** were tested positive (7/655)	Hagvall et al., 2013
Patch test data, consecutive patients	Geraniol, **air-exposed for 10 weeks**, 4% (in pet.)	Study of 655 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2010-2011.	0.9% were tested positive (6/655)	Hagvall et al., 2013
Patch test data, consecutive patients	Geraniol, **air-exposed for 10 weeks**, 6% (in pet.)	Study of 655 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2010-2011.	**2.3%** were tested positive (15/655)	Hagvall et al., 2013
Patch test data, consecutive patients	Geraniol, **air-exposed for 10 weeks**, 11% (in pet.)	Study of 653 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2010-2011.	**4.6%** were tested positive (30/653)	Hagvall et al., 2013
Patch test data, consecutive patients	Geraniol, 2% (in pet.)	Study of 2227 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2006-	0.1% were tested positive (3/2227)	Hagvall et al., 2012

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		2010.		
Patch test data, consecutive patients	Geraniol, **air-exposed for 10 weeks**, 2% (in pet.)	Study of 2179 unselected patients patch tested with geraniol. Data from Department of Dermatology, Sahlgrenska University Hospital, Gothenburg, Sweden. Data obtained 2006-2010.	0.6% were tested positive (12/2179)	Hagvall et al., 2012
Patch test data, consecutive patients	Geraniol, 1% (in pet.)	Study of 1502 unselected eczema patients patch tested with geraniol. Data from Department of Dermato-Allergology, Copenhagen University Hospital Gentofte, Denmark. Data obtained 2008-2010.	0% were tested positive (0/1502)	Heisterberg et al., 2011
Patch test data, consecutive patients	Geraniol, 1% (in pet.)	Study of 1214 unselected patients patch tested with geraniol. Data from IVDK multicentre project (IVDK: Information Network of Departments of Dermatology in Germany, Austria and Switzerland). Data obtained 2005-2008.	0.4% (95% CI: 0.1-0.69%) were tested positive (5/1214)	Uter et al., 2010
Patch test data, consecutive patients	Geraniol, 2% (in pet.)	Study of 320 eczema patients suspected of being contact allergic to fragrances or cosmetics patch tested with geraniol. Data from the University Medical Centre in Groningen, the Netherlands. Data obtained 2005-2007.	0.6% were tested positive (2/320)	Van Oosten et al., 2009
Patch test data, consecutive patients	Geraniol, 1% (in pet.)	Study of 37065 unselected dermatitis patients patch tested with geraniol. Data from the Department of Cutaneous Allergy at St John's Institute of Dermatology, UK. Data obtained 1982-2007.	0.2% were tested positive (89/37065)	White et al., 2009
Patch test data, consecutive patients	Geraniol, 1% (in pet.)	Study on 2063 unselected patients patch tested with geraniol. Data from IVDK multicentre project (IVDK: Information Network of Departments of Dermatology in Germany, Austria and Switzerland). Data obtained 2003-2004.	0.5% (95% CI: 0.1-0.7%) were tested positive (10/2063)	Schnuch et al., 2007
Patch test data, consecutive patients	Geraniol, 5% (in pet.)	A study on fragrance allergy in 658 hand eczema patients from three dermatological departments in Denmark and Sweden (Gentofte, Odense, Malmö). Data obtained in 2001-2002.	0.9% were tested positive (6/658)	Heydorn et al., 2003
Patch test data,	Geraniol, 1%	Study of 4900 unselected patients	**1.2%** were tested	Schnuch al.,

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
consecutive patients	(in pet.)	patch tested with geraniol. Data from IVDK multicentre project (IVDK: Information Network of Departments of Dermatology in Germany, Austria and Switzerland). Data obtained 1996-1999.	positive (60/4900)	2002
Patch test data, consecutive patients	Geraniol, 1% (in pet. with or without SSO (1%))	Study of 702 unselected patients patch tested with geraniol. Data from a multicentre study of the European Environmental and Contact Dermatitis Research Group.	0.7% (5/702) and 0.4% (3/702) were tested positive with and without SSO, respectively.	Frosch et al., 1995a
Patch test data, consecutive patients	Geraniol, 0.1 and 1% (in pet.)	Study of 106 unselected patients patch tested with geraniol. Data from Test centre Camarasa, Barcelona, as part of a multicentre study of the European Environmental and Contact Dermatitis Research Group.	0% were tested positive at both concentrations (0/106)	Frosch et al., 1995b
Patch test data, consecutive patients	Geraniol, 1% (in pet. with SSO 1%)	Study of 1072 unselected patients patch tested with geraniol. Data from a multicentre study involving 9 European centres of the European Environmental and Contact Dermatitis Research Group.	0.8% were tested positive (8/1072)	Frosch et al., 1995b
Patch test data, consecutive patients	Geraniol, 3-1% (pet.)	Study of 1967 patients patch tested with geraniol. Data from Department of Dermatology, South-Saimaa Central Hospital, Lappeenranta, Finland. Data obtained 1982-1985.	0.7% were tested positive (14/200)	Malanin & Ohela 1989
Patch test data, consecutive patients	Geraniol, 5% (vehicle not reported)	Study of 680 unselected patients with eczema or dermatitis patch tested with geraniol. Data obtained 1978-1985.	0.4% were tested positive (3/680)	Itoh et al., 1986
Patch test data, consecutive patients	Geraniol, 2% (yellow soft paraffin)	Study of 241 unselected patients patch tested with geraniol. Data obtained 1981-1983.	**4.1%** were tested positive (10/241)	Ferguson & Sharma 1984
Patch test data, consecutive patients	Geraniol, 5% (vehicle not reported)	Study of 212 unselected patients with cosmetic dermatitis patch tested with geraniol. Data obtained 1979-1982.	0.5% were tested positive (1/212)	Nishimura et al., 1984
Patch test data, consecutive patients	Geraniol, 5% (vehicle not reported)	Study of 35 unselected patients with facial patch tested with geraniol. Data obtained 1979-1982.	0% were tested positive (0/35)	Nishimura et al., 1984
Patch test data, consecutive patients	Geraniol, 5% (vehicle not reported)	Study of 275 unselected patients non-cosmetic dermatitis or eczema patch tested with geraniol. Data obtained 1979-	0.7% were tested positive (2/275)	Nishimura et al., 1984

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
		1982.		
Patch test data, consecutive patients	Geraniol, 1% (pet.)	Study of 242 unselected patients patch tested with geraniol.	0% were tested positive (0/667)	Van Joost et al., 1984
Patch test data, consecutive patients	Geraniol, **2%** (vaseline)	Study of 120 unselected patients with cosmetic dermatitis patch tested with geraniol.	0% were tested positive (0/120)	Ishihara et al., 1979
Patch test data, consecutive patients	Geraniol, **5%** (vaseline)	Study of 120 unselected patients with cosmetic dermatitis patch tested with geraniol.	**1.7%** were tested positive (2/120)	Ishihara et al., 1979
Patch test data, consecutive patients	Geraniol, 2% (pet.)	Study of 1033 unselected female patients patch tested with geraniol. Data from St. John's Hospital for Diseases of the Skin, London, UK. Data obtained 1984.	0.6% were tested positive (6/1033)	Cronin 1978
Patch test data, consecutive patients	Geraniol, 2% (pet.)	Study of 803 unselected male patients patch tested with geraniol. Data from St. John's Hospital for Diseases of the Skin, London, UK. Data obtained 1984.	0.5% were tested positive (4/803)	Cronin 1978
Patch test data, consecutive patients	Geraniol, 2% (pet.)	Study of 2461 unselected patients patch tested with geraniol. Data from St. John's Hospital for Diseases of the Skin, London, UK. Data obtained 1979-1980.	0.3% were tested positive (7/2461)	Cronin 1978
Patch test data, consecutive patients	Geraniol, 10% (pet.)	Study of 792 unselected eczema patients patch tested with geraniol.	0.5% were tested positive (4/792)	Fregert & Hjorth 1969, as cited in Hostynek & Maibach 2004
Patch Tests, other patients/studies				
Experimental study, selected patients	Geraniol, 1% (in pet.)	Single-centre, double-blind volunteer study of 100 selected patients with contact allergy to FM I and/or FM II. The patients were patch tested with commercial patch test fragrances incl. geraniol. Data from Department of Dermatology of the VU University Medical Centre, The Netherlands. Data obtained 2005-2010.	**9.0%** (9/100)	Nagtegaal et al., 2012
Patch test data, patients	Geraniol, 2% (in pet.)	Study of 15 patients with eczematous reactions from ketoprofen-containing gels concerning cross-reactivity and concomitant reactions patch tested with geraniol. Data from Italy. Data obtained 2006-2007.	0% were tested positive (0/15)	Foti et al., 2008
Patch test data, patients	Geraniol, 7% (vehicle not reported)	Study of 242 patients with contact allergy patch tested with geraniol.	0.4% were tested positive (1/242)	Van Joost et al., 1985

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
Patch test data, patients	Geraniol, 2% (vehicle not reported)	Study of 467 patients patch tested with geraniol.	0.2% were tested positive (1/467)	Ohela & Saramies
Human Repeat Insult Patch Tests (HRIPT's)				
HRIPT	Geraniol 2% (3:1 DEP:EtOH) (2362 µg/cm^2)	Study of 110 volunteers patch tested with geraniol.	0% were tested positive (0/110)	Unpublished report RIFM 2000, as cited in Lapczynski et al., 2008
HRIPT	Geraniol 5% and 0.5% tocopherol (3:1 DEP:EtOH) (5905 µg/cm^2)	Study of 109 volunteers patch tested with geraniol.	0.9% were tested positive (1/109)	Unpublished report RIFM 2002, as cited in Lapczynski et al., 2008
HRIPT	Geraniol 10% (3:1 DEP:EtOH) (11810 µg/cm^2)	Study of 112 volunteers patch tested with geraniol.	2.7% were tested positive (3/112)	Unpublished report RIFM 2004, as cited in Lapczynski et al., 2008
HRIPT	Geraniol 5% (alcohol SDA 39C) (3876 µg/cm^2)	Study of 40 volunteers patch tested with geraniol.	0% were tested positive (0/40)	Unpublished report RIFM 1964, as cited in Lapczynski et al., 2008
HRIPT	Geraniol 12.5% (EtOH) (9690 µg/cm^2)	Study of 41 volunteers patch tested with geraniol.	0% were tested positive (0/41)	Unpublished report RIFM 1964a, as cited in Lapczynski et al., 2008
HRIPT (modified Draize procedure)	Geraniol 10% (pet.)	Study of 104 volunteers patch tested with geraniol.	0% were tested positive (0/104)	Marzulli & Maibach, 1980 (also cited in REACH reg.)
HRIPT (modified Draize procedure)	Geraniol 10% (ethanol)	Study of 73 volunteers patch tested with geraniol.	2.7% were tested positive (2/73)	Marzulli & Maibach, 1980 (also cited in REACH reg.)
Human Maximation Tests (HMT's)				
HMT	Geraniol 6% (vehicle not reported)	Study of 25 volunteers patch tested with geraniol.	0% tests were positive (0/25)	Study report from 1986, as cited in REACH reg.
HMT	Geraniol 6% (pet.)	Study of 25 volunteers patch tested with geraniol.	0% were tested positive (0/25)	Marzulli & Maibach, 1980
HMT	Geraniol 6%	Study of 24 volunteers patch tested with geraniol.	0% tests were positive (0/24)	Unpublished report RIFM

Type of data/report	Test substance,	Relevant information about the study (as applicable)	Observations	Reference
	(pet.) (4140 µg/cm^2)			1979, as cited in Lapczynski et al., 2008
HMT	Geraniol 6% (pet.) (4140 µg/cm^2)	Study of 26 volunteers patch tested with geraniol.	3.8% tests were positive (1/26)	Unpublished report RIFM 1979a, as cited in Lapczynski et al., 2008
HMT	Geraniol 6% (pet.) (4140 µg/cm^2)	Study of 25 volunteers patch tested with geraniol.	0% tests were positive (0/25)	Grief 1967, cited from Lapczynski et al., 2008 (also cited in REACH reg.)
Case studies				
Case study	Geraniol 2% (pet.)	Patch test, one 54-year old female bartender with chronic hand dermatitis (Department of Dermatology, Oregon Health & State University, Portland, OR, USA, year not reported)	Positive reaction to geraniol	Swerdlin et al., 2010
Case study	Geraniol (concentration and vehicle not reported)	Patch test, one 48-year old male metalworker with recurrent hand dermatitis (Germany, 2007-2008)	Positive reaction to geraniol	Tanko et al., 2009
Case study	Geraniol, 20% (in pet.)	Patch test, 7 patients sensitive to farnesol patch tested with geraniol. Data from the Contact Allergy Unit, Department of Dermatits, University Hospital St. Rafaël, Kapucijnenvoer 33, B-3000 Leuven, Belgium.	43% were tested positive (3/7)	Goossens & Merckx 1997
Case study	Geraniol, 1% (acetone)	Study of 3 eczema patients patch tested with geraniol.	33% were tested positive (1/3)	Keil 1947 (also cited in REACH reg.)

10.8 Short summary and overall relevance of the provided information on skin sensitisation

The sensitising properties of geraniol have been intensively studied in both animals and humans. Numerous animal studies confirming the sensitising properties of geraniol are available. The animal studies reported in table 8 represent guideline studies as well as older studies based on testing principles that are equivalent to current test guidelines for skin sensitisation. According to the CLP criteria the results of LLNA (OECD 429), GPMT and Buehler tests (OECD 406) are directly applicable for classification and sub-categorisation of skin sensitisation.

Furthermore, a large number of publications are available on the sensitising properties of geraniol seen in human patch tests. For diagnostic testing of contact allergy to fragrances in humans, standardised fragrance mixtures (FM I and FM II) are used in the European baseline series used for standardised patch testing in dermatological clinics. Geraniol is a component of FM I, which has routinely been used for diagnostic patch testing in Europe (and elsewhere). FM I contains 1% geraniol and a total of 8% fragrance allergens (SCCS

2012), when tested individually the recommended concentration for geraniol in petrolatum is 2% (Recommendation of the European Society of Contact Dermatitis). Follow-up testing of the single fragrance substances showing positive reactions in patch tests with FM I and FM II is routinely done in many dermatological clinics and the sensitising properties of geraniol are well documented in humans. Patch tests with geraniol involving several thousand dermatitis patients from dermatological clinics in various countries in Europe, North America and Asia are thus available. Diagnostic patch test data are generally seen as the primary source of clinical information on the occurrence of skin sensitisation and are considered to represent the most important human data in relation to this classification proposal.

Results of human volunteer studies (which are no longer performed due to ethical reasons) are also available for geraniol and may according to the guideline of the application of the CLP criteria be used as weight of evidence for sub-categorisation (ECHA 2015).

10.8.1 Animal data

A total of 9 LLNAs, 1 *ex vivo* LLNA-BrdU ELISA, 5 GPMTs, and 1 Buehler test were identified for geraniol (Table 8).

The reported EC3 values in the LLNAs range between 5.6% and 25.8% in different vehicles. Most LLNAs were reported as being conducted according to or as being equivalent to OECD TG 429. The lowest EC3 value obtained with (non-oxidised) Geraniol (EC3 = 5.6%) was observed in a study where EtOH was used as a vehicle (SCCS 2012, Lalko et al., 2004). In two tests with the vehicle EtOH:DEP 3:1, the EC3 values were 11.4 and 25.8%, respectively (SCCS 2012, Lalko et al., 2004), whereas in two other tests with the same vehicle but in the ratio 1:3, the EC3 values were 11.4 and 20.4%, respectively (Lalko and Api 2006, SCCS 2012, Lalko et al., 2004). In one study with DEP as vehicle, the EC3 value was 11.8% (SCCS 2012, Lalko et al., 2004. In the study with AOO as the vehicle the EC3 value was 22.4% (Hagvall et al., 2007). A potential influence on the EC3 values of the vehicle used in the different tests cannot be evaluated. In the LLNA *ex vivo* BrdU tests an EC3 value of 13.1% was reported (Ulker et al., 2014). In two LLNA studies using air-exposed geraniol the EC3 values obtained were in the lower range compared to the results of the other LLNA studies (EC3 values of 4.4% and 5.8%, respectively) (Hagvall et al., 2007). As described in the SCCS opinion geraniol can be activated to other substances with increased sensitising capacity (such as geranial) both through autoxidation and metabolic oxidation. This may explain that lower EC3 values seem to be obtained with air exposed geraniol.

A positive reaction was observed in a GPMT with geraniol at an intradermal induction concentration of 0.1% in Dobs saline followed by topical application at 50% in acetone whereas no sensitisation was observed when followed by topical application at 50% in 70/30 acetone/PEG 400 (Lapczynski et al., 2008). Positive reactions were also observed in two GPMTs with geraniol (3/6 animals in one test) at intradermal induction concentrations of 5% in petrolatum followed by topical application of 25 or 30% in petrolatum, and in one GPMTs at an intradermal induction concentration of 10% followed by topical application at 10% (vehicle not reported) (Lapczynski et al., 2008, Klecak et al., 1977).

No sensitisation was observed in a Buehler test with an induction concentration of 25% in DEP (Lapczynski et al., 2008).

The above reported animal studies are relevant in terms of classification and generally confirm the sensitising properties of geraniol except from two of the studies (one GPMT and the Buehler test) in which no sensitisation was observed. For a number of the studies robust information is not available and the results are cited from reviews. Although the quality and reliability cannot be assessed in detail the results of the tests are, however, relatively consistent.

Other (and older) animal studies on the skin sensitising properties of geraniol have also been identified but have not been included in table 8. Such studies include Draize tests, Open Epicutaneous Tests (OET), Freund's Complete Adjuvant Tests (FCAT) and sensitisation tests. Both positive and negative results have been obtained in these studies. However, as these studies are not directly applicable for classification and sub-categorisation of skin sensitisers according to the CLP criteria and guidance, they are not included in the current CLH report as several currently accepted guideline studies are available.

10.8.2 Human data

A total of 88 diagnostic patch tests, 4 other patch test studies, 7 HRIPTs, 5 HMTs and 4 case studies were identified for geraniol (Table 9).

Diagnostic patch testing is conducted in order to diagnose contact allergy to a substance and is performed according to international standards by dermatologists (Johansen et al. 2015). The results of such patch tests are usually reported as number of patients/subjects having positive reactions in relation to the total number tested, i.e. the frequency of positive patch tests. An important factor when assessing the prevalence of positive reactions in diagnostic patch tests is how the group of patients are defined, i.e. selected patients versus consecutive (unselected) patients. Selected patients can be e.g. patients with dermatitis suspected of having contact allergy to fragrances or cosmetics or special occupational groups (aimed testing). Consecutive (unselected) patients are groups of patients for whom allergic contact dermatitis (ACD) is generally suspected.

The positive patch test frequencies from the 88 reported diagnostic patch tests vary between 0.1 and 30% in all dermatitis patients and the highest frequencies of positive patch test reactions with geraniol were generally seen in patch tests with selected patients. In the 56 patch tests with selected dermatitis patients the frequency of positive reactions ranges between 0.3 and 30%. Complete absence of positive reactions was observed in 8 of these tests. Whereas some of the highest frequencies of positive reactions (e.g. above 10%) were seen in tests including groups of less than 100 selected patients, high frequencies of positive reactions were also observed in patch tests with larger patient groups. In 36 out of 56 patch tests with selected patients positive patch test frequencies ≥2% were observed. In the 32 patch tests with consecutive (unselected) dermatitis patients the frequency of positive reactions was generally lower, ranging from 0.1 and 4.6%. Complete absence of positive reactions was only observed in 5 of these tests whereas relatively high frequencies of positive reactions (≥1.0%) were seen in 6 of these tests. In 2 of these 6 tests the patients were, however, exposed to air-oxidised geraniol (see below). Most of the patch tests with selected patients included large patient groups > 500 patients. Geraniol was typically tested in concentrations of 1-5% (in petrolatum) in the diagnostic patch tests. A concentration of 2% is currently recommended by the European Society of Contact Dermatitis. The total number of positive reactions in the published cases is > 900.

In some of the reported patch test studies both geraniol and air-exposed geraniol were tested in consecutive patients at different concentrations (Hagvall et al., 2012 and 2013). As geraniol can be activated to other substances with increased sensitising capacity (e.g. geranial) both through autoxidation and metabolic oxidation (SCCS 2012), patch testing with air-exposed geraniol may be foreseen to yield a higher response when compared to patch tests with unexposed geraniol. The results of the few available patch test studies using both air-exposed and unexposed geraniol seem to confirm that the air-exposed form generally increases the frequency of positive reactions relative to the unexposed form of geraniol and that testing with oxidised geraniol detects more cases of contact allergy than testing with pure geraniol (Hagvall et al., 2012, Hagvall et al., 2013). In relation to classification of geraniol for skin sensitisation the results obtained in patch tests using air-exposed geraniol are not directly applicable, as the increased sensitisation potential is considered to be a consequence of the transformation into more reactive metabolites/oxidation products of geraniol.

Four “other” patch test studies were identified. In an experimental study the possible role of skin irritation response in relation to polysensitisation to fragrances was investigated in 100 volunteer patients with confirmed fragrance contact allergy. All patients were patch tested (on the back) with 27 fragrance chemicals including geraniol. Furthermore a simultaneous patch test was done with sodium lauryl sulphate (a known skin irritant) on the upper arm of the patients. The study was not a clinical diagnostic patch test but the tests were nevertheless performed according to the guidelines of the International Contact Dermatitis Research Group. In this study 9.0% of the patients had positive reactions to geraniol (in 1% petrolatum). This result thus confirms the high frequencies of positive reactions to geraniol found in routine diagnostic patch testing with selected patients (Nagtegaal et al. 2012). In the three other studies sufficient information for identifying the nature of the patch test or the patient group was not available. Positive patch test frequencies between 0-0.4% were obtained for geraniol in these three studies.

The results of the many patch tests confirm that positive reactions to geraniol are commonly observed in dermatitis patients and with relatively high frequencies observed in a number of tests. The patch test data

collectively cover information from the last 3-4 decades and from many different dermatological clinics in different countries. Although it is not possible to directly compare these findings and draw conclusions on any tendencies in the sensitisation rates, it is obvious that high sensitisation frequencies have been observed for geraniol in recent years and that patients in many countries are affected.

Induction of sensitisation was also reported in 3 of 7 HRIPT studies after exposures to between 5-10% (>500 µg/cm^2) geraniol (different vehicles). Sensitisation was observed in 1 of 5 HMT studies after exposure to 6% (>500 µg/cm^2) geraniol (vehicle: petrolatum or not reported). The number of volunteers tested ranged from 40-112 in the HRIPT studies and 24-26 in the HMT studies. Concentrations lower than 500 µg/cm^2 geraniol were not tested in any of these studies. Robust study information is not available for these studies (Marzulli & Maibach, 1980, Lapczynski et al., 2008).

Four case studies are reported which confirm the general picture observed in the other patch tests with dermatitis patients described above.

The human tests identified are all relevant in terms of classification and confirm the sensitising properties of geraniol. The comprehensive set of diagnostic patch test data covering the last 3-4 decades with several of the tests being published very recently are seen as the key information for this classification proposal. The four case studies confirm the general picture observed in the other patch tests with dermatitis patients. For the HRIPTs and HMTs (older volunteer tests) robust study information is not available and the results are primarily cited from an older publication (Marzulli & Maibach, 1980) and a review article (Lapczynski et al., 2008). These data are seen as supporting evidence.

10.8.3 Human exposure

Geraniol is a fragrance that is manufactured in or imported to the EU in amounts of 1000-10,000 tonnes/year and is widely used in products on the EU market. The registered categories of use for consumers are cosmetics and a variety of household and professional cleaning and maintenance products. Data from the fragrance industry (cited in SCCS 2012) indicate that 80% of the total fragrance chemical volume is used in cosmetics and 20% in household products. Although cosmetics are assessed to be the main use category for geraniol, the use in other products (household and other products) may thus account for a substantial volume. As geraniol is widely used in many different types of consumer products the general population can be exposed from many different sources.

Geraniol is generally present in low concentrations in individual consumer products. The International Fragrance Association (IFRA) has established maximum recommended limits of geraniol in leave-on cosmetic products between 0.3-5.3% depending on the product category, between 5.0-8.6% in rinse-off cosmetic products, and of 2.5% for non-cosmetic consumer products with direct skin contact, as shown in Table 10 (IFRA 2007). (Note that other product types than those specifically mentioned in the table driving the category consumer exposure level are also covered under the different categories).

Table 10: The IFRA standard limits for geraniol in IFRA QRA (Quantitative Risk Assessment) product categories (IFRA 2007):

IFRA QRA product category	Product type that drives the category consumer exposure level	IFRA standard limits
Category 1	Lip products	0.3%
Category 2	Deodorants/antiperspirants	0.4%
Category 3	Hydroalcoholics for shaved skin	1.8%
Category 4	Hydroalcoholics for unshaved skin	5.3%
Category 5	Hand cream	2.8%
Category 6	Mouthwash	8.6%

IFRA QRA product category	Product type that drives the category consumer exposure level	IFRA standard limits
Category 7	Intimate wipes	0.9%
Category 8	Hair styling aids	2.0%
Category 9	Rinse-off hair conditioners	5.0%
Category 10	Hard surface cleaners	2.5%
Category 11	Incidental or non-skin contact	Not restricted

The SCCS opinion (SCCS 2012) refers to a number of surveys on the presence and content of the 26 fragrances subject to labelling requirements (for cosmetics and detergents) in various consumer products. The reported occurrence of the fragrances is mostly based on labelling information alone, i.e. whether the substances are mentioned on the label of the product. In one survey the content was verified by chemical analysis. Table 11 summarises the results of the surveys with respect to the occurrence of geraniol in various consumer products.

Table 11: Occurrence of geraniol in consumer products, different surveys (cited from SCCS 2012):

Product type	Number of products investigated	% products labelled to contain geraniol	Reference in SCCS 2012
Children's cosmetics	n.a	12%	Table 10.1, p. 74
Deodorants	88	48.9% (87% products found to contain geraniol; measured conc. from 1-399 ppm)	Table 10.2, p. 75
Consumer products (cosmetics, household products)	300	42%	Table 10.3, p. 77
Consumer products	516	22.1%	Table 10.4, p. 77
Consumer products	3000	Approx. 20%	Figure 10.1, p 78

Geraniol was found to be present in 12-49% of the products covered in the different surveys based on labelling information alone. One study of deodorants showed that the occurrence of geraniol was even more frequent than expected based on subsequent chemical analysis. It was concluded by SCCS (SCCS 2012) that taking the total exposure into account, exposure to all 26 allergenic fragrances is foreseeable in daily life.

The Danish EPA has conducted surveys and assessments of a broad range of consumer products on the Danish market over the last decades. Geraniol has been identified in many different types of products but mostly in cosmetic products, including day-to-day cosmetic products such as deodorants, soaps, shampoos/conditioner, lotions and creams as well as in e.g. massage oils. Geraniol has also been found in household products such as cleaning agents, stain removers and air care products and in articles such as pens. Generally geraniol is found in low concentrations (>0 - <0.15%) in the investigated products except air fresheners (up to 0.9%) and massage oils (up to 23%) (DK EPA database, search February 2017).

The Danish Product Register contains information of hazardous substances in mixtures for professional use. Data from the Register confirm that geraniol is used in a wide range of products on the market, especially cleaning products. The concentrations are generally lower than 0.1% in the majority of the products. However, concentrations above 1% are found in fragrance mixtures and scented oils (Danish Product Register, 2016).

Human exposure to geraniol generally seems to be low based on the IFRA recommendations and reported contents in various consumer products. The exposure is, however, assessed to be frequent due to the widespread uses, primarily as a fragrance in consumer products, and the high tonnage level of geraniol. It is thus difficult for consumers to avoid exposure. According to the data from IFRA the exposure to geraniol when used as a fragrance in cosmetics is relatively low with established maximum recommended limits in most leave-on products being below 2-3% (except for IFRA QRA Product Category 4 and 5). For rinse-off cosmetics higher maximum recommended limits (5.0-8.6%) have been established, but a lower exposure is expected due to the intermedient character of the exposure and shorter duration of exposure compared to leave-on products. For non-cosmetic consumer products with direct skin contact a maximum recommended limit of 2.5% has been established.

10.9 Comparison with the CLP criteria

Geraniol is a widely used fragrance and a well known skin sensitizer. Geraniol has no harmonized classification but is generally self-classified as a Category 1 Skin sensitizer according to the C&L Inventory. An assessment of the skin sensitizing properties of geraniol has been conducted according to the current classification criteria including an assessment of the appropriate sub-category for this hazard class

According to the classification criteria sub-category 1A represent "*Substances showing a high frequency of occurrence in humans and/or a high potency in animals can be presumed to have the potential to produce significant sensitisation in humans. Severity of reaction may also be considered*" (CLP table 3.4.2).

According to the classification criteria sub-category 1B represent "*Substances showing a low to moderate frequency of occurrence in humans and/or a low to moderate potency in animals can be presumed to have the potential to produce sensitisation in humans. Severity of reaction may also be considered*" (CLP table 3.4.2).

10.9.1 Animal data

According to the classification criteria evidence from animal tests for sub-category 1A and 1B, respectively, can include the following types of data and results (CLP Tables 3.4.3 and 3.4.4):

	Animal data	
Sub-category 1A	LLNA	EC3 value ≤ 2 %
	GPMT	≥ 30 % responding at ≤ 0,1 % intradermal induction dose or ≥ 60 % responding at > 0,1 % to ≤ 1 % intradermal induction dose
	Buehler	≥ 15 % responding at ≤ 0,2 % topical induction dose or ≥ 60 % responding at > 0,2 % to ≤ 20 % topical induction dose
Sub-category 1B	LLNA	EC3 value > 2 %
	GPMT	≥ 30 % to < 60 % responding at > 0,1 % to ≤ 1 % intradermal induction dose or ≥ 30 % responding at > 1 % intradermal induction dose
	Buehler	≥ 15 % to < 60 % responding at > 0,2 % to ≤ 20 % topical induction dose or ≥ 15 % responding at > 20 % topical induction dose

Test results from the LLNA, GPMT and Buehler tests can be used directly for classification and potency assessment. The reported EC3 values in the LLNAs (n=7) performed with geraniol range between 5.6% and 25.8% indicating a moderate skin sensitisation potency of geraniol (i.e. Cat 1B). The reported EC3 values in the LLNAs (n=2) performed with geraniol air-exposed for 10 or 45 weeks, respectively, were 4.4% and 5.8%, respectively, indicating a moderate skin sensitisation potency of air-exposed geraniol (i.e. Cat 1B). The reported EC3 value in the *ex vivo* LLNA-BrdU ELISA performed with geraniol was 13.1%; however, the result of this study cannot be used for sub-categorisation according to the CLP guidance (ECHA 2015).

Five GPMTs are available. In one GPMT with an intradermal induction concentration of 5%, a positive response was seen in 50% of the animals (3/6), indicating a moderate potency (i.e. Cat 1B). In three GPMTs with intradermal induction doses of 0.1, 5 and 10% geraniol, respectively, sensitisation was observed but not quantified (i.e. the number of animals affected was not reported) and a decision on sub-categorisation is thus not possible based on these studies. In one GPMT with an intradermal induction concentration of 0.1%, no sensitisation was observed.

No sensitisation was observed in a Buehler test with an induction concentration of 25% indicating that geraniol was not identified as a skin sensitiser in this test.

Other and older animal tests on the skin sensitising properties of geraniol show conflicting results. However, such tests are not directly applicable for sub-categorisation of skin sensitisers according to the CLP criteria and guidance.

In summary the animal data either indicate that geraniol is a skin sensitizer of moderate potency or do not allow conclusions on potency due to the design of the tests (doses used, lack of quantification of response). For most of the tests robust study information is not available to assess the quality more precisely. Caution should thus be exerted in drawing firm conclusions on sub-categorisation based on the animal data alone. Collectively, the results of the animal tests confirm the sensitizing properties of geraniol in a relatively consistent manner with a moderate potency.

10.9.2 Human data

According to the classification criteria human evidence for sub-category 1A and 1B, respectively, can include the following types of data (CLP section 3.4.2.2.2):

	Human data
Sub-category 1A	(a) positive responses at ≤ 500 μg/cm^2 (HRIPT, HMT — induction threshold); (b) diagnostic patch test data where there is a relatively high and substantial incidence of reactions in a defined population in relation to relatively low exposure; (c) other epidemiological evidence where there is a relatively high and substantial incidence of allergic contact dermatitis in relation to relatively low exposure.
Sub-category 1B	(a) positive responses at > 500 μg/cm^2 (HRIPT, HMT — induction threshold); (b) diagnostic patch test data where there is a relatively low but substantial incidence of reactions in a defined population in relation to relatively high exposure; (c) other epidemiological evidence where there is a relatively low but substantial incidence of allergic contact dermatitis in relation to relatively high exposure.

The guidance on the application of the CLP criteria further outlines how high or low frequency of occurrence of skin sensitization shall be assessed. The exposure level is determined according to Table 3.4.2-b in the guidance as shown below (ECHA 2015).

Table 3.4.2-b Relatively high or low exposure* (copied from ECHA 2015)

Human diagnostic patch test data	High frequency	Low frequency
General population studies	≥ 0.2 %	< 0.2 %
Dermatitis patients (unselected, consecutive)	≥ 1.0 %	< 1.0 %
Selected dermatitis patients (aimed testing, usually special test series)	≥ 2.0 %	< 2.0 %
Work place studies: 1: all or randomly selected workers 2: selected workers with known exposure or dermatitis	 ≥ 0.4 % ≥ 1.0 %	 < 0.4 % < 1.0 %
Number of published cases	≥ 100 cases	< 100 cases

* Only one or two types of information may be sufficient for sub-categorisation.

The key evidence for the assessment of the potency of geraniol in this classification proposal is the human data from diagnostic patch tests. Patch test data are available from several dermatological clinics in many different countries in and outside EU. In the patch tests summarized in Table 9, relatively high frequencies of positive reactions are seen upon exposure to geraniol in a high number of published cases. For selected dermatitis patients positive reactions range between 0.3 and 30% with frequencies ≥2% in 36 of 56 tests. For consecutive (unselected) dermatitis patients positive reactions range between 0.1 and 4.6% with 6* of 32 tests reporting frequencies ≥1% (*hereof two patch tests with oxidized geraniol). These tests represent more than 900 published cases of positive patch test reactions to geraniol.

The collected data from patch tests thus show that

- a high frequency (≥1%) of occurrence of skin sensitization is observed in some (6* of 32) of the patch tests with consecutive (unselected) dermatitis patients (*hereof two patch tests with oxidized geraniol).
- a high frequency (≥2%) of occurrence of skin sensitization is observed in the majority (36 of 56) of the patch tests with selected dermatitis patients
- the number of tested dermatitis patients showing positive reactions to geraniol is well above 100 (>900 cases)

These findings show a high frequency of occurrence of sensitization for geraniol in humans. For deciding on the appropriate sub-category the data from patch tests need to be seen in conjunction with the estimated exposure (see chapter 10.9.1.3 below).

Furthermore, four case studies of ACD are available. Geraniol was found to be among the causative agents of the dermatitis. These case studies are seen as supportive evidence for the findings of the patch tests.

The positive responses reported at relatively high concentrations > 500 µg/cm² in three HRIPTs and in one HMT indicate a moderate sensitisation potential of geraniol. The HRIPTs and HMTs are non-clinical tests based on healthy volunteers representing the general population (and are no longer conducted due to ethical reasons). Robust study information is not available for the HRIPTs and HMTs. The estimated induction concentrations (>500 µg/cm²) are calculated by fragrance industry and the original data have not been published. They are considered of low relevance for this classification proposal.

In an experimental volunteer study sensitisation to geraniol was reported in 9% of the fragrance allergy patients patch tested with 27 fragrance chemicals.

10.9.3 Exposure considerations

The occurrence of skin sensitization in human tests needs to be seen in conjunction with the level of exposure in order to make a decision on sub-categorisation of skin sensitisers. As described in chapter 10.8.3 the exposure to geraniol is generally considered to be relatively low, partly based on the current IFRA standard limits and on information of the actual concentrations of geraniol in various consumer products reported in different surveys.

According to the guidance on the application of the CLP criteria an additive exposure index shall be set in order to decide on the appropriate sub-category for skin sensitisers (when based on human data). An additive exposure index of 1-4 equates to relatively low exposure, whereas 5-6 reflects relatively high exposure. The exposure index is determined according to Table 3.4.2-c in the guidance as shown below (ECHA 2015).

Table 3.4.2-c Relatively high or low exposure (adapted from ECHA 2015)

Exposure data	**Relatively low exposure (weighting)**	**Relatively high exposure (weighting)**	**Score for geraniol**
Concentration / dose	< 1.0% < 500µg/cm^2 (score 0)	≥ 1.0% ≥ 500µg/cm^2 (score 2)	0
Repeated exposure	< once/daily (score 1)	≥ once/daily (score 2)	2
Number of exposures (irrespective of concentration of sensitizer)	<100 exposures (score 0)	≥ 100 exposures (score 2)	2

To achieve the exposure index a response in each row in Table 3.4.2-c above is necessary. The exposure index of geraniol is estimated based on the following assumptions:

- **Score 0** for concentration/dose: based on expected and observed concentrations < 1.0% of geraniol in relevant (consumer) products on the market.
- **Score 2** for repeated exposure: based on the frequent occurrence of geraniol in consumer products with estimated daily use.
- **Score 2** for number of exposures: based on an anticipated exposure of sensitised individuals to geraniol at least more than 100 times.

An additive exposure index of maximum 4 (0+2+2) is thus estimated indicating a relatively low exposure. A decision on the appropriate sub-category for skin sensitisers based on human data is done according to Table 3.4.2-d in the guidance:

Table 3.4.2-d Sub-categorisation decision table (from ECHA 2015)

Exposure data	**Relatively low frequency of occurrence of skin sensitisation**	**Relatively high frequency of occurrence of skin sensitisation**
Relatively high exposure (score 5-6)	Sub-category 1B	Category 1 or case by case evaluation
Relatively low exposure (score 1-4)	Category 1 or case by case evaluation	**Sub-category 1A**

10.9.1 Weight of Evidence

Both animal and human data are available documenting the skin sensitizing properties of geraniol. These data are considered in a weight of evidence assessment (WoE) according to the CLP criteria and guidance.

The animal data either indicate that geraniol is a skin sensitizer of moderate potency or do not allow conclusions on potency due to the design of the tests (doses used, lack of quantification of response). Among the standardized animal tests for skin sensitization the LLNA is considered best suited for potency assessment (Basketter et al., 2005 and ECHA 2015). All the available LLNAs suitable for classification of geraniol (i.e. excluding the LLNA BrdU ELISA and the LLNAs with air-exposed geraniol) show a moderate

potency with EC3 values >2%. Whereas one GPMT indicates a moderate potency, the remaining animal studies only indicate “sensitization” (3 GPMTs) or “no sensitization” (1 GPMT and 1 Buehler test). For most of the animal studies robust study information is not available to assess the quality more precisely. Collectively, the results of the animal tests confirm the sensitizing properties of geraniol in a relatively consistent manner with a moderate potency.

The human data available provide substantial evidence of strong sensitising effects of geraniol especially based on the results of patch tests with selected patients. Diagnostic patch test data obtained from eczema patients attending individual dermatology clinics or collected clinic data is the primary source of clinical information on the occurrence of skin sensitisation (ECHA 2015) and diagnostic patch tests are generally performed under internationally standardised conditions. Human patch tests with geraniol show a high frequency of occurrence of skin sensitisation of geraniol according to the classification criteria. According to the guidance the following three types of human information confirm the high frequency of occurrence of skin sensitisation: Data from unselected and selected dermatitis patients as well as a high number of published cases (>100). The comprehensive set of patch test data include thousands of dermatitis patients tested in dermatological clinics in different countries, mostly in EU. The four case studies confirm the general picture observed in the other patch tests with dermatitis patients. Some of the older volunteer tests in humans (HRIPTs and HMTs) generally confirm the sensitising properties of geraniol and indicate a moderate potency; however, original study information is generally not available for these non-clinical experimental studies.

Although frequent/daily exposure to geraniol is anticipated the overall exposure to geraniol is estimated to be relatively low based on information on the use in consumer products such as cosmetics and cleaning agents, but also in professional cleaning products.

Based on the high frequency of skin sensitisation observed in human patch tests with geraniol (≥2.0% in 36 of 56 patch tests with selected dermatitis patients and ≥1.0% in 6* of 32 patch tests with unselected dermatitis patients [*hereof two tests with oxidised geraniol]) and the high number of published cases combined with the estimated relatively low exposure, a classification of geraniol as a strong skin sensitiser in sub-category 1A is justified.

10.10 Conclusion on classification and labelling for skin sensitisation

Based on the high frequency of skin sensitisation observed in a large number of human patch tests (approximately 90 tests) combined with the relatively low estimated exposure to geraniol, a classification in sub-category 1A is justified.

Specific concentration limits can be set for skin sensitisers when reliable and adequate information is available to support that the specific hazard is evident below (or above) the GCL. The setting of an SCL for sensitisers is based on potency. For skin sensitisers the guidance clearly describes how an SCL can be set based on the results of certain animal studies (i.e. when a high response level is observed below a certain low dose). Further, relevant information e.g. from workplaces with known exposure levels can be used to justify a different SCL than those recommended based on the results of the animal studies.

The guidance does not provide any information on how an SCL may be set based on human data alone. Whereas the human patch test data support that geraniol is a strong sensitizer fulfilling the criteria for Category 1A these data do not provide clear dose-response information or specific information on the previous exposure regime for these patients. These data alone are thus not considered to support the establishment of an SCL.

10.11 Germ cell mutagenicity

Hazard class not assessed in this dossier.

10.12 Carcinogenicity

Hazard class not assessed in this dossier.

10.13 Reproductive toxicity

Hazard class not assessed in this dossier.

10.14 Specific target organ toxicity-single exposure

Hazard class not assessed in this dossier.

10.15 Specific target organ toxicity-repeated exposure

Hazard class not assessed in this dossier.

10.16 Aspiration hazard

Hazard class not assessed in this dossier.

11 EVALUATION OF ENVIRONMENTAL HAZARDS

Environmental hazards have not been assessed in this dossier.

12 EVALUATION OF ADDITIONAL HAZARDS

Additional hazards have not been assessed in this dossier.

13 ADDITIONAL LABELLING

Given that geraniol is classified as a skin sensitiser in Category 1A, labelling with EUH 208 will apply when geraniol is present in mixtures in concentrations ≥ 0.01%.

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15 ANNEXES

Annex I: detailed study summaries