# Safety Assessment of *Rosa damascena*-Derived Ingredients as Used in Cosmetics

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|---|---|
| Status: | Draft Final Report for Panel Review |
| Release Date: | February 11, 2022 |
| Panel Meeting Date: | March 7-8, 2022 |

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: Lisa, A. Peterson, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Preethi S. Raj, M.Sc., Senior Scientific Analyst/ Writer, CIR.



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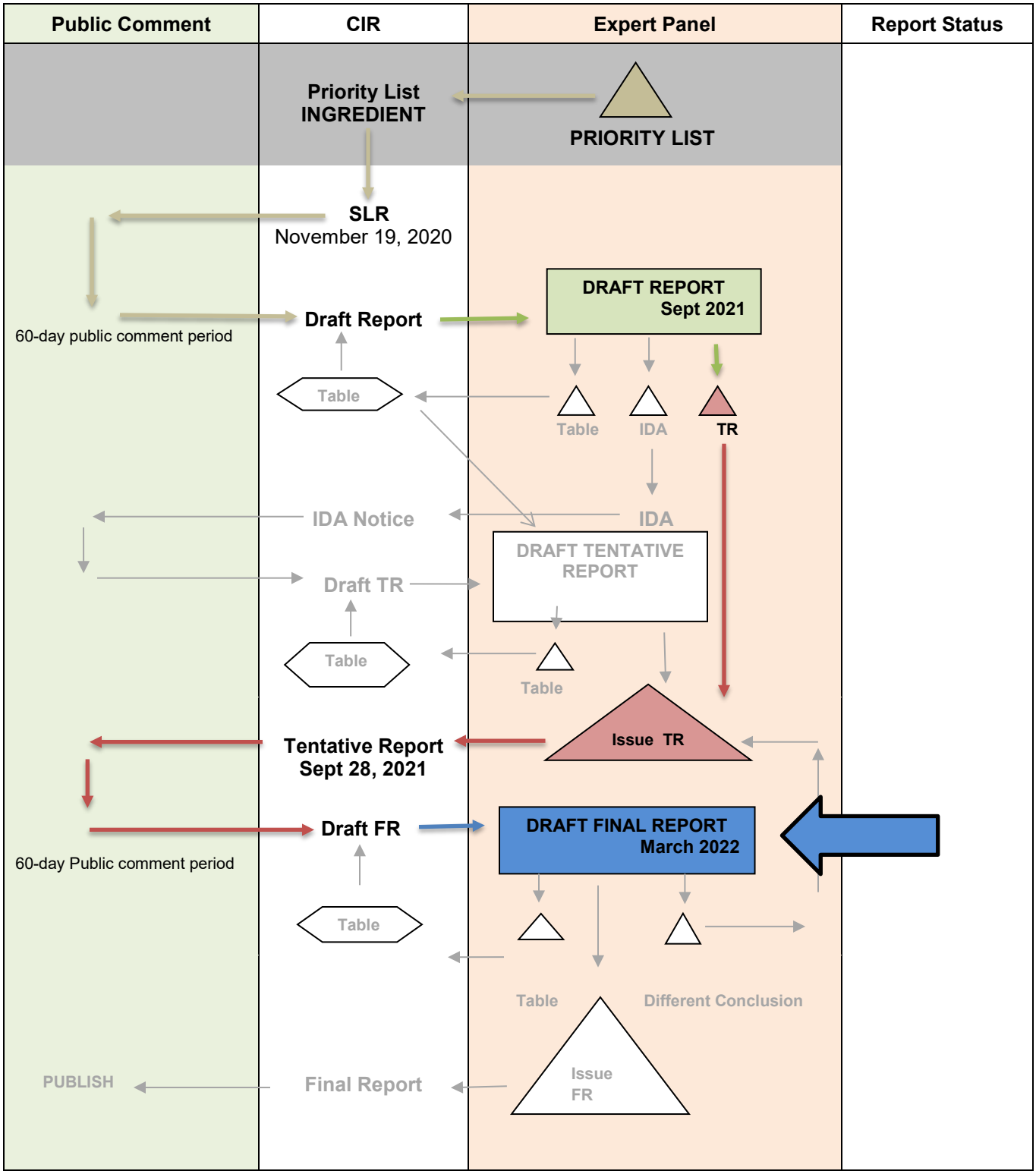
# SAFETY ASSESSMENT FLOW CHART

**INGREDIENT/FAMILY** *Rosa damascena*-derived ingredients

**MEETING** March 2022



Cosmetic Ingredient Review

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**Memorandum**

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons

From: Preethi S. Raj, M.Sc.
Senior Scientific Analyst/Writer, CIR

Date: February 11, 2022

Subject: Safety Assessment of *Rosa damascena*-Derived Ingredients as Used in Cosmetics

Enclosed is the Draft Final Report of the Safety Assessment of *Rosa damascena*-Derived Ingredients as Used in Cosmetics (identified as *report_RosaDamascena_032022* in the pdf). This is the second time the Panel is seeing a safety assessment of these 10 cosmetic ingredients. At the September 2021 Panel meeting, the Panel issued a Tentative Report for public comment with the conclusion that these ingredients are safe as used in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing.

Data from 2022 FDA VCRP were received and have been incorporated (*VCRP_RosaDamascena_032022*). Of note in the newly reported uses, is the increase from 22 to 74 reported used for Rosa Damascena Flower Extract in lipsticks. Also, updated concentration of use data were received from the Council in September 2021, and have been incorporated in the report (*data_RosaDamascena_032022*). This updated submission was prompted by the Panel's request to clarify the dubiously high maximum use concentration reported for Rosa Damascena Flower Water at 32.7% in face and neck, non-spray, products (which was verified to be 0.94%). Additionally, a supplier confirmed that the ingredient with the highest reported concentration of use for these ingredients, Rosa Damascena Flower Oil (at up to 10.8% in other skincare preparations) is an essential oil which is sold with instructions to dilute before use. The second highest reported concentration of use is now Rosa Damascena Flower Water, at up to 1.9% in foundations. Changes reflecting updated VCRP and concentration of use data are highlighted in yellow.

Comments on the Tentative Report that were received from the Council (*PCPCcomments_RosaDamascena_032022*) have been addressed. A comments response checklist is also included (*responsePCPC*comments*_RosaDamascena_032022*). Also included in this package, for your review, are a flow chart (*flow_RosaDamascena_032022*), minutes from the previous meeting (*transcripts_RosaDamascena_032022*), literature search strategy (*search_RosaDamascena_032022*), ingredient data profile (*dataprofile_RosaDamascena_032022*), and ingredient history (*history_RosaDamascena_032022*).

The Panel should carefully consider the newly added data, the Abstract, Discussion, and Conclusion, and be prepared to issue a Final Report.

Personal Care Products Council
Committed to Safety, Quality & Innovation

**Memorandum**

**TO:** Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

**FROM:** Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

**DATE:** October 7, 2021

**SUBJECT:** Tentative Report: Safety Assessment of *Rosa damascena*-Derived Ingredients as Used in Cosmetics (release date September 28, 2021)

The Personal Care Products Council respectfully submits the following comments on the tentative report, Safety Assessment of *Rosa damascena*-Derived Ingredients as Used in Cosmetics.

Key Issue

As there are no specific physiological or clinical effects caused by these ingredients, it is not clear why the studies need to be in a separate section (called Other Physiological and Biochemical Effects). The information in this section should be presented in the duration appropriate toxicity sections. If the studies are left in a separate section, the details described in this section should be added to Table 6, so at least all the details of one study are presented in one place (this is done for reference 61, it needs to be completed for all studies in this section).

Additional Considerations

Cosmetic Use, Summary, Table 4 – The corrected use information provided by PCPC on September 23, 2021, needs to be added to the report. The 10.8% concentration for Rosa Damascena Flower Oil in other skincare preparations is for an essential oil that is sold with instructions to dilute the product before use. The 32.7% use concentration for Rosa Damascena Flower Water was corrected to 0.94%.

Short-Term and Subchronic – It should be stated if there were other endpoints examined in the study described in reference 62. It is not clear what is meant by "organ tissue". Did they complete histopathologic examinations of the organs? If so, which organs were examined?

Case Reports – In the following sentence, there are 3 substances but only two values. It is not clear what the values represent. "Citronellol, geraniol, and nerol were identified as the main components (33.4% and 18.5%, respectively)."

Summary – All of the information from the study described in reference 62 should be presented together.

Table 1 – Rather than stating "The accepted scientific name for *Rosa damascena* is *Rosa* x *damascena*." with each definition, a footnote should be added to the table to indicate that this is stated in every definition.

Table 3 – NF is missing from the footnote. The meaning of "Not reported" is not clear. When NR is stated, does this mean they looked for it and did not find the component? Or does it mean that an analysis of the component was not completed?

| *Rosa damascena* – derived Ingredients - March 7-8th, 2022 Panel Meeting – Preethi Raj | | | |
|---|---|---|---|
| **Comment Submitter: Personal Care Products Council**<br>**Date of Submission: October 7, 2021 (comments received on Tentative Report after September 2021 meeting)** | | | |
| **#** | **Report section/Comment** | **Response/Action** | **Needs Panel Input** |
| 1 | Key Issue – move studies from 'Other Physiological…Effects' to tox section, or if left in same section, details should be added to Table 6 | Defer to Panel | |
| 2 | Cosmetic Use, Summary, and Table 4 – update conc of use data for RD Flower Water (32.7% → 0.94%) and include footnote for RD Flower Oil | Have updated and added footnote | |
| 3 | Short-Term and Subchronic – state if there were other endpoints examined in ref 62 (now **ref 63** – Saleh 2015)<br>Clarify what is meant by "organ tissue" | Have specified the organs in parentheses | |
| 4 | Case reports – clarify what the 3 percentages represent | Have include neral percentage (clarified) | |
| 5 | Summary – all of the info from the study described in ref 62 (now **ref 63**) should be presented together | Defer to Panel | |
| 6 | Table 1 – add a footnote to state *Rosa damascena* is *Rosa* x *damascena* | Added footnote | |
| 7 | Table 3 – add NF as a footnote, for not found (provide clarity to NR footnote) | NF (not found) was denoted by the first footnote - (not found) | |

# CIR History of:

# *Rosa damascena*-derived Ingredients

**July 2019**

-Concentration of use data submitted by Council

**November 2020**

- SLR posted on the CIR website

**December 2020**

Data received:

- December 2, 2020: Information for a trade name mixture that contains 0.1-1.0% Rosa Damascena Flower Water and 0.1-1% Rosa Damascena Flower Oil in Pentylene Glycol
- December 10, 2020: Rosa Damascena Flower Water in a trade name mixture with Butylene Glycol (method of manufacture and impurities).

**February 2021**

Data received:

- February 18, 2021: Two HRIPTs of fragrance products, containing 0.1068% Rosa Damascena Flower Water and 0.7794% Rosa Damascena Flower Extract
- February 18, 2021: HRIPT of a mask formulation, containing 0.1260% Rosa Damascena Flower Oil

**January 2021**

New VCRP data were received

**September 2021**

A Draft Report was presented to the Panel. The Panel issued a Tentative Report for public comment with the conclusion that these ingredients are safe as used in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing. The Panel discussed that most of these ingredients are derived from plant parts which are considered GRAS for intended food use, according to the US FDA. Subsequently, concerns regarding the potential for systemic toxicity were mitigated.

**October 2021**

Comments on the Tentative Report were received from Council

**January 2022**

New VCRP data were received

**March 2022**

**A Draft Final Report is being presented for Panel review.**

| *Rosa damascena*-derived Ingredients Data Profile* – March 7-8, 2022 – Writer, Preethi Raj | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Toxicokinetics | | | Acute Tox | | | Repeated Dose Tox | | | DART | | Genotox | | Carci | | Dermal Irritation | | | Dermal Sensitization | | | | Ocular Irritation | | Clinical Studies | |
| | Reported Use | Method of Mfg | Impurities | log P/log $K_{ow}$ | Dermal Penetration | ADME | Dermal | Oral | Inhalation | Dermal | Oral | Inhalation | Dermal | Oral | In Vitro | In Vivo | Dermal | Oral | In Vitro | Animal | Human | In Vitro | Animal | Human | Phototoxicity | In Vitro | Animal | Retrospective/ Multicenter | Case Reports |
| **Hydrolyzed Rosa Damascena Flower Extract** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Rosa Damascena Bud Extract** | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Rosa Damascena Extract** | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Rosa Damascena Flower** | X | | X | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Rosa Damascena Flower Extract** | X | X | | | | | | X | | | X | | | | | | | | | | | | | X | | | | | | |
| **Rosa Damascena Flower Oil** | X | X | X | | | | X | X | | | | | | | X | | | | X | X | X | X | | X | X | X | | X | X |
| **Rosa Damascena Flower Powder** | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| **Rosa Damascena Flower Water** | X | X | X | | | | | X | | | | | | | X | | | | X | | X | X | | X | X | X | | | |
| **Rosa Damascena Flower Water Extract** | X | X | | | | | | X | | | X | | | | | | | | | | | | | | | | | | | |
| **Rosa Damascena Flower Wax** | X | X | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

* "X" indicates that data were available in a category for the ingredient

## *Rosa damascena*- derived ingredients – (10 ingredients – March 7-8, 2022 Panel Meeting

| Ingredient/CAS # | InfoB | PubMed | TOXNET | FDA | EU | ECHA | IUCLID | SIDS | ECETOC | HPVIS | NICNAS | NTIS | NTP | WHO | FAO | NIOSH | FEMA | Web |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Hydrolyzed Rosa Damascena Flower Extract** | ✓ | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | NR | |
| **Rosa Damascena Bud Extract** 90106-38-0 | ✓ | NR | NR | ✓ | ✓* | NR | NR | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | NR | |
| **Rosa Damascena Extract** 90106-38-0 | ✓ | ✓* | ✓ | NR | ✓* | ✓ | NR | NR | NR | NR | ✓* | ✓ | NR | NR | NR | NR | NR | ✓ |
| **Rosa Damascena Flower** 90106-38-0 | ✓ | ✓* | ✓ | ✓ | ✓* | NR | NR | NR | NR | NR | ✓* | ✓ | NR | NR | NR | NR | NR | ✓ |
| **Rosa Damascena Flower Extract** 90106-38-0 | ✓ | ✓* | ✓* | NR | ✓* | NR | NR | NR | NR | NR | ✓* | ✓ | NR | NR | NR | NR | NR | |
| **Rosa Damascena Flower Oil** 8007-01-0 90106-38-0 | ✓ | ✓* | ✓* | ✓ | ✓* | ✓* | NR | NR | NR | NR | ✓* | ✓ | NR | NR | ✓ | NR | ✓ | ✓ |
| **Rosa Damascena Flower Powder** 90106-38-0 | ✓ | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | NR | |
| **Rosa Damascena Flower Water** 90106-38-0 | ✓ | ✓* | ✓* | NR | ✓* | NR | NR | NR | NR | NR | ✓* | ✓ | NR | NR | NR | NR | NR | |
| **Rosa Damascena Flower Water Extract** 90106-38-0 | ✓ | ✓* | ✓* | NR | ✓* | NR | NR | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | NR | ✓ |
| **Rosa Damascena Flower Wax** 90106-38-0 | ✓ | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | ✓* | NR | NR | NR | NR | NR | NR | |

✓ - data pertaining to safety was found
✓* - reported, but no data relevant to safety was found
NR- not reported

**Botanical and/or Fragrance Websites (if applicable)**

| Ingredient | CAS # | Dr. Duke's | Taxonomy | GRIN # | Sigma-Aldrich | IFRA | RIFM |
|---|---|---|---|---|---|---|---|
| Hydrolyzed Rosa Damascena Flower Extract | | | | | | | |
| Rosa Damascena Bud Extract | 90106-38-0 | | | | | | |
| Rosa Damascena Extract | 90106-38-0 | ✓ | ✓ | 5328 | ✓* | ✓ | |
| Rosa Damascena Flower | 90106-38-0 | | | | | | |
| Rosa Damascena Flower Extract | 90106-38-0 | | | | | | |
| Rosa Damascena Flower Oil | 8007-01-0 90106-38-0 | | | | | ✓ | ✓ |
| Rosa Damascena Flower Powder | 90106-38-0 | | | | | | |
| Rosa Damascena Flower Water | 90106-38-0 | | | | | | |
| Rosa Damascena Flower Water Extract | 90106-38-0 | | | | | | |
| Rosa Damascena Flower Wax | 90106-38-0 | | | | | | |

**Updated search on 1/19/2022:** ((((((((((rosa damascena extract) OR (hydrolyzed rosa damascena flower extract)) OR (rosa damascena bud extract)) OR (rosa damascena flower)) OR (rosa damascena flower extract)) OR (rosa damascena flower oil)) OR (rosa damascena flower powder)) OR (rosa damascena flower water)) OR (rosa damascena flower water extract)) OR (rosa damascena flower wax)) AND (toxicity) – 19/1 (not relevant)

**Search Strategy in PubMed** [*# useful hits / total # of hits*]
Hydrolyzed Rosa damascena flower extract – 0/0
Rosa damascena bud extract – 0/1
Rosa damascena extract - 18/90
Rosa damascena flower – 11/49
Rosa damascena flower extract – 8/26
Rosa damascena flower oil – 15/19
Rosa damascena flower powder – 0/1
Rosa damascena flower water – 7/14
Rosa damascena flower water extract – 2/5
Rosa damascena flower wax – 0/0
Rosa damascene/a HRIPT – 0/0
Rosa damascena toxicity – 2/17
Rosa damascene – 3/31
Rosa damascena oil allergy – 0/0
Rose oil dermatitis - 3/8
Rose oil contact allergen- 1/1
Rose oil sensitization – 0/5
Rose oil photosensitization – 0/5
Rose oil depigmentation – 0/0
((((((((((hydrolyzed rosa damascena flower extract) OR rosa damascena bud extract) OR rosa damascena extract) OR rosa damascena flower) OR rosa damascena flower extract) OR rosa damascena flower oil) OR rosa damascena flower powder) OR rosa damascena flower water) OR rosa damascena flower water extract) OR rosa damascena flower wax) OR 90106-38-0) OR 8007-01-0) AND:
Toxicity -0/1
Cosmetic toxicity – 1/2
Reproductive effects- 0/4
Ocular irritation- 0/0
Skin irritation – 0/0
Inhalation toxicity – 0/0
Ocular toxicity – 0/0
Teratogenicity – 0/0
Immune – 2/3
(rosa damascene) OR (90106-38-0) AND (toxicity) – 2/20
((rosa damascena extract) OR (90106-38-0)) AND (toxicity) – 0/15
tox [subset] AND (rosa damascena extract) OR (90106-38-0) – 7/34

**General Web Search Strategy** [*# useful hits / total # of hits*]
Hydrolyzed rosa damascene flower extract – 0/159,000
Rosa damascene/a HRIPT -0/0; 2/310
Rosa damascena skin or dermal sensitization/irritation -0/0
Rosa damascena oil allergy – 0/263,000

## LINKS

**Search Engines**

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://toxnet.nlm.nih.gov/); (includes Toxline; HSDB; ChemIDPlus; DART; IRIS; CCRIS; CPDB; GENE-TOX)

Connected Papers - https://www.connectedpapers.com/

**Pertinent Websites**

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true

- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://iaspub.epa.gov/oppthpv/public_search.html_page
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program ) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

**Botanical Websites, if applicable**

- Dr. Duke's - https://phytochem.nal.usda.gov/phytochem/search
- Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
- GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
- Sigma Aldrich plant profiler- http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html
- American Herbal Products Association Botanical Safety Handbook (database) - http://www.ahpa.org/Resources/BotanicalSafetyHandbook.aspx
- European Medicines Agency Herbal Medicines - http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp
- National Agricultural Library NAL Catalog (AGRICOLA) https://agricola.nal.usda.gov/
- The Seasoning and Spice Association List of Culinary Herbs and Spices
- http://www.seasoningandspice.org.uk/ssa/background_culinary-herbs-spices.aspx

**Fragrance Websites, if applicable**

- IFRA (International Fragrance Association) – http://www.ifraorg.org/
- Research Institute for Fragrance Materials (RIFM)

**SEPTEMBER 2021 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT**

**Belsito Team – September 13, 2021**

**DR. BELSITO:** Okay. So, then we're moving on to Rosa Damascena. This is the first time we're looking at it, ten cosmetic ingredients. Use concentration data comments information for a trade name mixture of 0.1 to 1 percent of the flower water and the flower oil composition, allergen certificates characteristic, molecular certificates, tox file, method of manufacturing impurities. We've got a whole bunch of data, HRIPT for a fragrance product at 0.1 percent and another one at point essentially eight percent of the flower extract in a mask formulation at 0.13 percent.

It's reported to 223 formulations and quite a number of them are leave-on. It goes up to 32.7 percent face and neck products and 10.8 in other skincare preparations, and the flower extract and the bud extract have no reported uses.

So, before we start this, I just had a question as a side of a dermatologist who's patch testing patients and propylene glycol is not an overwhelmingly frequent allergen, but we see a fair amount of it. And so, if this is extracted, the flower oil and the flower water in these formulations that contain other ingredients -- in this case, pentalene glycol -- would those end up on the label of a product, or would it just be rose flower oil?

**MS. FIUME:** Jay, can you address that? You're on mute.

**DR. SNYDER:** I can address it tomorrow. We have a shampoo in our shower that has rose oil in it. I just noticed this morning.

**DR. ANSELL:** I'm sorry, was that to me?

**DR. BELSITO:** Yes, Jay.

**DR. ANSELL:** If it were a mixture, it would include both. If it was a residual, not necessarily, but if there was other glycols in there, they may be added up for purposes of predominance. So, it would really depend on how much is there. If it's trivial and non-functional, it doesn't require a disclosure. If it's a function of part of the product, it would.

**DR. BELSITO:** Okay, so what would be considered trivial?

**DR. ANSELL:** It would have to not contribute to the product. It would have to be non-functioning and low. So, I'm not sure that I have a sense of what that would be numerically.

**DR. BELSITO:** Well, propylene glycol is usually used as an emulsifier so I would imagine it would make an oil mix with something else in a lotion or a liquid that contains water.

**DR. ANSELL:** Okay. In that case, the product would be labeled as a -- its INCI name would be rosa and glycol.

**MS. RAJ:** Dr. Belsito, you mean pentylene glycol, right?

**DR. BELSITO:** Yeah, I mean, but it's come up with a number of particularly these botanical products, and I've been meaning to raise it for a while where there -- a small percentage of the product is supplied as a small percentage of the actual botanical in a vehicle that contains other constituents. I was always wondering if, when I'm reading product labels -- so I see a patient and they're using Paul's shampoo and they have a facial and neck dermatitis and they end up being allergic to pentylene glycol and it's not on the label. Does that mean it could be in the product; it's just not labeled? It's just labeled as rose flower oil?

**DR. ANSELL:** No, I think if it was an essence diluted in a vehicle that the vehicle would be part of the labeling.

**MS. FIUME:** But from what I've understood from Bart, this should be a trade name mixture technically and that there is this percent cutoff, and that, if it's in the product, it needs to be on the label. I would think looking at the breakdown for this trade name mixture, pentylene glycol probably makes up about 98 percent of that product.

**DR. ANSELL:** Yeah, so that would be --

**MS. FIUME**: Yeah.

**DR. BELSITO:** So, it would be labeled.

**DR. ANSELL:** Yeah.

**DR. BELSITO:** Okay, okay, so I had my little piece of contact dermatitis and allergies. So, we have a couple. So, the ones on the introduction on page 11 that are bolded and italicized are fragrance only, but it's not being reviewed by RIFM, so we're reviewing. Is that correct?

**MS. FIUME:** That's correct. Right, Preethi? RIFM said they are not doing a monograph of these right now, so it's being reviewed by CIR?

**MS. RAJ:** Yeah.

**DR. BELSITO:** Okay. Then PDF page 13, the flower wax, it says, "Volatile, hydrocarbon solvents, ethel alcohol, hexane, petroleum ether, benzene, are often used to extract," but do we know residual levels? Are we going to have to set that or discuss it? It just says, "traces of solvent were removed in a vacuum evaporator."

**DR. LIEBLER:** Yeah, I think what this is, is we actually saw this, Don, for RIFM when we toured that plant in (audio skip) where they're extracting the naturals, and they described making these waxes or concretes, which are very similar. They use various solvents. I think they would hopefully avoid benzene. But they use various solvents to extract the organic solubles, and then they evaporate everything down to essentially a solid cake. They can do additional alcoholic extracts with that sometimes, but that's what we end up with. I would not have concern about residual solvents in a process like that.

**DR. BELSITO:** Okay, but I guess my point is, is your concern so low that you wouldn't discuss it, or would you discuss it?

**DR. LIEBLER:** It's so low that I wouldn't discuss it.

**DR. BELSITO:** Okay.

**DR. LIEBLER:** Because they can't get to a wax if you get residual solvent in there.

**DR. BELSITO:** Right. Okay.

**DR. LIEBLER:** So, I thought that the method of manufacture for the flower extract really covered us for -- it contains just about everything. It represents the other ingredients. So, we've got I think composition, impurities for the, let's see, the extract, flower extract, and the flower oil. I thought we were actually pretty well covered for these ingredients. Method of manufacture, composition, and impurities are okay. GRAS food additives mitigate the limited tox data profile, and then it's just a question of sensitization.

**DR. BELSITO:** Yeah.

**DR. SNYDER**: That's all I had was sensitization. It's used up to 32.7 percent, and the max we have is the flower extract at 0.8 percent.

**DR. BELSITO:** Okay, and then, before we get to sensitization, PDF page 14 into the flower water, 90 parts per million of methanol. Is that concerning?

**DR. LIEBLER:** No. Very low.

**DR. BELSITO:** And then always, I mean the question is like when we're saying that the flower oil, the highest concentration of use is up to 32.7 percent in face and neck products, is that really the flower oil or is that the trade name mixture which contains a low amount of the flower oil?

**DR. SNYDER:** I would've gone with the flower water.

**MS. RAJ:** Yeah, whatever's reported in the Cosmetic Use section is coming from Council, Dr. Belsito, so it's not a trade mixture. It is the actual ingredients.

**MS. FIUME:** So, I think, Don, what you're talking about, I believe Carol's response to this -- and Jay you can correct me if I'm wrong -- it's as reported to them is how she passes it along to us. That they ask for the ingredient but, whatever information they are given, I don't think she always knows. Is that correct, Jay?

**DR. ANSELL:** Yeah.

**DR. BELSITO:** Jay, you're muted.

**DR. ANSELL:** Yeah. No, no. Yeah, she asks, and in cases like this where there's some confusion, we go back and ask whether -- what they meant. What is the activity, essentially?

**DR. BELSITO:** Okay. So we're presuming that 32.7 percent is the actual concentration?

**MS. FIUME:** That's what we presume when we put it in unless we're told otherwise.

**DR. ANSELL:** If it looks odd you know, I would go back and said, is that your 32 percent of the commercial product? What percent of that commercial product is actually the extract itself?

**DR. BELSITO:** Okay. Okey-doke, and then we're going to need the respiratory boilerplate which I think was there. So, we're going to have the issue of sensitization. We already know that the methyl eugenol is restricted by IFRA to 0.01 percent in fine fragrances, 0.004 percent in eau de toilettes, and down to 0.0002 percent.

I guess we're going to have to really go with the absence of knowing the amounts in these ingredients that we're using. That's going to be tough because it contains a lot of sensitizers.

Genotox, that micronucleus assay on page 16 for the flower oil. The flower oil is GRAS for FDA, so I didn't think so, but does it need to go into the discussion?

**DR. SNYDER:** I think that gives it too much attention. I think we can just default to the data package and the GRAS data says being sufficient for safety determination for cosmetic use.

**DR. BELSITO:** Okay, same with the in vitro cell transformation and the carcinogenicity?

**DR. SNYDER:** Yes.

**DR. BELSITO:** Okay. Question for you, Preethi, in the dermal irritation and desensitization. The in vitro study of the trade mixture with the pentylene glycol, do you know if they use pentylene glycol as the control?

**MS. RAJ:** Which one are you referring to, Dr. Belsito?

**DR. BELSITO:** So, PDF page 17, the in vitro study of the trade name mixture on the 0.1 to 1 percent demas, rosa demas in the flower oil and flower water, and pentylene glycol was predicted to be non-sensitizing in the EpiSkin model. Then they did an h-CLAT in vitro assay and --

**MS. RAJ:** Yeah, there appear to be three separate in vitro studies, Dr. Belsito, if you look under Table 7. So maybe are you referring to the first one because it looks like it was in DMSO, but you said the control.

**DR. BELSITO:** Okay.

**MS. RAJ:** Is the control PBS? I'm trying to look.

**DR. BELSITO:** So, it's non-sensitizing in EpiSkin. The h-CLAT was sensitizing and the KeratinoSens was negative, so we have one positive and one negative in vitro. We don't have a DPRA, but I'm assuming given the composition these are going to bind to protein, wouldn't you think, Dan?

**DR. LIEBLER:** I can't venture an opinion based on a complex mixture.

**MS. RAJ:** Dr. Belsito, on PDF page 65, that third paragraph under experimental procedure, does that answer your question? It says for each analysis, "three negative controls (PBS, olive oil, and DMSO-treated skins)."

**DR. BELSITO:** Yeah, okay. Thank you. They did an irritation control, okay. Okay, so we get rid of that comment. So, the botanical and respiratory boilerplates, emit total fragrance sensitizers and finished products to IFRA standards. Dan, you said you were okay with manufacturing and composition?

**DR. LIEBLER:** Yes.

**DR. BELSITO:** Okay. The data is almost exclusively on the flower oil and water. Do these cover the other flower ingredients?

**DR. LIEBLER:** Yes, they do.

**DR. BELSITO:** What about the bud?

**DR. LIEBLER:** The bud is not really, no.

**DR. BELSITO:** So, are we insufficient for that?

**DR. SNYDER:** Well, the rosebud is GRAS.

**DR. BELSITO:** Okay. It is GRAS?

**DR. SNYDER:** Yeah. Yeah.

**DR. BELSITO:** Okay.

**DR. LIEBLER:** You're right about that, Paul. Strictly speaking, the bud isn't handled in the -- oh, no, we're okay with the bud on method of manufacture and impurities. It's right there under composition impurities. It says via hydrodistillation, so that's steam distillation.

**DR. BELSITO:** Okay. So, we don't have sensitization/irritation at reported concentrations of 32.7 for flower and water, and 10.8 for flower oil. But we're going to have to come back with formulate to be non-sensitizing just based upon the components. So, do we need these? I mean, in the end? (Inaudible). What, Paul?

**DR. SNYDER:** Isn't that what we usually do for botanicals?

**DR BELSITO:** Well, that's what I mean. Particularly with this one where it contains a lot of sensitizers. We're going to say safe when formulated to be non-sensitizing, so we don't have sensitization and irritation data. But we're going to restrict it

based on sensitization, so do we need to go insufficient and say we want sensitization data up to 32.7 percent? Or we simply say, well, our conclusion is going to take care of that anyway?

**DR. SNYDER:** I'd say move it along and use the latter because we're likely not going to get it.

**DR. BELSITO:** Well, we could, but, I mean, the point is, is that we're going to ask for data that's not going to change. If it proves to be a sensitizer, we're going to say when formulated to be non-sensitizing. I mean, I'm fine. I mean, the point is I'm fine without asking for the data because of the way we handle botanicals when they have things like eugenol and geraniol or all of these fragrance sensitizers that have different standards.

**DR. LIEBLER:** Yeah, you're right, it's not going to have an effect on how we deal with the report, so.

**DR. BELSITO:** Okay, so then I think my conclusion after reading this was safe as used when formulated to be non-sensitizing.

**DR. LIEBLER:** I'm in the same place.

**MS. FIUME:** Don, I may actually go back to Carol and have her check that 32.7 because it is so different than all of the other data. I don't think anything else is even close to one percent for concentration of use, and it's just so our report is correct, not that it would have anything to do with what you were just talking about.

**DR. BELSITO:** Right.

**DR. ANSELL:** I would agree. It just doesn't sound right. But we can follow up and follow up and make sure that it isn't 32 percent of the product, which, itself, is one percent active.

**DR. BELSITO:** Okay. Okay, so it's 2:25. The next ingredient are the red algae. Do we want to take a break before we get into seaweed?

**DR. LIEBLER:** I don't think this one's going to take that long.

**DR. BELSITO:** Okay.

**DR. LIEBLER:** If anybody needs to take a break, we can take like a five minute. Okay, let's take a five-minute break. Come back at 2:30. I just need to stretch.

**DR. LIEBLER:** Sure.

**DR. BELSITO:** Okay.

**Cohen Team – September 13, 2021**

**DR. COHEN:** Okay, if there aren't any further comments, we can move on to Rosa damascena. Preethi, this is yours also. This is a draft report. It's the first time we're reviewing this, and this safety assessment is on ten derived ingredients. It's used as a skin conditioner and a fragrance, but there was a comment that RIFM has not and does not plan to review this.

Highest concentration of use is for the flower oil at 32.7 percent in face and neck products, and 10.8 percent in other skincare products. We have a frequency of use reported. Looks we have method of manufacturing on everything, but the plain extract, and the term extract is used under the heading of flower extract, so I'll get some more information. It's used as a food, and the impurities are provided.

My comments and thoughts were that the -- in the hydrodistillation process of the blossoms, there's citronellol, geraniol, limonene, and linalool, which are certainly known sensitizers. I have some further comments, but I'll stop and ask for the team to bring their thoughts in. Lisa, do you want to start?

**DR. PETERSON:** I didn't think there were really any deficiencies from the chemistry point of view because all the ingredients were derived from the flower and that the -- yeah, I actually thought that overall. I didn't have any requests, and I felt that the ingredients were safe with the qualification of the allergens.

**DR. COHEN:** Yeah, I mean, I think we need irritancy and sensitization at max use concentrations.

**DR. SHANK:** Yes.

**DR. COHEN:** Ron, other thoughts?

**DR. SHANK:** No, just insufficient for skin sensitization for the flower water at 32.7 percent and flower oil at 10.6 percent. Those are the highest concentrations of use. So, we need skin sensitization, flower water, and flower oil.

**DR. SLAGA:** I agree, and the rest of the data looks very good.

**DR. COHEN:** Yeah, the photoabsorption data looked okay. Again, one thought is this rosality contains 0.1 to 1 percent flower water and up to 1 percent flower oil and pentylene glycol, so, when we see irritancy studies, we're looking at a

percentage of a percentage, right? So, we're using commercial oil that has a small percentage of the actual chemical in it and then they're using just a fraction of that, so it can get a little confusing what the final concentration is being used. But I assume that, when we're looking at method of manufacturing, we're looking at that to see what products are being tested and what the common use is. I have that correct I assume.

**DR. SLAGA:** Yes.

**DR. BERGFELD:** Could I ask a question of Ron? Ron, it said in our documentation that flower water and wax was previously reviewed by the CIR Panel and safe at one percent.

**DR. SHANK:** Where's that?

**DR. BERGFELD:** It's within the text. I pulled it out. See if I can find it.

**DR. SHANK:** Let me look.

**DR. BERGFELD:** Bart, can you isolate that? I'm having trouble finding where I found that.

**DR. HELDRETH:** I'm also looking for it.

**DR. BERGFELD:** Oh, I think it's under uses.

**MS. RAJ:** I don't recall seeing this, Dr. Bergfeld, but perhaps I missed it.

**DR. BERGFELD:** I have a tendency to write things down when I see them that sound --

**DR. COHEN:** Wilma, can you just repeat your concern again?

**DR. BERGFELD:** It wasn't a concern; it was a fact that I had found that, in the text somewhere, that the flower water and flower wax had been previously reviewed and was safe at one percent.

**DR. SLAGA:** That would probably be in the introduction, wouldn't it?

**DR. BERGFELD:** It might be.

**DR. COHEN:** I couldn't find it searching the word previously.

**MS. RAJ:** Yeah, perhaps Bart can verify, but I don't think these ingredients were reviewed before.

**DR. HELDRETH:** Right, yeah, I just looked through our database of reports that we've done previously, and we don't have any of the Rosa damascena, but we certainly have other species within the Rosa genus, the centifolia and the caninae, including those waxes and oils, that the Panel has looked at and considered safe as used. So those compositions may be somewhat similar, but they're certainly from a different species.

**DR. BERGFELD:** Okay.

**DR. COHEN:** Okay, so we'll proceed with an IDA on that and make our comments tomorrow. We have red algae.

**DR. EISENMANN:** I was wondering if we could discuss the concern we have about the paragraph in a lot of the -- if you want to do it now or in another report, in the introduction to the botanicals about mixtures. I have been uncomfortable with that statement. I'm not sure it's needed to begin with, but I always thought it was the opposite, that usually you test individual components and then say that they don't always represent what the mixture would do, and that's why you're not including the individual components.

Rather than saying mixtures might not replicate that. And I'm not sure if it should be biological activity, both biological activity and then of the individual components. I think the statement should be opposite of what it is now or not put in the report at all. I'm not sure. As it stands, I'm not sure it adds anything to the report.

**DR. SHANK:** Where are you, Carol?

**DR. BERGFELD:** It's in several reports.

**DR. EISENMANN:** Right, it's in the introduction, and it's in the introduction of all the botanical reports.

**DR. BERGFELD:** Yeah.

**DR. SHANK:** For the Rosa?

**DR. PETERSON:** It's page 11.

**DR. EISENMANN:** Yeah, it's in the Rosa.

**DR. PETERSON:** And it's the one, two, three, four, fifth paragraph of the introduction, or sixth, depending on how you -- sixth paragraph. Second to the last paragraph.

**DR. COHEN:** One, two, three, four, five, six. Mixtures of different chemical compounds may not replicate, is that the sentence?

**MS. RAJ:** May contain hundreds of constituents. Botanicals such as Rosa damascena, derived ingredients may contain hundreds of constituents.

**DR. COHEN:** Hmm.

**DR. HELDRETH:** So typically, we've inserted this paragraph, although, you know, we're certainly open to changing the verbiage of it, but we've inserted this paragraph because typically when we look at botanicals (audio gap) and basing safety off of test data on the whole material, the mixture, versus looking at specific components therein individually.

A big part of that is because often, even though we may know that something like eugenol or some other constituent of potential concern is in there, often we have no clue what the concentration is going to be in there. So, typically, we will be seeing (audio gap). For example, say on a Rosa damascena extract, then we can (audio gap) some data there that is the most applicable, as compared to looking at the NHRIPT on eugenol or some other component therein. But (audio gap) should change here, and we're absolutely open to that.

**DR. COHEN:** You know, I was going to bring this issue up when we have our read across discussion. It somehow fits into this discussion a little bit when I looked at that manuscript though.

**DR. EISENMANN:** I think it could end after complex substance, period. Or you switch the reason why you're not considering -- or the opposite is what I've said. That toxicity from single components may not predict a potential toxicity of mixtures, and that's the reason why you're not putting in the individual component data. The way it's written now, I don't think it adds anything, the last phrase. So, I'm all right with it up to "complex substance," but the rest of it I think is either not necessary or should be opposite.

**DR. PETERSON:** I agree with the opposite because I think we do make some judgment on the mixture based on the individual components, but the reality is, is that you can't know how the individual component is going to behave in the mixture. So, I do get your point and I would -- I think it's important to phrase it -- say something, but I think to put it as the opposite so that -- and almost exactly how you said it.

**DR. COHEN:** Yeah, I get that too.

**DR. PETERSON:** Because then, conversely, all of the other individual ingredients should be, you know, we don't really know how the -- you know, we have this data on the individual chemical, but we don't how it's going to behave in the mixture of the cosmetic ingredients, and that's a true statement too.

I mean, I study tobacco smoke individual chemicals, but when you put the whole gamish together, they probably interact with one another to make overall toxicological properties. And I do like the word of toxicity as opposed to biological activity because we're really addressing the safety and the toxicity, and we're not really dealing with the -- you know, the biological activity could be both toxicity and beneficial effects. So, I would focus on the harmful effect, which is toxicity.

**DR. COHEN:** You know, ultimately, when we look at these mixtures, our sensitization and irritancy data is not based on individual ingredients; it's based on these mixtures, right? And our tox data's also based on these mixtures. We're not going in there and have -- we don't have HRIPT on isoeugenol, right? We have it on this mixture knowing there may be some of that in there, or limonene and linalool, but we don't -- we're not presented with limonene data.

**DR. SLAGA:** Right.

**DR. COHEN:** We just know it's in there, so we are looking at mixtures in aggregate, and in the back of our minds we understand the toxicities and sensitization potential of individual ingredients, but that's just part of the discussion in our minds, not how we're looking at this.

**DR. SLAGA:** Yeah. It's the toxicity of the total mixture. The ((inaudible).

**DR. PETERSON:** But there's always is some discussion about the individual chemicals, so I thought that it's worth putting something to put it in -- you know, put that discussion in context, but I'm okay. I mean, you've got a point about eliminating it too.

**DR. COHEN:** I think the sentence can be reworked a little bit, but we can't lose sight of the fact that the group looks at mixtures and, in fact, we can't -- we don't know how the individual components are working in this. We just don't.

If we get a positive sensitization on Rosa, let's say this comes back, we really don't know which component is doing it. We have suspicions that there may be a basket of sensitizers in there, but we don't know which one it is. So, I think that sort of verifies why the sentence looks the way it is, but I completely get this discussion, and maybe offline we can rework that a little bit.

**DR. BERGFELD:** We can turn it back to the group, the administrator scientist there to rework it. Bart, Monice?

**DR. HELDRETH:** For sure, for sure.

**DR. COHEN:** That was a punt back, Preethi, it sounded like. But I think it's worth it.

**DR. BERGFELD:** But I think there's a lot that's been discussed regarding that, so I think they could do that.

**DR. COHEN:** Okay, I'm good with that. Okay.

**MS. RAJ:** Thank you.

**DR. BERGFELD:** Can I ask a question to Bart? Since RIFM has not reviewed this, how will this particular document stand in the public or with them? Or are we totally different because we're looking at other uses other than fragrance?

**DR. HELDRETH:** Commonly, according to our procedures, the expert panel may exclude review of an ingredient if it's only used as a fragrance and some other safety assessment team has reviewed it or plans to review it in the near future. The whole point, of course, is to not duplicate efforts. But, in those cases where it is a fragrance ingredient, at least that's (audio gap) and there is no (audio gap) safety assessment, and RIFM does not have it on their near future docket. I'm always afraid (audio gap) something just our end, it's in public use, but nobody's going to look at the safety assessment of it.

So, in those cases, we typically keep that ingredient in the report and we're looking at its fragrance ingredient use in that position as one of the potential uses. If RIFM doesn't plan to look at it, I don't know who else is going -- but it is always the Panel's prerogative if they (audio gap) don't want to bring it, that they can throw it out.

**DR. COHEN:** Bart, you're coming in and out. I don't know if it's happening to everyone or just me.

**DR. BERGFELD:** Yeah, me.

**DR. SHANK:** Terribly.

**DR. HELDRETH:** Okay, I'm sorry.

**DR. COHEN:** I think --

**DR. HELDRETH:** Can you hear me clearly now? I (audio gap).

**DR. COHEN:** I think we got the general gist that we're going to keep it in. It's reported to us as a skin conditioning agent and a fragrance. The material that we have doesn't distinguish which use the data is presented to us as, so we're getting it as all-comer data. Right?

**DR. SHANK:** Right.

**DR. HELDRETH:** Yes, I mean, and that's true for any ingredient and any use type. Let me turn off my video, maybe that'll help the signal come through a little better.

Whenever we see a use reported, that's just a very general term that was reported to the nomenclature dictionary. We don't know that that necessarily applies in any given formulation, which type of use is actually being used there. In some cases, an ingredient may be in there for uses that aren't reported to the dictionary, or more than one use. To some extent, it's a little bit arbitrary looking at those uses, but the main reason we've looked at fragrance before as a potential exclusionary use type is because we were trying to avoid duplication of efforts with RIFM.

**Full Panel – September 14, 2021**

**DR. COHEN**: So, we have Rosa damascena, this is a draft report. It's the first time we're reviewing this. It's a safety assessment for 10 derived ingredients. It's used as a skin conditioning agent and a fragrance, but it appears RIFM has not and does not plan to review this. We have max concentration for Flower Water at 32.7 percent, and Flower Oil at 10 percent. The frequency of use is reported. This is also used as a food.

Our team came through with an insufficient data announcement. We needed an irritancy and sensitization data at max use concentration. The products have been reported to have sensitizers like benzyl alcohol, eugenol, limonene, linalool in these derived ingredients. That's our motion.

**DR. BERGFELD:** Is there a second, if not, a discussion?

**DR. BELSITO**: No.

**DR. BERGFELD:** You said no?

**DR. BELSITO**: No, there is no second.

**DR. BERGFELD:** No second. You want to discuss why you're not seconding it?

**DR. BELSITO**: Well, our conclusion that it's safe as used when formulated to be non-sensitizing. These components that are sensitizers are going to be present in other botanicals, so it's not going to really help you to have a HRIPT on Rose Water alone to see how high you can go with Rose Water, because in fact if Rose Water is combined with another botanical containing eugenol or Isoeugenol, then you're getting sensitization. So, why ask for something that we're not going to use?

**DR. BERGFELD:** David?

**DR. COHEN**: Yeah, you know, Don, I think it's a very provocative point. And, we didn't adjudicate it that way because it was a draft report; we didn't cut right to that. But, I understand and appreciate that take on it. And I would just ask our team if they had any other comments. Because if it's used as a food I don't think we have any other toxicology issues, and we sort of bypassed, as you said, Don, if it's formulated to be non-sensitizing and we know there're sensitizers in there, I find that okay. Lisa, Tom, Ron?

**DR. SLAGA:** I agree.

**DR. SHANK:** It's okay.

**DR. PETERSON**: I agree.

**DR. LIEBLER**: This has been what we've used for botanicals for just about as long as I've been on the panel.

**DR. SHANK:** Can you hear me now?

**DR. BELSITO**: Yes.

**DR. COHEN**: Yes.

**DR. BELSITO**: Yay, Ron.

**DR. SHANK:** All right.

**DR. HELDRETH**: So, I would just like to --

**DR. BERGFELD:** Ron, did you have something to say, because Bart has something?

**DR. SHANK:** Okay, I would just add if you say when formulated to be non-sensitizing that's okay. I was pushing for sensitization data, but you would see the same level of safety if you say when formulated to be non-sensitizing.

**DR. BERGFELD:** All right, Bart?

**DR. SNYDER**: I think also we were going to get clarification whether that 32.7 percent was of the product or how that was measured. Because that was kind of an outlier percentage when all the rest of them are very, very, low. So, I think some of this may go away if we get clarification as to what that 32.7 percent represents.

**DR. BERGFELD:** Bart, I'm sorry, we're trying to get you to speak.

**DR. HELDRETH**: That's okay, thank you. So, of course, it's the panel's prerogative to go forward with this conclusion as is, but I just wanted to remind you historically with botanical, when we add the caveat of formulated to be non-sensitizing, that caveat is typically not used for the ingredient itself but for cumulative exposure when multiple ingredients with the same constituents of concern are used in the same formulation.

So typically, when we add that caveat for botanicals, we have some language in the discussion that essentially tells the reader that, you know, these ingredients themselves are fine, there's not a concern for sensitization, but you may get above a threshold of concern if you combine multiple ingredients that have those same constituents of concern. So, it's fine if the panel wants to go with this. I just wanted to say it's a break from the historical path, and it'll require some different language in the discussion.

**DR. BELSITO**: Well, it's probably a break from the historical path, but let me just tell you how the Expert Panel for Fragrance Safety would approach this in the absence of data on the actual product. So, we would look at the sensitizers, and those are mentioned in the report. We would look at the sensitizer with the lowest NESL, and that's mentioned in the report. And then we would apply it across the QRA categories.

So, that information is available to manufacturers if they want to look at what would be the safe level of the standard for this. So, the data that's needed is really out there in the literature and could be supplemented to this report. And, that's where we would derive, at least from the dermal aspect, a safety for sensitization on a whole botanical where we did not have any data on the actual complex mixture.

We would look at the various sensitizers. We'd obtain the lowest NESL. If we didn't have data we'd use reactive or nonreactive DST and then run it through QRA. So, there is data there; there's just not a HRIPT on the whole ingredient.

**DR. BERGFELD:** Don, are you suggesting that be done?

**DR. BELSITO**: No, I don't think it needs to be done. I mean, that's not our duty that's manufacturers' duty. The data is there; the IFRA standards, the NESL, on all the sensitizers have been published.

**DR. BERGFELD:** Okay.

**DR. COHEN**: Don? Yeah, just a question, again, it's a hypothetical. If we got a HRIPT on Flower Oil at 10 percent, and a quarter of the panelist were reacting, would our conclusion shift at all?

**DR. BELSITO**: Well, you know, I mean, again, the problem with the botanicals, David, is that the concentration of individual ingredients are going to vary depending upon the harvest, where it actually was grown, how it was extracted, yada, yada, yada. So, that particular product at 10 percent may induce sensitization, whereas another Rose Water that's manufactured by a different method, coming from a different country, harvested at a different time in its lifecycle, may not.

So, that's the complexity and the reason I think you would share my sentiment that I hate trying to patch test with botanicals, because I don't know if I'm really missing the problem.

**DR. COHEN**: I share your dislike of it. So, if my team is okay with this I would move to revise my motion.

**DR. SLAGA:** I agree.

**DR. COHEN**: The motion would be safe as used in current concentration and practice when formulated to not be sensitizing.

**DR. BELSITO**: Second.

**DR. BERGFELD:** Any further discussion by the team members, or the panel?

**DR. BELSITO**: I just think the change in that paragraph in the introduction regarding botanicals.

**DR. BERGFELD:** Okay. All right, no other discussion?

**DR. BELSITO**: No.

**DR. BERGFELD:** Okay, all those opposed? Abstaining? Unanimous approval of the Rosa damascena. Okay, then moving on to the third ingredient in this list, Dr. Belsito, the Saccharum officinarum.

# Safety Assessment of *Rosa damascena*-Derived Ingredients as Used in Cosmetics

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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: Lisa, A. Peterson, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Preethi S. Raj, M.Sc., Senior Scientific Analyst/ Writer, CIR.


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## ABBREVIATIONS

| | |
|---|---|
| ALP | alkaline phosphatase |
| ALT | alanine aminotransferase |
| AST | aspartate aminotransferase |
| CAS | Chemical Abstracts Service |
| CIR | Cosmetic Ingredient Review |
| Council | Personal Care Products Council |
| Cyt B | cytochalasin B |
| *Dictionary* | *International Cosmetic Ingredient Dictionary and Handbook* |
| DMEM | Dulbecco's modified Eagle's medium |
| DMSO | dimethyl sulfoxide |
| EC | maximal effective concentration |
| ECHA | European Chemicals Agency |
| FBS | fetal bovine serum |
| FDA | Food and Drug Administration |
| GAE | gallic acid equivalents |
| GC-MS | gas chromatography – mass spectroscopy |
| GRAS | generally recognized as safe |
| HCA | hydroxycitric acid |
| h-CLAT | human cell line activation test assay |
| HeLa | human cervical cancer cell line |
| HDL | high-density lipoprotein |
| HRIPT | human repeat insult patch test |
| IFRA | International Fragrance Association |
| LD | lethal dose |
| LDL | low-density lipoprotein |
| MIT | minimum induction threshold |
| MMC | mitomycin C |
| MTT | 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide |
| N/A | not applicable |
| NR | not reported/none reported |
| NS | not specified |
| OECD | Organisation for Economic Co-operation and Development |
| OTC | over-the-counter |
| Panel | Expert Panel for Cosmetic Ingredient Safety |
| PBS | phosphate-buffered saline |
| PHA | phytohemagglutinin |
| RIFM | Research Institute for Fragrance Materials |
| RPMI | Roswell Park Memorial Institute |
| SCCS | Scientific Committee on Consumer Safety |
| SLS | sodium lauryl sulfate |
| TG | test guideline |
| TG | triglyceride |
| THP-1 | human monocytic leukemia cell lines |
| TNBS | trinitrobenzenesulfonic acid |
| US | United States |
| VCRP | Voluntary Cosmetic Registration Program |

## ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 10 *Rosa damascena*- derived ingredients as used in cosmetic formulations, which are reported to function in cosmetics mostly as skin conditioning agents and fragrance ingredients. Because final product formulations may contain multiple botanicals, each containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. With *Rosa damascena* – derived ingredients, the Panel was concerned about the presence of benzyl alcohol, eugenol, methyl eugenol, geraniol, citronellol, limonene, linalool, and farnesol as potential allergens in cosmetics. Industry should use good manufacturing practices to minimize impurities that could be present in botanical ingredients. The Panel considered all the data and concluded that these ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-sensitizing.


## INTRODUCTION

This assessment reviews the safety for the following 10 *Rosa damascena*-derived ingredients, as used in cosmetic formulations:

Hydrolyzed Rosa Damascena Flower Extract
Rosa Damascena Bud Extract
Rosa Damascena Extract
Rosa Damascena Flower
Rosa Damascena Flower Extract
Rosa Damascena Flower Oil
Rosa Damascena Flower Powder
Rosa Damascena Flower Water
Rosa Damascena Flower Water Extract
Rosa Damascena Flower Wax

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), some *Rosa damascena*-derived ingredients are reported to function as skin conditioning agents and fragrance ingredients in cosmetic products (Table 1).[1] Additionally, these ingredients are sometimes reported to function as antioxidants and cosmetic astringents. Common names for *Rosa damascena* include damask rose, pink rose, Turkish rose, and Bulgarian rose.[2]

The Expert Panel for Cosmetic Ingredient Safety (Panel) does not review ingredients that function only as fragrance ingredients because, as fragrances, the safety of these ingredients is evaluated by the Research Institute for Fragrance Materials (RIFM). Rosa Damascena Extract, Rosa Damascena Flower Extract, Rosa Damascena Flower Powder, and Rosa Damascena Flower Wax are reported to function only as fragrance ingredients, according to the wINCI *Dictionary*. However, according to personal communications with RIFM in May-June 2020, these ingredients have not been reviewed, and are not currently scheduled for review by RIFM; thus, the Panel is reviewing the safety of these ingredients.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline ). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Botanicals, such as *Rosa damascena*-derived ingredients, often contain hundreds of constituents, some of which have the potential to cause adverse effects. For example, geraniol, citronellol, and linalool are known potential dermal sensitizers. In this assessment, the Panel is evaluating the potential toxicity of each of these *Rosa damascena* – derived ingredients as a whole, complex substance; toxicity from single components may not predict the potential toxicity of botanical ingredients.

Also, with botanicals, it is often not known how the substance being tested in a study compares to the cosmetic ingredient. In the report text, if it is known that the material being tested is a cosmetic ingredient, the INCI naming convention is used (i.e., the names of cosmetic ingredients are capitalized, without italics (e.g., Rosa Damascena Extract)). If it is not known that the test substance is the same as the cosmetic ingredient, the taxonomic naming conventions (i.e. with genus and species name italicized (e.g., a *Rosa damascena* extract)) is used.

## CHEMISTRY

### Definition and Plant Identification

Definitions of the 10 *Rosa damascena*-derived ingredients reviewed in this safety assessment are presented in Table 1.[1] Generically, the bud is defined as a not yet developed shoot in the axil of a leaf, often covered with scales, or a young flower that has not bloomed. The flower is defined as the reproductive shoot in flowering plants, usually with sepals, petals, stamens, and pistil(s).

*Rosa damascena* is an ornamental, old garden rose hybrid, belonging to the Rosaceae family, with more than 200 species and 18,000 cultivars around the world.[3] Thought to originate in the Mediterranean or Asia, *Rosa damascena* is mainly grown in Turkey, Bulgaria, Morocco, Iran, Egypt, France, China, and India, with Turkey and Bulgaria reported to be the largest producers.[2] Commonly known as the damask rose, *Rosa damascena* is one of the few rose species which possesses the

characteristic rose fragrance, owing to its highly valuable aromatic oil.[2] The total world production of *Rosa damascena* oil and *Rosa damascena* concrete (flower wax) is estimated to be 15 - 20 tons.

*Rosa damascena* is a thorny shrub, up to 2.5 m in height, that blooms in the spring.[4] The stem has numerous stout and hooked prickles, occasionally mixed with glandular bristles, while the leaves are pinnate and compound with 5 - 7 leaflets that are 2.5 - 6.3 cm long, ovate-oblong, and have serrated edges.[5] Flowers have an average of 33 petals, which are arranged in a corymb, and can range in color from white to light red; most *Rosa damascena* flowers are light pink or magenta in hue.[4,5]

## Chemical Properties

A summary of chemical properties described for *Rosa damascena*-derived ingredients are provided in Table 2.

*Rosa Damascena Flower Oil and Rosa Damascena Flower Water*

A supplier described a trade mixture, comprising 0.1 - 1 % Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower Water formulated in pentylene glycol, as a transparent, colorless liquid with a characteristic odor.[6] At 20 °C, the refractive index of this trade mixture is 1.434 - 1.444.

## Method of Manufacture

Most of the methods below are general to the processing of *Rosa damascena*-derived materials, and it is unknown if these apply to cosmetic ingredient manufacturing. In some cases, the definition of the ingredients, as given in the *Dictionary*, provides insight as to the method of manufacture.[1]

*Rosa Damascena Bud Extract*

In a method of preparing a *Rosa damascena* bud extract, 1700 g of air-dried, whole buds of *Rosa damascena* were coarsely powdered and extracted with distilled water at 100 °C for 2 h.[7] Upon removal of the water under vacuum, 720 g of a *Rosa damascena* bud extract were obtained, suspended in distilled water, and sequentially partitioned with n-hexane, chloroform, ethyl acetate, and n-butanol to create multiple fractions.

*Rosa Damascena Flower Extract*

In a pharmacological analysis of *Rosa damascena* petals, 100 g of dried *Rosa damascena* flower powder was passed through a sieve and macerated, separately, with water, ethanol, chloroform, ethyl acetate, and petroleum ether for 7 d, with occasional agitation.[8] The extracts were filtered through muslin cloth, and the filtrates were evaporated under reduced pressure, vacuum dried, and stored.

*Rosa Damascena Flower Oil*

A large quantity of *Rosa damascena* flowers yields a relatively small amount of a *Rosa damascena* flower oil (e.g., 4000 kg of flowers yields 1 kg of oil).[9] Optimal yield and higher quality *Rosa damascena* flower oil is produced from roses freshly picked in either the early morning hours or colder temperatures, compared to roses subject to heat or fermentation, due to minimal evaporation.[2,10]

A *Rosa damascena* flower oil has been manufactured traditionally for centuries, using copper stills, loosely connected to a condensing apparatus.[11] In the present-day, a *Rosa damascena* flower oil is often produced industrially in well-sealed, steel stills, producing oils with a richer constituent profile, which are of higher quality.[12]

*Rosa Damascena Flower Oil and Rosa Damascena Flower Water*

A *Rosa damascena* flower water is often a by-product of the hydrodistillation process to produce a *Rosa damascena* flower oil.[2] Both fresh and dried *Rosa damascena* flowers can be utilized in the manufacture of a *Rosa damascena* flower oil and water.[13,14] In a study using fresh *Rosa damascena* flowers, 400 g of fresh flower petals were hydrodistilled with 2 l of water for 4 h in a Clevenger apparatus, to yield 800 ml of a *Rosa damascena* flower water.[13] In a study using shade-dried *Rosa damascena* petals, 60 g of rose petals (with 79.3% moisture removed) were hydrodistilled with 1.5 l of water for 4 h to prepare 800 ml of a *Rosa damascena* flower water.[14]

*Rosa damascena* flower oil, and consequently *Rosa damascena* flower water, are often produced by the hydrodistillation of *Rosa damascena* flowers in a Clevenger apparatus, or via an analogous steam distillation procedure.[14] In a method of preparing a *Rosa damascena* flower oil, a cauldron was filled with 200 kg of fresh *Rosa damascena* flowers and water, and boiled for approximately an hour.[9] After boiling, steam transported through an attached condensing pipe to a refrigerator yielded a distillation product of a *Rosa damascena* flower water. This *Rosa damascena* flower water moved from the first Floridian container, where a very small quantity of oil (~15%) was segregated, and the water was boiled for about 2.5 h, twice, before condensing in a separate refrigerated pipe, where it passed through a second Floridian container, and separated from the remaining oil. After repeated distillations, rose oil from both Floridian containers was combined and passed through a clean filter; a final yield of 50 - 60 g of a *Rosa damascena* flower oil was obtained.

*Rosa Damascena Flower Powder*

*Rosa damascena* flower petals were separated from the sepals and shade-dried.[8] The dried petals were then ground into a fine powder, resulting in a *Rosa damascena* flower powder.

*Rosa Damascena Flower Water*

A supplier has reported that Rosa Damascena Flower Water is also produced from dried raw material.[15] The water phase of dried *Rosa damascena* flowers processed via steam distillation is further concentrated and added to a 80%, 1,3-butylene glycolic solution.

*Rosa Damascena Flower Water Extract*

Fresh *Rosa damascena* flowers (2.0 kg) were soaked in 12.5 l water overnight to yield 1.0 l of a *Rosa damascena* flower water.[16] Well-stirred *Rosa damascena* flower water (500 ml) was extracted with dichloromethane (250 ml x 5) and dried over fused calcium chloride/anhydrous sodium sulfate. After the solvent was removed by distillation, a *Rosa damascena* flower water extract (dichloromethane) was stored at -5 °C.

*Rosa Damascena Flower Wax*

Volatile, hydrocarbon solvents, such as ethyl alcohol, hexane, petroleum ether, and benzene, are often used to extract *Rosa damascena* absolute and concrete, a semisolid, waxy substance from *Rosa damascena* flowers.[11,17] During the industrial production of this *Rosa damascena* flower wax, 600 - 750 kg of *Rosa damascena* flowers were added to a 3000 l extraction vessel, filled half-way with n-hexane, and extracted in two cycles for 20 min at 60 - 65 °C.[17] The resulting extracts were combined in an evaporator, and traces of the solvent were removed in a vacuum evaporator, to yield > 1 kg of a *Rosa damascena* flower wax.

## Composition and Impurities

Solid residues, containing mainly straight-chain saturated hydrocarbons and the esters of carboxylic acids, were identified in a gas chromatography-mass spectrometry (GC-MS) analysis of *Rosa damascena* flower extracts (absolute), produced from a *Rosa damascena* flower wax (concrete).[18]

Of the 26 fragrance allergens defined by the European Union Cosmetic Directive, benzyl alcohol, eugenol, geraniol, citronellol, limonene, linalool, and farnesol are present in *Rosa damascena*-derived ingredients.[2,13,14,16,17,19-22] The components identified in *Rosa damascena*-derived ingredients can vary greatly, depending upon extraction solvent and method,[14] part of the plant,[7] or growth and harvest conditions.[23,24] A percent-composition profile of constituents found in a *Rosa damascena* flower oil, a flower water, a flower water extract, and a flower wax, produced from dried and fresh flowers, is presented in Table 3.

*Rosa Damascena Bud Extract*

A *Rosa damascena* bud extract (720 g), obtained via hydrodistillation, was used to create concentrated fractions with n-hexane (0.5 g), chloroform (2.8 g), ethyl acetate (124.7 g), n-butanol (274.4 g), and water (317.6 g).[7] Repeated silica gel, octadecyl silane, and Sephadex LH-20 column chromatography of the ethyl acetate fraction yielded five main flavonoids, including: isoquercitrin, afzelin, cyanidin-3-*O*-β-glucoside, quercetin gentiobioside, and kaempferol-3-*O*-β-D-glucopyranosyl(1→4)-β-D-xylopyranoside.

*Rosa Damascena Extract*

Flavonoids, such as kaempferol, quercetin, and pectolinargenin, were identified as the major components in hydroalcoholic, ethyl acetate: ethanol, and ether extracts of dried and powdered *Rosa damascena* flowers.[25]

In an compositional analysis of *Rosa damascena* fruit extracts, a 5 g sample of *Rosa damascena* fruit yielded 332 mg/100 g ascorbic acid, while a 2 g sample of *Rosa damascena* fruit yielded 7.10 µg/g α- tocopherol, and 3.70 µg/g β- carotene.[26] The fatty acid content was determined to be 93.18% in *Rosa damascena* fruit seed oil.

*Rosa Damascena Flower*

In a reversed phase high performance liquid chromatography test of fresh *Rosa damascena* flowers, the following components were identified, in µg/ml: gallic acid (125.41), rutin (84.98), quercitrin (360.87), myricetin (170.43), quercetin (81.35), and kaempferol (2.36).[27] Trace amounts of catechin were also identified.

*Rosa Damascena Flower Extract*

The total phenolic content of fresh and spent *Rosa damascena* flowers, used in the hydrodistillation process, was measured in gallic acid equivalents (GAE/g).[28] The GAE of these *Rosa damascena* flowers, extracted with methanol, were measured at 276.02 ± 2.93 mg GAE for fresh flowers, and 248.97 ± 2.96 mg GAE, for spent flowers. A *Rosa damascena* extract, produced from rose blossoms spent in the hydrodistillation process, produced sufficient amounts of citronellol, nerol, geraniol, and β-phenethyl alcohol, suggesting the utility of rose waste in obtaining valuable extracts.[18]

*Rosa Damascena Flower Oil*

*Rosa damascena* flower oil is characterized by high percentages of monoterpene alcohols, including citronellol (35.1%), geraniol (17.9%), nerol (8.4%), phenethyl alcohol (2.5%), and linalool (1%).[2] Additionally, various hydrocarbons, oxides, ethers, esters, aldehydes, and phenols are found in *Rosa damascena* flower oil. Citronellol is the major component which determines rose oil quality. Methyl eugenol levels may be over 2.5%, especially in the oils distilled from rose flowers subject to excess or long-term fermentation.[2]

According to International Fragrance Research Association (IFRA) standards, *Rosa damascena* absolute can comprise 0.1% benzyl alcohol, 0.5% methyl eugenol, 2.3% eugenol, 5% geraniol, and 6% citronellol.[29-34] Additionally, *Rosa damascena* oil is reported to contain 0.02% benzyl alcohol,1% farnesol, 1.2% eugenol, 2% methyl eugenol, 20% geraniol, and 34% citronellol, according to IFRA standards.

*Rosa Damascena Flower Oil and Rosa Damascena Flower Water*

Specifications provided by a supplier indicate that a trade mixture containing 0.1 - 1% Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower Water, formulated in pentylene glycol, should contain 0.15 – 0.35 % phenethyl alcohol and < 10 ppm methyl eugenol.[35] In this trade mixture, most of the 26 allergens defined by the European Union Cosmetic Directive are below the level of detection (< 1ppm), with the following exceptions: benzyl alcohol (41 ppm), citral (16 ppm), citronellol (1080 ppm), farnesol (6 ppm), geraniol (365 ppm), and linalool (33 ppm).[36]

This supplier measured the mean concentration of several constituents in the *Rosa damascena* fraction mixture, using 3 batches of the same trade mixture.[37] It was determined that the *Rosa damascena* fraction mixture could contain 1 ppm of benzaldehyde, 2 ppm of pinene, 36 ppm of isobutenyl methyltetrahydropyran, 40 ppm of terpineols, 48 ppm of β-caryophyllene, 50 ppm of citronellal, 150 ppm of 1-nonadecene, 350 ppm of nonadecane, and 400 ppm of nerol.

*Rosa Damascena Flower Water*

Due to an increased solubility in water, phenethyl alcohol is the major component collected in a *Rosa damascena* flower water, during the hydrodistillation of roses to produce *Rosa damascena* flower oil.[2] In a GC-MS analysis of *Rosa damascena* flower water samples, phenethyl alcohol was present at up to 39.53%, geraniol at up to 24.01%, and β-citronellol at up to 10.26%.[20]

Methanol and ethanol, produced via plant fiber fermentation, were measured in 90 commercial herbal distillates, including 9 *Rosa damascena* water samples, by GC-MS.[38] The methanol content in *Rosa damascena* flower water samples was 9.04 mg/dl. Two *Rosa damascena* flower water samples were found to have the highest average ethanol content (56.77 mg/dl and 38.97 mg/dl).

A supplier reported that Rosa Damascena Flower Water, formulated in a trade mixture with butylene glycol, contained no more than 20 ppm heavy metals and 2 ppm arsenic.[15] No further details were provided.

*Rosa Damascena Flower Water Extract*

Dichloromethane extracts of a *Rosa damascena* flower water produced from fresh flowers contained up to 50% more *Rosa damascena* flower oil than flower water produced from dried flowers.[16] These fresh flower dichloromethane extracts also contained mostly phenethyl alcohol (69.7 - 81.6%), linalool (1.5 - 3.3%), citronellol (1.8 - 7.2%), nerol (0.2 - 4.2%), and geraniol (0.9 - 7.0%).

*Rosa Damascena Flower Wax*

Phenethyl alcohol is present at over 50% in a *Rosa damascena* flower wax.[2] Although citronellol, geraniol, and nerol contents are relatively lower, the phenethyl alcohol content is higher in a *Rosa damascena* flower wax than in a *Rosa damascena* flower oil. As per IFRA standards, *Rosa damascena* concrete can naturally comprise 0.5% methyl eugenol, 1% eugenol, 2.7% geraniol, and 4.7% citronellol.[30,31,33,34]

## USE

### Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2022 VCRP survey data, Rosa Damascena Flower Water is reported to be used in 302 formulations, Rosa Damascena Flower Extract is reported to be used in 293 formulations, and Rosa Damascena Flower Oil is reported to be used in 229 formulations (Table 4).[39] Rosa Damascena Flower Oil is reported to be used at up to 10.8% in other skincare

preparations, and according to a manufacturer, is sold with instructions to dilute the product before use, hence, resulting in much lower use concentrations in finished products.[40,41] The highest reported leave-on use concentration for Rosa Damascena Flower Oil is at up to 0.16% in non-spray face and neck products. Results from the concentration of use surveys, conducted in 2019 by the Council, indicate that the highest reported leave-on, use concentration for Rosa Damascena Flower Water is at up to 1.9% in foundations. Hydrolyzed Rosa Damascena Flower Extract and Rosa Damascena Bud Extract are not in reported to be in use, according to the VCRP and industry survey.

These ingredients have been reported to be used in products that may lead to incidental ingestion and exposure to mucous membranes, such as in lipstick; for example, Rosa Damascena Flower Oil and Rosa Damascena Flower Wax are reported to be used at up to 0.01% and 1.1% in lipsticks, respectively. Additionally, some of these ingredients are reported to be used in products applied near the eye (e.g., up to 0.13% Rosa Damascena Flower Wax in eyeliners).

Several of these ingredients are used in cosmetic products that could possibly be inhaled; for example, Rosa Damascena Flower Oil is reported to be used at up to 0.0003% in aerosol hair spray, Rosa Damascena Extract is reported to be used at up to 0.00007% in aerosol spray deodorant formulations, and Rosa Damascena Flower Extract is reported to be used in face powder formulations (concentration of use not reported). In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.[42,43] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[44,45] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[44] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[46-48]

The *Rosa damascena*-derived ingredients named in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[49] However, according to Regulation EC No 1223/2009, restrictions for methyl eugenol, a minor component of *Rosa damascena*, include a maximum concentration of 0.001% in rinse-off products and 0.0002% in other leave-on and oral products that are ready for use.[50] Additionally, the same regulation states that citronellol, eugenol, farnesol, geraniol, limonene, and linalool (fragrance allergens) are required to be included in cosmetic labelling when use concentrations for these individual constituents in formulation exceed 0.001% for leave-on products and 0.01% for rinse-off products.

### Non-Cosmetic

According to the US FDA, the essential oils, oleoresins (solvent-free), and natural extractives/distillates of *Rosa damascena* rose absolute, rose otto, rose buds, rose flowers, and rose fruit are generally recognized as safe (GRAS) for their intended use in foods [21CFR182.20].

Traditionally, *Rosa damascena* flowers and derived products have a wide range of uses in religious ceremonies, pharmaceuticals, and food, especially in the Middle East and Southeast Asia.[4,14,20] Dried *Rosa damascena* flower petals and flower water are added to flavor and embellish food, and are consumed in Iran as a digestive aide.[4,14] In traditional medicine, *Rosa damascena* flower oil and flower water are considered to possess antibacterial, analgesic, antioxidant, and anti-inflammatory properties.[51] Consequently, these ingredients have been used in aromatherapy,[52,53] and for the treatment of many conditions, including skin, eye, and oral ailments,[51] arthritis,[54] dysmennorhea,[55] pediatric seizures,[56] depression, and cognitive decline.[57]

## TOXICOKINETIC STUDIES

No relevant toxicokinetic studies on *Rosa damascena*-derived ingredients were found in the published literature, and unpublished data were not submitted. In general, toxicokinetic data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

## TOXICOLOGICAL STUDIES

### Acute Toxicity Studies

The acute dermal and oral toxicity studies summarized below are described in Table 5.

The acute dermal $LD_{50}$ of *Rosa damascena* flower oil was determined to be > 2500 mg/kg in rabbits.[58-60] No toxic effects were observed and the acute oral $LD_{50}$ of a *Rosa damascena* flower extract, prepared in 0.7% carboxymethylcellulose, was > 2000 mg/kg in male and female Swiss albino mice.[61] In one study, the acute oral $LD_{50}$ of *Rosa damascena* flower oil was determined to be > 5000 mg/kg in rats.[58-60] In subsequent oral toxicity studies, the acute oral $LD_{50}$ of *Rosa damascena* flower oil was determined to be 5525 mg/kg in male rats, and 2975 mg/kg and 3972 mg/kg, in mature and immature female

rats, respectively.[59] Swiss albino mice dosed orally with up to 6000 mg/kg of a *Rosa damascena* flower water extract did not die during the 24-h post-treatment observation period, and the acute $LD_{50}$ was determined to be > 6000 mg/kg.[62]

### Short-Term and Subchronic Toxicity Studies

Details of the short-term and subchronic oral toxicity studies summarized below are provided in Table 6.

Groups of 10 Wistar rats were administered 0, 2.5, 5, 25, or 50 mg/kg/d aqueous *Rosa damascena* flower extract, via gavage, for 30 d.[63] Body weight gain was greater in all test groups compared to controls, but the percent weight gains were not statistically significant. Groups of 5 dogs were administered distilled water or lactulose (controls), or, 90, 180, 360, 720, or 1440 mg/kg/d aqueous *Rosa damascena* flower extract, in the diet, for 10 d.[64] No significant differences were observed between groups for respiration, temperature, or cardiac response. A dose-dependent increase of diarrhea was observed, starting with the lowest dose of 90 mg/kg/d. Animals in the 720 and 1440 mg/kg/d groups exhibited slight weight loss after day 7, which was attributed to possible diarrhea-induced malabsorption, or dehydration. Fifteen Swiss albino mice (compared to 10 controls) were orally administered 300 mg/kg/d *Rosa damascena* flower water extract for 28 d.[62] No significant differences from controls in body or organ (liver, intestine, heart, lungs, kidneys and spleen) weights, tissue, mortality, or hematological biomarkers were observed upon sacrifice. Groups of 25 Swiss albino mice were orally dosed with 0 or 300 mg/kg/d *Rosa damascena* flower water extract for 90 d.[62] Two control and 2 treated mice died in the first month, one control mouse and 2 treated mice died in the second month, and no mortality occurred in the third month of observation. Mice killed after the first, second, and third month (number not specified), progressively exhibited mild hydroponic degeneration in the liver, congestion in coronary blood vessels, and peribronchiolar aggregation of round cells in the lungs. No significant differences were observed in body and organ weights, and various hematological markers, compared to the control group.

## DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity studies were not found in the published literature, and unpublished data were not submitted.

## GENOTOXICITY

### In Vitro

*Rosa Damascena Flower Oil*

In a micronucleus assay, doses of 1, 10, 50, 100, 150, or 200 µg/ml *Rosa damascena* flower oil were added to whole blood samples treated with Roswell Park Memorial Institute (RPMI) culture medium supplemented with fetal bovine serum (FBS) containing L-glutamine, antibiotics, and phytohemagglutinin (PHA).[65] Cytochalasin B (Cyt B) was added at a concentration of 6 µg/ml 44 h after PHA stimulation. The frequency of micronuclei in binucleated lymphocytes was significantly greater ($p < 0.05$) in samples treated with > 50 µg/ml *Rosa damascena* flower oil, compared to negative and 1% dimethyl sulfoxide (DMSO)-treated controls.

No inhibition of mitotic activity was observed when a *Rosa damascena* flower oil (absolute) and a *Rosa damascena* flower oil (extracted from fresh flowers) were tested on cultures of normal human blood lymphocytes at doses of 10 µg/ml.[66] *Rosa damascena* flower absolute oil showed significant antimutagenic activity ($p < 0.001$) when added at a dose of 10 µg/ml to a blood lymphocyte culture treated with 300 ng/ml mitomycin C (MMC).

*Rosa Damascena Flower Oil and Rosa Damascena Flower Water*

A trade mixture of 0.1 - 1% Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower Water, in pentylene glycol, was tested in an Ames test using *Salmonella typhimurium* strains TA 98, TA 100, TA 102, TA 1535, TA 1537, at up to 5000 µg/plate, with and without metabolic activation.[67] No signs of precipitate or dose responses were found at any concentration. The test material was not deemed genotoxic.

## CARCINOGENICITY STUDIES

Carcinogenicity studies on the *Rosa damascena* - derived ingredients were not found in the published literature, and unpublished data were not submitted.

## OTHER RELEVANT STUDIES

### Cytotoxicity

*Rosa Damascena Flower Extract*

A methanolic extract of dried *Rosa damascena* flowers was used in an 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) colorimetric assay to evaluate in vitro activity against human cervical cancer (HeLa) and African green monkey kidney epithelial (Vero) cell lines.[68] Studies examining the effect of increasing doses of the extract upon cytotoxicity exhibited $IC_{50}$ values at 265 µg/ml and > 1000 µg/ml *Rosa damascena* flower extract on the HeLa and Vero

cells, respectively. Additionally, a selectivity index (SI), of > 3.8 for the *Rosa damascena* flower extract indicated minimal concerns for concurrent cytotoxic effects in normal cells.

*Rosa Damascena Flower Oil and Rosa Damascena Flower Water*

The cytotoxicity of a trade mixture of 0.1 - 1.0% Rosa Damascena Flower Water and 0.1 - 1.0% Rosa Damascena Flower Oil formulated in pentylene glycol was estimated by measuring the intake of neutral red dye by murine fibroblast cells treated with either 1.4 - 50 mg/ml of the test article or 10 - 100 µg/ml sodium lauryl sulfate (SLS), for 48 h, in an vitro cytotoxicity assay, in accordance with the Organisation for Economic Cooperation and Development (OECD) test guideline (TG) 129.[67] A mean $IC_{50}$ value of 6.68 mg/ml was determined.

**In Vitro Cell Transformation**

*Rosa Damascena Flower Oil*

Human colon carcinoma SW742 cell lines and human fibroblast cell lines were prepared for an MTT assay with RPMI-1640 medium, combined with FBS (10% v/v), streptomycin (100 µg/ml), and penicillin (100 µg/ml).[69] Doses of 0, 1, 2, 3, 4, 5, or 10 µl of a *Rosa damascena* flower oil were introduced, in triplicate, to cells for 48 h. Outer and inner controls were used, in which cells not exposed to the flower oil were cultured in separate, or the same, dishes as cell lines treated with flower oil. Both morphology and cell survival rates of cancer and fibroblast cells were affected by *Rosa damascena* flower oil exposure. The evaporated (non-soluble) phase of the oil was shown to have an inhibitory effect on cell growth, especially in the inner controls, while the water-soluble phase of the oil significantly increased cell growth by nine-fold, compared to the inner controls. Both SW742 cells and fibroblasts showed cell growth induction when exposed to 10 µl of *Rosa damascena* flower oil, while at lower concentrations a potent induction effect was only seen in fibroblasts.

**Other Physiological and Biochemical Effects**

*Rosa Damascena Flower Extract*

Groups of 10 Wistar rats were administered 0, 2.5, 5, 25, or 50 mg/kg/d aqueous *Rosa damascena* flower extract, via gavage, for 30 d.[63] Blood samples were collected on days 0 and 30 to assess hematological parameters and biochemical changes. Significant decreases in total white blood cell count was noted in the 2.5 and 50 mg/kg/d groups, while platelet counts were significantly increased in all test groups. Fasting glucose, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels were significantly decreased and alkaline phosphatase (ALP) levels were significantly increased in all test groups. Increased triglyceride (TG) levels were statistically significant in only the 50 mg/kg/d group, while the cholesterol/high-density lipoprotein (HDL) ratio and low-density lipoprotein (LDL)/HDL ratios were significantly decreased in the 2.5, 5, and 25 mg/kg/d groups.

A methanolic, *Rosa damascena* flower extract was administered at 1.5 g, via diet, to rabbits (number not specified) for 45 d.[70] Animals were anesthetized at the end of the experiment, and under intubation, had pressure transducer cannulae inserted into the left carotid artery and left ventricle, to record heart rate, arterial blood pressure, and left ventricular pressure, respectively. A fasting blood sample was taken on days 1 and 46 to measure the total cholesterol, TG, LDL, and HDL levels. TG levels were significantly higher than controls at the end of the experiment. No other significant differences in lipid profiles, pulse, or cardiac indices were observed.

Groups of 5 dogs were administered distilled water or lactulose (controls), or, 90, 180, 360, 720, or 1440 mg/kg/d aqueous *Rosa damascena* flower extract, in food, for 10 d.[71] Serum levels of urea, creatinine, ALP, ALT, bilirubin, albumin, and protein were measured in all experimental groups at day 0, 1, 3, 7, and 10. Except for a significant increase in bilirubin levels on day 3 and ALT on day 10 in animals in the 1440 mg/kg bw/d group, there were no statistically significant differences with controls.

*Rosa Damascena Flower Water*

Groups of 10 male albino rabbits were orally dosed with either 250 or 500 mg/kg bw/d *Rosa damascena* flower water for 60 d.[72] Blood samples were collected for hematological testing on day 31 and day 61; compared to controls, no significant differences were observed between hemoglobin, white blood cells, red blood cells, and platelets after 30 and 60 days of dosing. The 250 mg/kg/d group had a significant increase in red blood cell count, and a higher platelet count was observed for both doses, at day 60 compared to day 30.

## DERMAL IRRITATION AND SENSITIZATION

The dermal irritation and sensitization studies summarized below are described in Table 7.

In an in vitro study, 30 µl of a trade mixture containing 0.1 - 1% Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower Water, in pentylene glycol, was predicted to be non-irritating and non-sensitizing when applied neat to an EpiSkin™ model.[67] Human monocytic leukemia cell lines (THP-1) exposed to up to 5000 µg/ml of the same trade mixture, undiluted, in a human cell line activation test (h-CLAT) in vitro assay were considered to be sensitized (minimum induction threshold of 923 µg/ml).[67] The trade mixture of 0.1 - 1% Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower

Water was not considered sensitizing when evaluated in a luciferase assay (KeratinoSens™ model), undiluted, at up to 400 µg/ml.[67]

Undiluted *Rosa damascena* flower oil was not irritating to the skin of mice and pigs, but was moderately irritating when applied to the intact or abraded skin of rabbits for 24 h; no further details were provided.[58,60] A trade mixture of 0.1-1% Rosa Damascena Flower Oil and 0.1-1% Rosa Flower Water, in pentylene glycol, was not irritating when applied as a single, semi-occlusive application of 160 µl, at a concentration of 20% in distilled water, to 11 subjects.[67] *Rosa damascena* flower oil, 2% in petrolatum, was not irritating in a single, occlusive, 48-h patch test (number of subjects not specified) and was also not sensitizing in a maximization test using 25 subjects (additional details not provided).[58,60] Two fragrance products, one containing 0.7794% Rosa Damascena Flower Extract and one containing 0.1068% Rosa Damascena Flower Water, both in 100 subjects, and one mask formulation containing 0.1260% Rosa Damascena Flower Oil, in 107 subjects, were not sensitizing in 3 separate HRIPTs.[73-75]

### Photosensitization/Phototoxicity

#### In Vitro

*Rosa Damascena Flower Oil and Rosa Damascena Flower Water*

In an ultraviolet-visible spectrophotometric analysis of a trade mixture of 0.1 - 1% Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower Water, formulated in pentylene glycol, diluted to 10% in water, a very low UV absorption was observed between 290 - 400 nm.[67] The test article was not considered to have phototoxic potential.

#### Animal

*Rosa Damascena Flower Oil*

No phototoxic effects were reported when undiluted *Rosa damascena* flower oil was applied on hairless mice and swine.[58,60] No further details were provided.

## OCULAR IRRITATION STUDIES

#### In Vitro

*Rosa Damascena Flower Oil and Rosa Damascena Flower Water*

The potential of a trade mixture comprising 0.1 - 1.0% Rosa Damascena Flower Oil and 0.1 - 1.0% Rosa Damascena Flower Water formulated in pentylene glycol to cause ocular irritation was investigated in a neutral red release assay.[67] Rabbit cornea fibroblast cells (SIRC cell line) were preloaded with neutral red dye (amount not specified) for 3 h at 37 °C. The dyed cells were then treated with either 500 µl of the test article diluted at 0, 25, or 50% (in water), sodium dodecyl sulfate diluted at 0.2%, 0.05%, or 0.01% in saline solution (positive control), or saline solution (negative control), for 60 s. Upon removal of the test article and controls, the amount of dye, released solely by surviving cells, was measured at an optical density of 540 nm. The resulting cell death percentages were plotted against the corresponding test article concentrations to determine $IC_{50}$ values. Under these experimental conditions, the trade mixture exhibited negligible cytotoxicity (≤ 20% cell death at 50% dilution), with the positive controls producing expected results. The test article was not considered an ocular irritant.

## CLINICAL STUDIES

### Dermatological Patch Test Studies

*Rosa Damascena Flower Oil*

Patients in Japan (n= 1483), suspected of having contact dermatitis, were enrolled in an 8-yr study (1990-1998), in which they were annually patch tested with a series of essential oils.[76] A *Rosa damascena* flower oil (2% pet.) was one of the 10 fragrance oils applied on the upper back of patients, in a 2-d close patch test, using Finn Chambers and Scanpor tape. Readings were taken at 1 h and 1 d after removal, according to International Contact Dermatitis Group recommendations. The average patch test positivity rate for this *Rosa damascena* flower oil, over 8 yr, was 0.4%.

### Case Reports

A 48-yr old woman with a history of allergy to imitation jewelry reported experiencing an intense scalp itch in response to a hair dye application.[77] The subject was treated with oral antihistamines and topical corticosteroids, and symptoms resolved within 2 d. Three months later, itching and erythema occurred at sites which came in contact with a cologne containing *Rosa damascena* flower oil; itchy papules appeared as much on untouched areas as on those in contact with the cologne. Standard and additional patch tests (Chemotechnique fragrance series), scored on day 2 and day 4, revealed a + reaction to the fragrance mix at 8% in petrolatum, a ++reaction to nickel sulfate at 5% in petrolatum and to *Rosa damascena flower* oil at 2% in petrolatum, and a +++ reaction to geraniol at 2% in petrolatum. Since this was the first patient with suspected contact dermatitis from perfumes to show a positive reaction to *Rosa damascena* flower oil following patch-testing with this series (a total of 326 had been tested), a chromatographic analysis of the oil was conducted. Citronellol, geraniol, and neral were

identified as the main components (33.4%, 18.5%, and 5.9%, respectively). *Rosa damascena* flower oil contains approximately 20% geraniol, which led the researchers to surmise that the woman's reaction was possibly attributed to this component in the cologne.

A 71-yr old woman reported painful, pruritic, palmar eruptions, lasting 3 mo, shortly after a first-time exposure to a household cleaner.[78] The patient presented with hyperkeratotic plaques and bilateral fissures on her palms and fingers. The differential diagnosis included irritant, as opposed to allergic contact, dermatitis. Treatment with over-the-counter (OTC) products and the use of a fragrance-free soap did not alleviate the condition. Patch test results, graded according to the North American Contact Dermatitis Group, revealed numerous positive reactions to fragrance chemicals at 48 and 72 h, including a 1+ reaction to *Rosa damascena* flower oil and a 1+ reaction to geraniol. It was determined that the fragrance-free soap contained rose oil. The observed dermatitis only partly diminished after discontinued use of the fragrance-free soap and other recommendations based on test results and case history.

## SUMMARY

The safety of 10 *Rosa damascena*-derived ingredients as used in cosmetics is reviewed in this safety assessment. According to the *Dictionary*, some of these ingredients are reported to function as skin-conditioning and fragrance ingredients, while a few are reported to function as antioxidants and cosmetic astringents, in cosmetic products. Some constituents of concern, such as the fragrance allergens eugenol, geraniol, citronellol, limonene, linalool, and farnesol, are found in *Rosa damascena*-derived ingredients, with amounts varying based on time of harvest, as well as the timing and method of extraction.

According to 2022 VCRP survey data, Rosa Damascena Flower Water is reported to be used in 302 formulations, at a maximum concentration of 1.9% in foundations, Rosa Damascena Flower Extract is reported to be used in 293 formulations, and Rosa Damascena Flower Oil is reported to be used in 229 formulations, at a maximum concentration of 0.16% in non-spray, face and neck products. Rosa Damascena Flower Oil is used at up to 10.8% in other skincare preparations, and has been indicated to be sold with instructions to dilute before use, resulting in much lower use concentrations in finished products. Incidental ingestion and mucous membrane exposure are possible; for example, Rosa Damascena Flower Wax is reported to be used at a maximum of up to 1.1% in lipsticks. Additionally, these ingredients are used in cosmetic sprays and powders, and could possibly be inhaled. For example, Rosa Damascena Flower Extract is reported to be used at up to 0.00007% in aerosol spray deodorant formulations, and Rosa Damascena Flower Oil is reported to be used at up to 0.0003% in hair spray. Rosa Damascena Flower Extract is reported to be used in face powder formulations (concentration of use not reported)

The acute dermal $LD_{50}$ of *Rosa damascena* flower oil was determined to be ≥ 2500 mg/kg in rabbits. A single oral dose of 2000 mg/kg ethyl acetate *Rosa damascena* flower extract did not cause toxic effects in groups of 3 male and 3 female Swiss albino mice. The acute oral $LD_{50}$ of *Rosa damascena* flower oil was determined to be > 5000 mg/kg in rats, and in another study, was determined to be up to 5525 mg/kg in male rats and 2975 mg/kg in mature, and 3972 mg/kg in immature, female rats, respectively. No deaths were observed in groups of 6 Swiss albino mice orally dosed with up to 6000 mg/kg *Rosa damascena* flower water extract, and the acute $LD_{50}$ in mice was determined to be > 6000 mg/kg.

Groups of 10 Wistar rats administered 0, 2.5, 5, 25, or 50 mg/kg/d aqueous *Rosa damascena* flower extract, via gavage, for 30 d, exhibited greater body weight gain in all test groups compared to controls, but the percent weight gain was not statistically significant. Groups of 5 dogs administered 0, 90, 180, 720, or 1440 mg/kg/d aqueous *Rosa damascena* flower extract, in the diet, for 10 d exhibited a dose dependent increase of diarrhea, and animals in the 720 and 1440 mg/kg/d groups exhibited slight, but not significant, weight loss after day 7. No significant differences in body or organ (liver, intestine, heart, lungs, kidneys and spleen) weights, organ tissue, mortality, or hematological biomarkers were observed in 15 Swiss albino mice orally administered 300 mg/kg/d *Rosa damascena* flower water extract for 28 d (compared to 10 controls). Groups of 25 Swiss albino mice were orally dosed with 0 or 300 mg/kg/d *Rosa damascena* flower water extract for 90 d. Two control mice and 2 treated mice died in the first month, 1 control mouse and 2 treated mice died in the second month, and no mortality occurred during the third month of observation. Mice killed after the first, second, and third month (number not specified), progressively exhibited mild hydroponic degeneration in the liver, congestion in coronary blood vessels, and peribronchiolar aggregation of round cells in the lungs. No significant differences were observed in body and weights, and various hematological markers, compared to the control group.

Whole blood samples exposed to up to 200 µg/ml of a *Rosa damascena* flower oil, followed by PHA stimulation and the addition of Cyt B, exhibited a significantly greater frequency of micronuclei at doses > 50 µg/ml, compared to controls. Concentrations of 10 µg/ml of a *Rosa damascena* flower oil (absolute) and a *Rosa damascena* flower oil (extracted from whole flowers) did not inhibit mitotic activity in normal human blood lymphocytes. *Rosa damascena* flower oil (absolute) exhibited significant ($p < 0.001$) antimutagenic activity when added to a blood lymphocyte culture treated with 300 ng/ml MMC. A trade mixture of 0.1 - 1% Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower Water, in pentylene glycol was not considered genotoxic when tested in an Ames test using *S. typhimurium* strains TA 98, TA100, TA 102, TA 1535, TA 1537, at up to 5000 µg/plate.

In two separate MTT assays, a methanolic *Rosa damascena* flower extract exhibited $IC_{50}$ values of 265 µg/ml and > 1000 µg/ml on HeLa and Vero cell lines, respectively. Murine fibroblast cell lines treated with up to 50 mg/ml of a trade mixture

comprising 0.1 – 1% Rosa Damascena Flower Oil and 0.1 – 1% Rosa Damascena Flower Water formulated in pentylene glycol, yielded a mean $IC_{50}$ value of 6.68 mg/ml. Human colon carcinoma cell lines dosed with up to 10 µl of a *Rosa damascena* flower oil in an MTT assay exhibited a significant cell growth induction at the highest dose, while an induction effect was observed at lower concentrations in human fibroblast cells.

Wistar rats orally administered up to 50 mg/kg/d aqueous *Rosa damascena* flower extract for 30 d exhibited significant decreases in the cholesterol/HDL and LDL/HDL ratios in the 2.5 and 50 mg/kg/d groups, and a significant TG increase in the 50 mg/kg/d group. A methanolic, *Rosa damascena* flower extract was administered at 1.5 g, via diet, to rabbits (number not specified) for 45 d. Comparison of fasting blood samples on day 1 and 1 d after the experiment revealed significantly higher TG levels in treated animals compared to the controls. No other significant differences in lipid profiles, pulse, or cardiac indices were observed. Groups of 5 dogs were administered up to 1440 mg/kg bw/d aqueous *Rosa damascena* flower extract in food for 10 d. Except for a significant increase in bilirubin levels on day 3 and ALT on day 10 in animals in the 1440 mg/kg bw/d group, there were no statistically significant differences from controls. Blood samples collected from groups of 10 male albino rabbits orally dosed with either 250 or 500 mg/kg bw/d *Rosa damascena* flower water for 60 d only showed a statistically significant increase in red blood cell counts for the 250 mg/kg group, and an increase in platelet counts for both groups, at day 60, compared to day 30 of dosing.

In an in vitro study, 30 µl of a trade mixture of 0.1-1% Rosa Damascena Flower Oil and 0.1-1% Rosa Damascena Flower Water, formulated in pentylene glycol did not cause irritation or sensitization when applied to an EpiSkin™ model. Human monocytic leukemia cell lines (THP-1) exposed to up to 5000 µg/ml of the same trade mixture, undiluted, in an h-CLAT in vitro assay were sensitized, with a minimum induction threshold of 923 µg/ml. The aforementioned trade mixture was not considered sensitizing when evaluated in a luciferase assay (KeratinoSens™ model), undiluted, at up to 400 µg/ml. No dermal irritation or phototoxic effects were observed when *Rosa damascena* flower oil was applied to the backs of hairless mice and swine. Rabbits with intact or abraded skin exposed to undiluted *Rosa damascena* flower oil for 24 h under occlusion showed signs of moderate irritation. The same trade mixture of Rosa Damascena Flower Oil and Rosa Damascena Flower Water, in pentylene glycol was not irritating when applied, at a concentration of 20% in distilled water, at160 µl in a single, semi-occlusive patch test of 11 subjects. *Rosa damascena* flower oil, 2% in petrolatum, did not produce irritation in a 48-h closed patch test, or, sensitization reactions in a maximization test using 25 human subjects. Sensitization was not observed in 3 separate HRIPTs testing the sensitizing potential of two fragrance products containing 0.7794% Rosa Damascena Flower Extract, 0.1068% Rosa Damascena Flower Water, and a mask formulation containing 0.1260% Rosa Damascena Flower Oil, in either 100 or 107 subjects.

A trade mixture of 0.1 - 1% Rosa Damascena Flower Oil and 0.1 - 1% Rosa Damascena Flower Water, in pentylene glycol, diluted to 10% in water, had very low UV absorption between 290 - 400 nm, and was considered not phototoxic. Undiluted *Rosa damascena* flower oil was not considered phototoxic to mice and swine skin. The same trade mixture, applied at a dose of 500 µl, neat or 25 or 50%, in water, to neutral red dye treated-rabbit cornea fibroblast cells for 60 s did not exhibit cytotoxicity and was not considered an ocular irritant.

In an 8-yr, annual essential oil patch study of 1483 patients susceptible to contact dermatitis, among the 10 fragrance oils used, the average patch test positivity rate for *Rosa damascena* flower oil (2% pet.) was 0.4%. A 48-yr old woman, with prior allergic reactions to imitation jewelry and hair dye experienced itching and erythema from exposure to a cologne containing *Rosa damascena* flower oil; in subsequent patch-testing, the woman had a ++ reaction to *Rosa damascena flower* oil (2% pet.), a +++ reaction to geraniol. Pruritic, palmar eruptions experienced by a 71-yr old woman, after exposure to a household cleaner did not diminish with use of treatment with OTC products or the use of a fragrance-free soap. Discontinued use of the soap, which was determined to contain *Rosa damascena* flower oil (for which the subject patch tested positive, +1), led to only partial diminishing of the symptoms.

## DISCUSSION

This assessment reviews the safety of 10 *Rosa damascena*-derived ingredients as used in cosmetic formulations. The Panel concluded that that these 10 *Rosa damascena*-ingredients are safe in the present practices of use and concentrations described in this safety assessment when formulated to be non-sensitizing.

The need for systemic toxicity data were mitigated, as all of the ingredients described in this report are composed from plant parts that are used in foods or are considered GRAS for intended food use, according to the US FDA. Since systemic exposure from food is expected to be far greater than exposure via cosmetics, the Panel considered the toxicity data in this review sufficient.

The Panel expressed concern regarding pesticide residues. heavy metals, and other plant species that may be present in botanical ingredients. The Panel stressed that the cosmetics industry should continue to use current good manufacturing practices to limit these impurities.

Additionally, because final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be

hazardous to consumers. For *Rosa damascena*-derived ingredients, examples of the constituents the Panel was concerned about include benzyl alcohol, eugenol, methyl eugenol, geraniol, citronellol, limonene, and linalool, which are possible sensitizers. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents that may cause sensitization.

The Panel discussed the issue of incidental inhalation exposure that could result with the use of some of these ingredients (e.g., up to 0.0003% Rosa Damascena Flower Oil in aerosol hair spray). Inhalation toxicity data were not available. However, the Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

## CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 10 *Rosa damascena*- derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-sensitizing.

Hydrolyzed Rosa Damascena Flower Extract*
Rosa Damascena Bud Extract*
Rosa Damascena Extract
Rosa Damascena Flower
Rosa Damascena Flower Extract
Rosa Damascena Flower Oil
Rosa Damascena Flower Powder
Rosa Damascena Flower Water
Rosa Damascena Flower Water Extract
Rosa Damascena Flower Wax

* Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

# TABLES

**Table 1. Definitions and reported functions of *Rosa damascena* ingredients [1]**

| Ingredient/CAS No. | Definition | Function |
|---|---|---|
| Hydrolyzed Rosa Damascena Flower Extract | Hydrolyzed Rosa Damascena Flower Extract is the hydrolysate of Rosa Damascena Flower Extract derived by acid, enzyme, or other method of hydrolysis.* | Antioxidants |
| Rosa Damascena Bud Extract<br>90106-38-0 | Rosa Damascena Bud Extract is the extract of the buds of *Rosa damascena*.* | Skin-conditioning agents - miscellaneous |
| Rosa Damascena Extract<br>90106-38-0 | Rosa Damascena Extract is the extract of the rose, *Rosa damascena*.* | Fragrance ingredients |
| Rosa Damascena Flower<br>90106-38-0 | Rosa Damascena Flower are the flowers of *Rosa damascena.** | Skin-conditioning agents - miscellaneous |
| Rosa Damascena Flower Extract<br>906106-38-0 | Rosa Damascena Flower Extract is the extract of the flowers of *Rosa damascena*.* | Fragrance ingredients |
| Rosa Damascena Flower Oil<br>8007-01-0<br>90106-38-0 | Rosa Damascena Flower Oil is the volatile oil obtained from the flowers of *Rosa damascena.** | Fragrance ingredients; Skin-conditioning agents – miscellaneous |
| Rosa Damascena Flower Powder<br>90106-38-0 | Rosa Damascena Flower Powder is the powder obtained from the dried, ground flowers of *Rosa damascena.** | Fragrance ingredients |
| Rosa Damascena Flower Water<br>90106-38-0 | Rosa Damascena Flower Water is an aqueous solution of the steam distillate obtained from the flowers of *Rosa damascena.** | Fragrance ingredients; Skin-conditioning agents - miscellaneous |
| Rosa Damascena Flower Water Extract<br>90106-38-0 | Rosa Damascena Flower Water Extract is the extract of Rosa Damascena Flower Water.* | Antioxidants; Cosmetic astringents |
| Rosa Damascena Flower Wax<br>90106-38-0 | Rosa Damascena Flower Wax is a wax obtained from the flower of *Rosa damascena.** | Fragrance ingredients |

* The accepted scientific name for *Rosa damascena* is *Rosa* x *damascena.*

**Table 2. Chemical properties of *Rosa damascena*-derived ingredients**

| Property | Value | Reference |
|---|---|---|
| | **Rosa Damascena Extract** | |
| Physical Form (@ 20°C and 1013 hPa) | Viscous liquid; can contain crystallized product | [79] |
| Color | Orange-red | [79] |
| Density (g/ml) | 0.9804 | [79] |
| Vapor pressure (mmHg @ 20 ºC; 25°C) | 3.053; 3.960 | [79] |
| Boiling Point | Decomposed before boiling | [79] |
| | **Rosa Damascena Flower** | |
| Physical Form<br>(fresh petal width and length, in cm) | Heart/pear shape, soft and smooth petals;<br>0.9-3.8; 1.8-4.2 | [8] |
| Color | Magenta on base, light yellow near apex<br>pink | [2,8] |
| Odor | Aromatic distinct | [8] |
| Density (g/ml) | 0.202 | [8] |
| pH | 6.56 | [8] |
| Ash (% w/w upon burning); Total<br>Acid insoluble; Water soluble | 6.34<br>1.51; 2.48 | [8]<br>[8] |
| | **Rosa Damascena Flower Extract** | |
| UV Wavelengths and Absorbance (nm; AU)*<br>(UVA (315-400 nm), UVB (280-315 nm), UVC (100-280 nm))<br>Hydroalcoholic extract<br><br><br>Ether extract<br><br><br>Ethyl acetate:ethanol<br><br> | <br><br>228; 2.57 ($\lambda_{max}$)<br>226; 2.42<br>355; 0.9<br>269; 1.59 ($\lambda_{max}$)<br>238; 1.35<br>350; 0.85<br>270; 1.16 ($\lambda_{max}$)<br>354; 0.64 | [25] |
| | **Rosa Damascena Flower Oil** | |
| Physical Form | Liquid or crystallized | [80] |
| Color | Colorless, light yellow to yellow-green | [2,80,81] |
| Odor | Floral, rose | [80] |
| Density (g/ml @ 20 ºC) | 0.848-0.880 | [80] |
| | **Rosa Damascena Flower Water** | |
| Density (g/ml @ 20 ºC) | 0.9916; 0.9927 | [4,9] |
| Viscosity ($cm^2/s$) @ 25 ºC) | 104 | [9] |

**Table 2. Chemical properties of *Rosa damascena*-derived ingredients**

| | | |
|---|---|---|
| Melting Point (ºC) | 93 | [9] |
| pH | 7.2; 6.55 | [4,9] |
| **Rosa Damascena Flower Wax** | | |
| Melting Point (ºC) | | [17] |
| Turkish rose wax | 42 | |
| Bulgarian rose wax | 41.0-46.5 | |

**Table 3. Percent composition of constituents found in *Rosa damascena*-derived ingredients**[2,13,14,16,17,20-22]

| | **Shade-dried petals of *Rosa damascena*** | | **Fresh flowers of *Rosa damascena*** | | | |
|---|---|---|---|---|---|---|
| **Constituent** | **Hydrodistilled Essential Oil** | **Hexane Extract of Rose Water** | **Hydrodistilled Essential Oil** | **Rose Water** | **Rose Water Extract*** | **Rose Wax**** |
| α-bulnesene | 0.4% | 0.1% | NR | NR | NR | NR |
| α-guaiene | NF | 0.1% | 2.0% | NR | NR | NR |
| α-humulene | 0.3% | 0.2% | 0.6% | NR | NR | NR |
| α-pinene | 0.1% | 0.3% | 2.8% | 0.71%[20] | NR | NR |
| α-selinene | trace | trace | NR | NR | NR | NR |
| α-terpinene | trace | trace | NR | NR | NR | NR |
| α-terpineol | 0.1% | 0.2% | 1.6% | 0.12% | NR | NR |
| β-caryophyllene | trace | - | trace | NR | NR | NR |
| β-citronellol | NR | NR | NR | 28.70% | NR | NR |
| β-copaene | 0.1% | 0.2% | 2.0% | NR | NR | NR |
| β-damascenone | NR | NR | 0.5% | NR | NR | NR |
| β-elemene | 0.1% | - | NR | NR | NR | NR |
| β-myrcene | 0.2% | 0.2% | 2.4% | NR | NR | NR |
| β-pinene | NR | 0.1% | 0.3% | NR | NR | NR |
| β-selinene | 0.1 | - | NR | NR | NR | NR |
| δ-cadinene | - | 0.1% | NR | NR | NR | NR |
| δ-elemene | 0.1% | trace | NR | NR | NR | NR |
| (2*e*,6*e*)-farnesol | 0.4% | 0.3% | 0.6% | NR | NR | NR |
| e-β-ocimene | 0.3 | - | 0.8% | 1.06% | NR | NR |
| (*e*)-rose oxide | NR | NR | 0.7% | NR | trace | NR |
| (z)-rose oxide | NR | NR | 0.2% | NR | trace | NR |
| z-β-farnesene | 0.3% | 0.1% | NR | NR | NR | NR |
| z-β-ocimene | trace | - | 0.3% | 0.18% | NR | NR |
| (z)-9-nonadecene | NR | NR | 0.6% | NR | NR | NR |
| 1-eicosene | 0.1% | 0.1% | NR | NR | NR | NR |
| 1-nonadecene | 1.6% | 0.8% | 10.2%[2] | NR | NR | NR |
| 10-*epi*-γ-eudesmol | 0.1% | 0.1% | NR | NR | NR | NR |
| benzaldehyde | trace | 0.1% | NR | NR | NR | NR |
| benzyl alcohol | NR | NR | NR | 0.85% | NR | NR |
| caryophyllene oxide | 0.1% | 0.1% | NR | NR | NR | NR |
| *cis*-geraniol | NR | NR | NR | 10.81% | NR | NR |
| citronellal | 0.1% | 0.2% | NR | NR | NR | NR |
| citronellol | 7.1% | 2.2% | 35.3% | 29.44%[22] | 1.8-7.2% | 17% |
| citronellyl acetate | 0.1% | 0.3% | 0.5% | NR | NR | NR |
| citronellyl butyrate | 0.1 % | - | NR | NR | NR | NR |
| citronellyl formate | 0.2% | 0.3% | NR | NR | NR | NR |
| docasane | 1.1% | 1.4% | 0.6% | 0.4%[20] | NR | NR |
| eicosane | 2.5% | 2.4% | 0.5% | 0.45% | 0.2% | NR |
| ethanol | NR | NR | 2.1%[2] | NR | NR | NR |
| eugenol | NR | NR | 1.6%[2] | 2.26-17.75%[20] | 0.4% | 1% |
| farnesol | NR | NR | NR | 0.89% | NR | NR |
| geranial | 0.1% | trace | 0.7% | NR | NR | NR |
| geraniol | 4.1% | 2.5% | 18.7% | 30.74%[22] | 0.9-7.0% | 5% |
| geranyl acetate | 0.8% | 0.1% | 1.7% | 7.33% | NR | NR |
| geranyl formate | 0.5% | 1.5% | 1.0% | NR | NR | NR |
| geranyl propionate | trace | - | NR | NR | NR | NR |
| germacrene-d | trace | - | NR | NR | NR | NR |
| heneicosane | 19.7% | 15.7% | 2.6% | 0.56% | 1.4% | NR |
| heptadecane | 0.6% | 0.5% | 0.3% | 1.08%[20] | NR | NR |
| hexadecane | 0.1% | 0.4% | NR | 2.14% | NR | NR |
| isomenthone | 0.2% | 0.3% | NR | NR | NR | NR |
| limonene | NR | NR | 0.8% | NR | NR | NR |

**Table 3. Percent composition of constituents found in *Rosa damascena*-derived ingredients**[2,13,14,16,17,20-22]

| | Shade-dried petals of *Rosa damascena* | | Fresh flowers of *Rosa damascena* | | | |
|---|---|---|---|---|---|---|
| **Constituent** | **Hydrodistilled Essential Oil** | **Hexane Extract of Rose Water** | **Hydrodistilled Essential Oil** | **Rose Water** | **Rose Water Extract*** | **Rose Wax**** |
| linalool | 0.5% | 0.7% | 2.6% | 0.65-8.99%[20] | 1.5-3.3%* | NR |
| linalyl acetate | trace | trace | NR | NR | NR | NR |
| methyl eugenol | trace | 0.1% | 1.3% | 1.83% | 0.4% | 2% |
| methyl geranate | trace | - | NR | NR | NR | NR |
| n-decanal | NR | NR | trace | NR | NR | NR |
| neral | trace | 0.1% | 0.3% | NR | NR | NR |
| nerol | 0.1% | - | 7.2% | 16.12%[22] | 0.2-4.2% | 4% |
| nerol oxide | 0.2% | 0.1% | NR | NR | NR | NR |
| neryl acetate | 0.4% | - | NR | NR | NR | NR |
| nonane | NR | NR | NR | 0.31%[20] | NR | NR |
| n-nonanal | 0.4% | 0.4% | 0.2% | NR | NR | NR |
| nonadecane | 13.0% | 8.4% | 4.5% | 2.05% | 0.9% | 0.1% |
| nonadecene | NR | NR | NR | NR | 0.7% | - |
| octadecane | 0.2% | 0.9% | NR | NR | NR | NR |
| ***p***-cymene | 0.6% | 0.6% | NR | NR | NR | NR |
| pentacosane | 5.3% | 5.1% | 0.5% | NR | NR | NR |
| pentadecane | - | 0.2% | NR | 0.73% | NR | NR |
| phenethyl alcohol | 0.4% | 7.1% | 2.9% | 4.95%[21]; 23.70%[22] | 69.7-81.6% | 43% |
| terpinen-4-ol | 0.1% | 0.2% | 0.5% | NR | NR | NR |
| terpinolene | 0.1% | 0.1% | NR | NR | NR | NR |
| tetracosane | 0.9% | 1.1% | trace | NR | NR | NR |
| tetradecanol | 0.1% | - | NR | NR | NR | NR |
| *trans*-geraniol | NR | NR | NR | 16.44% | NR | NR |
| tricosane | 11.3% | 9.3% | 0.6% | NR | NR | NR |

* *Rosa damascena* flower extracts prepared with listed solvents (20 mg%)

Abbreviations: - (not found); NR- not reported; *dichloromethane extract; ** solid phase microextraction (SPME) analysis

**Table 4. Frequency (2022)[39] and concentration (2019)[40,41] of use of *Rosa damascena*-derived ingredients**

| | *# of Uses* | *Max Conc of Use (%)* | *# of Uses* | *Max Conc of Use (%)* | *# of Uses* | *Max Conc of Use (%)* |
|---|---|---|---|---|---|---|
| | **Rosa Damascena Extract** | | **Rosa Damascena Flower** | | **Rosa Damascena Flower Extract** | |
| **Totals*** | **59** | **0.000005-0.05** | **6** | **NR** | **293** | **0.0012-0.0018** |
| ***Duration of Use*** | | | | | | |
| *Leave-On* | *40* | *0.00001-0.014* | *5* | *NR* | *261* | *NR* |
| *Rinse-Off* | *19* | *0.000005-0.05* | *1* | *NR* | *30* | *0.0012-0.0018* |
| *Diluted for (Bath) Use* | *NR* | *NR* | *NR* | *NR* | *2* | *NR* |
| ***Exposure Type*** | | | | | | |
| Eye Area | 3 | NR | NR | NR | 70 | NR |
| Incidental Ingestion | NR | NR | NR | NR | 74 | NR |
| Incidental Inhalation-Spray | 5; 18[a]; 10[b] | 0.00001-0.00027; 0.00013-0.0065[a] | 2; 1[a]; 1[b] | NR | 19[a]; 22[b] | NR |
| Incidental Inhalation-Powder | 10[b]; 2[c] | 0.00077-0.014[c] | 1[b] | NR | 8; 22[b] | NR |
| Dermal Contact | 56 | 0.000005-0.05 | 6 | NR | 184 | 0.0018 |
| Deodorant (underarm) | 1[a] | aerosol: 0.00007; 0.00007 (not spray) | NR | NR | 2[a] | NR |
| Hair - Non-Coloring | 3 | 0.00001-0.0065 | NR | NR | 12 | 0.0012 |
| Hair-Coloring | NR | 0.0023 | NR | NR | NR | NR |
| Nail | NR | NR | NR | NR | 19 | NR |
| Mucous Membrane | 5 | 0.000005-0.05 | NR | NR | 86 | NR |
| Baby Products | 2 | NR | NR | NR | NR | NR |
| | **Rosa Damascena Flower Oil** | | **Rosa Damascena Flower Powder** | | **Rosa Damascena Flower Water** | |
| **Totals*** | **229** | **0.000059-0.31; 10.8**** | **1** | **NR** | **302** | **0.009-1.9** |
| ***Duration of Use*** | | | | | | |
| *Leave-On* | *184* | *0.00013-0.16; 10.8*** | *1* | *NR* | *246* | *0.09-1.9* |
| *Rinse Off* | *36* | *0.000059-0.31* | *NR* | *NR* | *56* | *0.009-0.99* |
| *Diluted for (Bath) Use* | *9* | *NR* | *NR* | *NR* | *NR* | *NR* |
| ***Exposure Type*** | | | | | | |
| Eye Area | 6 | 0.0095 | NR | NR | 22 | NR |
| Incidental Ingestion | 2 | 0.0002-0.01 | NR | NR | 10 | NR |
| Incidental Inhalation-Spray | 48; 61[a]; 46[b] | 0.00013-0.0003; 0.0012[a] | NR | NR | 4; 80[a]; 95[b] | NR |
| Incidental Inhalation-Powder | 46[b]; 2[c] | 0.005-0.16[c] | NR | NR | 95[b] | 0.94[c] |
| Dermal Contact | 217 | 0.00014-0.16; 10.8** | 1 | NR | 282 | 0.09-1.9 |
| Deodorant (underarm) | 2[a] | NR | NR | NR | NR | NR |
| Hair - Non-Coloring | 8 | 0.00013-0.0017 | NR | NR | 10 | 0.009 |
| Hair-Coloring | NR | 0.000059 | NR | NR | NR | 0.03-0.09 |
| Nail | NR | 0.005 | NR | NR | NR | NR |
| Mucous Membrane | 21 | 0.00014-0.01 | NR | NR | 16 | 0.09 |
| Baby Products | 2 | NR | NR | NR | NR | NR |

| | **Rosa Damascena Flower Water Extract** | | **Rosa Damascena Flower Wax** | |
|---|---|---|---|---|
| **Totals*** | **1** | **NR** | **7** | **0.015-1.1** |
| ***Duration of Use*** | | | | |
| *Leave-On* | *NR* | *NR* | *6* | *0.015-1.1* |
| *Rinse-Off* | *1* | *NR* | *1* | *0.05* |
| *Diluted for (Bath) Use* | *NR* | *NR* | *NR* | *NR* |
| ***Exposure Type*** | | | | |
| Eye Area | NR | NR | 1 | 0.13 |
| Incidental Ingestion | NR | NR | 2 | 1.1 |
| Incidental Inhalation-Spray | NR | NR | 1[b] | NR |
| Incidental Inhalation-Powder | NR | NR | 1[b] | 0.05[c] |
| Dermal Contact | 1 | NR | 4 | 0.015-0.13 |
| Deodorant (underarm) | NR | NR | NR | NR |
| Hair - Non-Coloring | NR | NR | NR | NR |
| Hair-Coloring | NR | NR | NR | NR |
| Nail | NR | NR | NR | NR |
| Mucous Membrane | NR | NR | 3 | 1.1 |
| Baby Products | NR | NR | NR | NR |

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

**According to a supplier, this product is an essential oil that is sold with instructions to dilute the product before use.[41]

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

[c] It is possible these products are powders, but it is not specified whether the reported uses are powders

NR – not reported

**Table 5. Acute toxicity studies**

| Ingredient | Animals | No./Group | Vehicle | Concentration/Dose/Protocol | $LD_{50}$/ Results | Reference |
|---|---|---|---|---|---|---|
| **DERMAL** | | | | | | |
| *Rosa damascena* flower oil | Rabbits | NR | NR | NR | $LD_{50}$ > 2500 mg/kg | 58-60 |
| **ORAL** | | | | | | |
| *Rosa damascena* flower extract | Male and female Swiss albino mice | 3/sex | 0.7% carboxy-methylcellulose | 2000 mg/kg ethyl acetate extract | $LD_{50}$ > 2000 mg/kg | 61 |
| *Rosa damascena* flower oil | rats | NR | NR | NR | $LD_{50}$ > 5000 mg/kg | 58-60 |
| *Rosa damascena* flower oil | Male and female rats | NR | NR | NR | $LD_{50}$ was determined to be 5525 mg/kg in male rats, and 2975 mg/kg and 3972 mg/kg in mature and immature female rats, respectively. | 58-60 |
| *Rosa damascena* flower water extract | Swiss albino mice | 6/group | NR | 500, 1000, 2000, 3000, 4000, 5000, or 6000 mg/kg | $LD_{50}$ > 6000 mg/kg | 62 |

DMEM – Dulbecco's modified Eagle's medium; NR – not reported; SLS – sodium lauryl sulfate

**Table 6. Short-term and subchronic oral toxicity studies**

| Ingredient | Animals/Group | Study Duration | Vehicle/Control | Dose/Concentration | Protocol/Results | Reference |
|---|---|---|---|---|---|---|
| *Rosa damascena* flower extract<br>Aqueous extract | Wistar rats; 10/group | 30 d | 0.9 % saline | 0, 2.5, 5, 25, or 50 mg/kg/d, via gavage | Body weight increased more in test groups than in controls, but the percent weight gains were not statistically significant. | 63 |
| *Rosa damascena* flower extract<br>Aqueous extract | Dogs (strain not specified);<br>5/group (test substance)<br>4/group (controls) | 10 d | Distilled water;<br>Negative control: distilled water<br>Positive control: lactulose | 0, 90, 180, 360, 720, or 1440 mg/kg/d, in the diet | Animals were monitored for changes in gastrointestinal performance, weight, electrocardiogram, temperature, respiration, and heart rates. No significant differences were observed between groups for respiration, temperature, or cardiac response. A dose-dependent increase of soft feces and diarrhea was observed, starting from the 90 mg/kg/d group. The animals in the 1440 mg/kg/d group showed sedation, and animals in the 720 and 1440 mg/kg/d groups exhibited slight weight loss, especially after day 7, which was statistically significant. However, animals treated with lactulose also experienced slight weight loss, and this effect was, therefore, attributed to possible diarrhea-induced malabsorption, or dehydration. No further changes or adverse effects were observed. | 64 |
| *Rosa damascena* flower water extract | Swiss albino mice; control: 10; treated: 15 | 28 d | NS | 0, 300 mg/kg/d, via gavage | Animal body weights were recorded prior to, and during, treatment. Animals were sacrificed 24 h after the end of treatment and vital organs were weighed and examined for histopathological changes. No significant differences in body or organ weights, organ tissue, or mortality were observed in treated mice. ALT, ALP, AST, urea, and creatinine levels were not significantly different from controls. | 62 |

**Table 6. Short-term and subchronic oral toxicity studies**

| Ingredient | Animals/Group | Study Duration | Vehicle/Control | Dose/Concentration | Protocol/Results | Reference |
|---|---|---|---|---|---|---|
| Rosa damascena flower water extract | Swiss albino mice; 25/group | 90 d | NS | 0, 300 mg/kg/d, via gavage | Mortality rates were recorded, and every month a group of mice (# not specified) was sacrificed. Total body and organ weights, and histopathological changes in the kidney and liver were assessed. Two control and 2 treated mice died in the first month (8%, both groups), one control and 2 treated mice in the second month (12.5% treated mice vs. 6.25% control mice), and no mortality occurred in the third month of observation. In the mice killed after the first month, the liver of treated mice showed mild hydropic degeneration and the heart showed slight congestion in coronary blood vessels with mild perivascular edema. In mice killed after the second month, the liver showed mild hydropic degeneration, and slight congestion of hepatic blood vessels, the kidneys had mild vacuolations and hydropic degeneration in the tubular epithelia, the heart showed granular eosinophilic sarcoplasm and slightly congested coronary blood vessels, and the lung had peribronchiolar aggregations of round cells with thickening of the adjacent interalveolar septa. In addition to the aforementioned effects, mice killed after the third month had focal hyaline degeneration in cardiac muscle fibers, the intestine showed an increase in the numbers of goblet cells and slight activation of Paneth cells, and the spleen exhibited sub capsular edema. No significant differences were observed in body and organ weights, or ALT, ALP, AST, urea, and creatinine levels in treated mice compared to the control group. (statistical significance not provided). | [62] |

ALT- alanine aminotransferase, ALP- alkaline phosphatase, AST- aspartate aminotransferase; HDL- high-density lipoprotein; LDL – low-density lipoprotein; NS- not specified; TG – triglyceride; TC – plasma total cholesterol

**Table 7. Dermal irritation and sensitization studies**

| Test Article | Concentration/Dose | Test Population | Procedure | Results | Reference |
|---|---|---|---|---|---|
| | | | **IN VITRO STUDIES** | | |
| 0.1-1% Rosa Damascena Flower Oil and 0.1-1% Rosa Damascena Flower Water, in pentylene glycol | Undiluted; 10%, or 50% v/v in DMSO; 10% v/v in PBS 30 µl of each dilution | EpiSkin™, Sens-IS | Test articles were applied to the model for 15 min, rinsed with PBS, and then incubated at 37 °C for 6 h. After incubation, the epidermis was collected, and RNA was extracted to analyze the expression of irritation and sensitization biomarker genes. Overexpression of at least 15 of 23 genes associated with irritation would classify the substance as an irritant. | Not sensitizing. Three negative controls (PBS, olive oil, and DMSO - treated skins), a positive irritation control (5% SLS), and two positive sensitization controls (50% HCA and 1% TNBS) were used for each experiment. | [67] |
| 0.1-1% Rosa Damascena Flower Oil and 0.1-1% Rosa Damascena Flower Water, in pentylene glycol | Undiluted; up to 5000 µg/ml | Human monocytic leukemia cell line (THP-1) | OECD TG 442E. In an h-CLAT in vitro assay, THP-1 cell lines were exposed to 8 concentrations of the test article ranging from 19.5 to 5000 µg/ml for 24 h. Post-exposure, the expression of two cell surface antigens, CD86 and CD54, was measured by flow cytometry. Vehicle control (RPMI), negative control (lactic acid), and positive controls (2,4-dinitrochlorobenzene or nickel sulfate) were also run in parallel. | Sensitizing; Based on linear regression, the median concentrations to induce a 150/200% expression of CD86/CD54 relative fluorescence intensity, were an $EC_{200}$ of 923 µg/ml and an $EC_{150}$ of 2125 µg/ml. The MIT was calculated as 923 µg/ml, from these $EC_{200}$ and $EC_{150}$ values. | [67] |

**Table 7. Dermal irritation and sensitization studies**

| Test Article | Concentration/Dose | Test Population | Procedure | Results | Reference |
|---|---|---|---|---|---|
| 0.1-1% Rosa Damascena Flower Oil and 0.1-1% Rosa Damascena Flower Water, in pentylene glycol | Undiluted, 0.2 µg/ml – 400 µg/ml (12 concentrations) | KeratinoSens™, transformed keratinocytes | OECD TG 442D. Luciferase induction was measured in keratinocytes transformed with the AKR1C2 gene (a gene which identifies skin sensitizers). Cinnamaldehyde and 1% DMSO were run in parallel as positive and negative controls, respectively. The experiment was repeated twice to calculate average values for luciferase induction, i.e., test article concentrations at which the luciferase activity was 1.5-fold higher than basal luciferase activity ($EC_{1.5}$), and cell viability ($IC_{70}$). | Not sensitizing. Luciferase induction was lower than 1.5-fold of base values, and $EC_{1.5}$ values were not determined. | [67] |
| **ANIMAL** | | | | | |
| *Rosa damascena* flower oil | NR | Mice and pigs (# and strain not stated) | NR | Not irritating | [58,60] |
| *Rosa damascena* flower oil | NR | Rabbits (# and strain not stated) | Intact or abraded rabbit skin was exposed to undiluted test article for 24 h, under occlusion. No further details provided. | Moderately irritating | [58,60] |
| **HUMAN** | | | | | |
| 0.1-1% Rosa Damascena Flower Oil and 0.1-1% Rosa Damascena Flower Water, in pentylene glycol | 20%, diluted in distilled water/ 160 µl | 11 subjects | A single, semi-occlusive application of the test article was made for 48 h. Readings were taken 30-40 min after removal of the patches. | Not irritating | [67] |
| *Rosa damascena* flower oil | NR; 2%, in petrolatum | NR | A one-time, occlusive application of the test article, was made for 48 h. No further details provided. | Not irritating | [58,60] |
| *Rosa damascena* flower oil | NR; 2% in petrolatum | 25 subjects | NR | Not sensitizing | [58,60] |
| Fragrance; 0.7794% Rosa Damascena Flower Extract | 0.2 ml | 100 subjects | In an HRIPT, 9 occlusive induction applications were applied for 24 h using 2 $cm^2$ patches, over 3 wk. Prior to each patch application, the test article was evaporated for 30 min. Test sites were scored and retested every 48 - 72 h. After a rest period of 10-15 d, a previously unexposed site was challenged with the test substance for 24 h. Challenge sites were scored 48 and 72 h after application. | Not sensitizing; 1 adverse event, which was not test article related, was reported. | [73] |
| Mask; 0.1260% Rosa Damascena Flower Oil | 0.2 ml | 107 subjects | In an HRIPT, 9 occlusive induction applications were applied for 24 h using 2 $cm^2$ patches, over 3 wk. Test sites were scored and retested every 48 h. After a rest period of 10-15 d, a previously unexposed site was challenged with the test substance for 24 h. Challenge sites were scored 48 and 72 h after application. | Not sensitizing | [75] |
| Fragrance; 0.1068% Rosa Damascena Flower Water | 0.2 ml | 100 subjects | In an HRIPT, 9 occlusive induction applications were applied for 24 h using 2 $cm^2$ patches , over 3 wk. Prior to each patch application, the test article was evaporated for 30 min. Test sites were scored and retested every 48 h. After a rest period of 10-15 d, a previously unexposed site was challenged with the test substance for 24 h. Challenge sites were scored 48 and 72 h after application. | Not sensitizing | [74] |

DMSO – dimethyl sulfoxide; EC - maximal effective concentration ; HCA- hydroxycitric acid; HRIPT – human repeated insult patch test; MIT – minimum induction threshold; NR – not reported; PBS- phosphate-buffered saline; RPMI – Roswell Park Memorial Institute; SLS – sodium lauryl sulfate; TNBS – trinitrobenzenesulfonic acid

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**Concentration of Use by FDA Product Category – *Rosa damascena*-Derived Ingredients***

Rosa Damascena Flower Oil
Hydrolyzed Rosa Damascena Flower Extract
Rosa Damascena Bud Extract
Rosa Damascena Extract
Rosa Damascena Flower
Rosa Damascena Flower Extract
Rosa Damascena Flower Powder
Rosa Damascena Flower Water
Rosa Damascena Flower Water Extract
Rosa Damascena Flower Wax

| Ingredient | Product Category | Maximum Concentration of Use |
|---|---|---|
| Rosa Damascena Flower Oil | Eye makeup removers | 0.0095% |
| Rosa Damascena Flower Oil | Hair conditioners | 0.0017% |
| Rosa Damascena Flower Oil | Hair sprays<br>Aerosol | <br>0.00013-0.0003% |
| Rosa Damascena Flower Oil | Shampoos (noncoloring) | 0.0011% |
| Rosa Damascena Flower Oil | Tonics, dressings and other hair grooming aids | 0.0012% |
| Rosa Damascena Flower Oil | Hair dyes and colors | 0.000059% |
| Rosa Damascena Flower Oil | Foundations | 0.027% |
| Rosa Damascena Flower Oil | Lipstick | 0.0002-0.01% |
| Rosa Damascena Flower Oil | Cuticle softeners | 0.005% |
| Rosa Damascena Flower Oil | Bath soaps and detergents | 0.00014% |
| Rosa Damascena Flower Oil | Skin cleansing (cold creams, cleansing lotions liquids and pads) | 0.001-0.31% |
| Rosa Damascena Flower Oil | Face and neck products<br>Not spray | <br>0.16% |
| Rosa Damascena Flower Oil | Body and hand products<br>Not spray | <br>0.005-0.01% |
| Rosa Damascena Flower Oil | Other skin care preparations | 10.8%** |
| Rosa Damascena Extract | Hair conditioners | 0.003% |
| Rosa Damascena Extract | Hair sprays<br>Aerosol | <br>0.00001-0.00027% |
| Rosa Damascena Extract | Shampoos (noncoloring) | 0.0003-0.003% |
| Rosa Damascena Extract | Tonics, dressings and other hair grooming aids | 0.0065% |
| Rosa Damascena Extract | Hair dyes and colors | 0.0023% |
| Rosa Damascena Extract | Foundations | 0.00026% |
| Rosa Damascena Extract | Bath soaps and detergents | 0.000005-0.05% |
| Rosa Damascena Extract | Deodorants<br>Not spray<br>Aerosol | <br>0.00007%<br>0.00007% |
| Rosa Damascena Extract | Skin cleansing (cold creams, cleansing lotions, liquids and pads) | 0.0025% |
| Rosa Damascena Extract | Face and neck products<br>Not spray | <br>0.00077-0.014% |
| Rosa Damascena Extract | Moisturizing products | |

| | | |
|---|---|---|
| | Not spray | 0.00005% |
| Rosa Damascena Extract | Skin fresheners | 0.00013% |
| Rosa Damascena Flower Extract | Hair conditioners | 0.0012% |
| Rosa Damascena Flower Extract | Shampoos (noncoloring) | 0.0012% |
| Rosa Damascena Flower Extract | Skin cleansing (cold creams, cleansing lotions, liquids and pads) | 0.0018% |
| Rosa Damascena Flower Water | Hair conditioners | 0.009% |
| Rosa Damascena Flower Water | Shampoos (noncoloring) | 0.009% |
| Rosa Damascena Flower Water | Hair dyes and colors | 0.03-0.09% |
| Rosa Damascena Flower Water | Other hair coloring preparations | 0.09% |
| Rosa Damascena Flower Water | Foundations | 0.09-1.9% |
| Rosa Damascena Flower Water | Makeup bases | 1.9% |
| Rosa Damascena Flower Water | Bath soaps and detergents | 0.09% |
| Rosa Damascena Flower Water | Skin cleansing (cold creams, cleansing lotions, liquids and pads) | 0.99% |
| Rosa Damascena Flower Water | Face and neck products<br>Not spray | 0.94% |
| Rosa Damascena Flower Water | Moisturizing products<br>Not spray | 0.09% |
| Rosa Damascena Flower Water | Other skin care preparations | 0.9% |
| Rosa Damascena Flower Wax | Eyeliners | 0.13% |
| Rosa Damascena Flower Wax | Foundations | 0.015% |
| Rosa Damascena Flower Wax | Lipstick | 1.1% |
| Rosa Damascena Flower Wax | Skin cleansing (cold creams, cleansing lotions, liquids and pads) | 0.05% |
| Rosa Damascena Flower Wax | Face and neck products<br>Not spray | 0.05% |

*Ingredients included in the title but not found in the table were included in the concentration of use survey, but no uses were reported.

**This product is an essential oil that is sold with instructions to dilute the product before use.

Information collected in 2019

Table prepared: July 23, 2019

September 22, 2021 essential oil footnote added; Rosa Damascena Flower Water in face and neck products corrected from 32.7% to 0.94%

**2022 VCRP Frequency of Use Data for *Rosa damascena*-derived Ingredients**

| INGREDIENT_NAME | CATEGORY CODE- DESCRIPTION | CPIS_COUNT |
|---|---|---|
| **Rosa Damascena (Damask Rose)Extract Total Uses: 59** | | |
| Rosa Damascena (Damask Rose) Extract | 02A- Bath Oils, Tablets, And Salts | 2 |
| Rosa Damascena (Damask Rose) Extract | 03E - Eye Makeup Remover | 1 |
| Rosa Damascena (Damask Rose) Extract | 03G - Other Eye Makeup Preparations | 2 |
| Rosa Damascena (Damask Rose) Extract | 04A - Cologne And Toilet Waters | 2 |
| Rosa Damascena (Damask Rose) Extract | 04B - Perfumes | 3 |
| Rosa Damascena (Damask Rose) Extract | 05A - Hair Conditioner | 1 |
| Rosa Damascena (Damask Rose) Extract | 05F - Shampoos (Non-Coloring) | 1 |
| Rosa Damascena (Damask Rose) Extract | 05G - Tonics, Dressings, And Other Hair Grooming Aids | 1 |
| Rosa Damascena (Damask Rose) Extract | 10A - Bath Soaps And Detergents | 5 |
| Rosa Damascena (Damask Rose) Extract | 10B - Deodorants (Underarm) | 1 |
| Rosa Damascena (Damask Rose) Extract | 12A - Cleansing | 8 |
| Rosa Damascena (Damask Rose) Extract | 12C - Face And Neck (Exc Shave) | 6 |
| Rosa Damascena (Damask Rose) Extract | 12D - Body And Hand (Exc Shave) | 4 |
| Rosa Damascena (Damask Rose) Extract | 12F - Moisturizing | 11 |
| Rosa Damascena (Damask Rose) Extract | 12G - Night | 5 |
| Rosa Damascena (Damask Rose) Extract | 12H - Paste Masks (Mud Packs) | 3 |
| Rosa Damascena (Damask Rose) Extract | 12I - Skin Fresheners | 1 |
| Rosa Damascena (Damask Rose) Extract | 12J - Other Skin Care Preps | 2 |
| **Rosa Damascena (Damask Rose) Flower Total Uses: 6** | | |
| Rosa Damascena (Damask Rose) Flower | 04B - Perfumes | 2 |
| Rosa Damascena (Damask Rose) Flower | 12C - Face And Neck (Exc Shave) | 1 |
| Rosa Damascena (Damask Rose) Flower | 12F - Moisturizing | 1 |
| Rosa Damascena (Damask Rose) Flower | 12H - Paste Masks (Mud Packs) | 1 |
| Rosa Damascena (Damask Rose) Flower | 12J - Other Skin Care Preps | 1 |
| **Rosa Damascena (Damask Rose) Flower Extract Total Uses: 293** | | |
| Rosa Damascena (Damask Rose) Flower Extract | 02B - Bubble Baths | 2 |
| Rosa Damascena (Damask Rose) Flower Extract | 03A - Eyebrow Pencil | 5 |
| Rosa Damascena (Damask Rose) Flower Extract | 03B - Eyeliner | 6 |
| Rosa Damascena (Damask Rose) Flower Extract | 03C - Eye Shadow | 49 |
| Rosa Damascena (Damask Rose) Flower Extract | 03D - Eye Lotion | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 03E – Eye Makeup Remover | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 03F - Mascara | 3 |
| Rosa Damascena (Damask Rose) Flower Extract | 03G - Other Eye Makeup Preparations | 5 |
| Rosa Damascena (Damask Rose) Flower Extract | 05A - Hair Conditioner | 3 |
| Rosa Damascena (Damask Rose) Flower Extract | 05E - Rinses (Non-Coloring) | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 05F - Shampoos (Non-Coloring) | 5 |
| Rosa Damascena (Damask Rose) Flower Extract | 05G - Tonics, Dressings, And Other Hair Grooming Aids | 2 |
| Rosa Damascena (Damask Rose) Flower Extract | 05I - Other Hair Preparations | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 07A - Blushers (All Types) | 20 |
| Rosa Damascena (Damask Rose) Flower Extract | 07B - Face Powders | 8 |
| Rosa Damascena (Damask Rose) Flower Extract | 07E - Lipstick | 74 |

| | | |
|---|---|---|
| Rosa Damascena (Damask Rose) Flower Extract | 07F- Makeup Bases | 3 |
| Rosa Damascena (Damask Rose) Flower Extract | 07G - Rouges | 8 |
| Rosa Damascena (Damask Rose) Flower Extract | 07I - Other Makeup Preparations | 4 |
| Rosa Damascena (Damask Rose) Flower Extract | 08A – Basecoats and Undercoats | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 08E – Nail Polish and Enamel | 18 |
| Rosa Damascena (Damask Rose) Flower Extract | 10A - Bath Soaps And Detergents | 5 |
| Rosa Damascena (Damask Rose) Flower Extract | 10B - Deodorants (Underarm) | 2 |
| Rosa Damascena (Damask Rose) Flower Extract | 10C - Douches | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 10E - Other Personal Cleanliness Products | 4 |
| Rosa Damascena (Damask Rose) Flower Extract | 12A - Cleansing | 9 |
| Rosa Damascena (Damask Rose) Flower Extract | 12C - Face And Neck (Exc Shave) | 16 |
| Rosa Damascena (Damask Rose) Flower Extract | 12D - Body And Hand (Exc Shave) | 6 |
| Rosa Damascena (Damask Rose) Flower Extract | 12F - Moisturizing | 16 |
| Rosa Damascena (Damask Rose) Flower Extract | 12H - Paste Masks (Mud Packs) | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 12I - Skin Fresheners | 1 |
| Rosa Damascena (Damask Rose) Flower Extract | 12J - Other Skin Care Preps | 12 |
| **Rosa Damascena (Damask Rose) Flower Oil Total Uses: 229** | | |
| Rosa Damascena (Damask Rose) Flower Oil | 01B - Baby Lotions, Oils, Powders, And Creams | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 02A - Bath Oils, Tablets, And Salts | 4 |
| Rosa Damascena (Damask Rose) Flower Oil | 02B - Bubble Baths | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 02D - Other Bath Preparations | 3 |
| Rosa Damascena (Damask Rose) Flower Oil | 03D - Eye Lotion | 3 |
| Rosa Damascena (Damask Rose) Flower Oil | 03E - Eye Makeup Remover | 1 |
| Rosa Damascena (Damask Rose) Flower Oil | 03G - Other Eye Makeup Preparations | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 04A - Cologne And Toilet Waters | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 04B - Perfumes | 38 |
| Rosa Damascena (Damask Rose) Flower Oil | 04E - Other Fragrance Preparation | 8 |
| Rosa Damascena (Damask Rose) Flower Oil | 05A - Hair Conditioner | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 05F - Shampoos (Non-Coloring) | 4 |
| Rosa Damascena (Damask Rose) Flower Oil | 05I - Other Hair Preparations | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 07E - Lipstick | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 10A - Bath Soaps And Detergents | 6 |
| Rosa Damascena (Damask Rose) Flower Oil | 10B - Deodorants (Underarm) | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 10C - Douches | 2 |
| Rosa Damascena (Damask Rose) Flower Oil | 10D - Feminine Deodorants | 1 |
| Rosa Damascena (Damask Rose) Flower Oil | 10E - Other Personal Cleanliness Products | 1 |
| Rosa Damascena (Damask Rose) Flower Oil | 12A - Cleansing | 15 |
| Rosa Damascena (Damask Rose) Flower Oil | 12C - Face And Neck (Exc Shave) | 30 |
| Rosa Damascena (Damask Rose) Flower Oil | 12D - Body And Hand (Exc Shave) | 15 |
| Rosa Damascena (Damask Rose) Flower Oil | 12F - Moisturizing | 44 |
| Rosa Damascena (Damask Rose) Flower Oil | 12G - Night | 10 |
| Rosa Damascena (Damask Rose) Flower Oil | 12H - Paste Masks (Mud Packs) | 5 |
| Rosa Damascena (Damask Rose) Flower Oil | 12I - Skin Fresheners | 4 |
| Rosa Damascena (Damask Rose) Flower Oil | 12J - Other Skin Care Preps | 16 |
| Rosa Damascena (Damask Rose) Flower Oil | 13B - Indoor Tanning Preparations | 2 |

| | | |
|---|---|---|
| Rosa Damascena (Damask Rose) Flower Oil | 13C - Other Suntan Preparations | 1 |

**Rosa Damascena (Damask Rose) Flower Powder**
**Total Uses: 1**

| | | |
|---|---|---|
| Rosa Damascena (Damask Rose) Flower Powder | 12J - Other Skin Care Preps | 1 |

**Rosa Damascena (Damask Rose) Flower Water**
**Total Uses: 302**

| | | |
|---|---|---|
| Rosa Damascena (Damask Rose) Flower Water | 03D - Eye Lotion | 13 |
| Rosa Damascena (Damask Rose) Flower Water | 03E - Eye Makeup Remover | 2 |
| Rosa Damascena (Damask Rose) Flower Water | 03G - Other Eye Makeup Preparations | 7 |
| Rosa Damascena (Damask Rose) Flower Water | 04B - Perfumes | 3 |
| Rosa Damascena (Damask Rose) Flower Water | 05A - Hair Conditioner | 2 |
| Rosa Damascena (Damask Rose) Flower Water | 05F - Shampoos (Non-Coloring) | 2 |
| Rosa Damascena (Damask Rose) Flower Water | 05G - Tonics, Dressings, And Other Hair Grooming Aids | 5 |
| Rosa Damascena (Damask Rose) Flower Water | 05I - Other Hair Preparations | 1 |
| Rosa Damascena (Damask Rose) Flower Water | 07C - Foundations | 10 |
| Rosa Damascena (Damask Rose) Flower Water | 07E - Lipstick | 8 |
| Rosa Damascena (Damask Rose) Flower Water | 07F - Makeup Bases | 5 |
| Rosa Damascena (Damask Rose) Flower Water | 07H - Makeup Fixatives | 3 |
| Rosa Damascena (Damask Rose) Flower Water | 07I - Other Makeup Preparations | 1 |
| Rosa Damascena (Damask Rose) Flower Water | 09A - Dentifrices | 1 |
| Rosa Damascena (Damask Rose) Flower Water | 09B - Mouthwashes And Breath Fresheners | 1 |
| Rosa Damascena (Damask Rose) Flower Water | 10A - Bath Soaps And Detergents | 2 |
| Rosa Damascena (Damask Rose) Flower Water | 10E - Other Personal Cleanliness Products | 4 |
| Rosa Damascena (Damask Rose) Flower Water | 11A - Aftershave Lotion | 1 |
| Rosa Damascena (Damask Rose) Flower Water | 12A - Cleansing | 31 |
| Rosa Damascena (Damask Rose) Flower Water | 12C - Face And Neck (Exc Shave) | 87 |
| Rosa Damascena (Damask Rose) Flower Water | 12D - Body And Hand (Exc Shave) | 8 |
| Rosa Damascena (Damask Rose) Flower Water | 12F - Moisturizing | 55 |
| Rosa Damascena (Damask Rose) Flower Water | 12G - Night | 3 |
| Rosa Damascena (Damask Rose) Flower Water | 12H - Paste Masks (Mud Packs) | 11 |
| Rosa Damascena (Damask Rose) Flower Water | 12I - Skin Fresheners | 15 |
| Rosa Damascena (Damask Rose) Flower Water | 12J - Other Skin Care Preps | 19 |
| Rosa Damascena (Damask Rose) Flower Water | 13A – Suntan Gels, Creams, and Liquids | 1 |
| Rosa Damascena (Damask Rose) Flower Water | 13B – Indoor Tanning Preparations | 1 |

**Rosa Damascena (Damask Rose) Flower Water Extract**
**Total Uses: 1**

| | | |
|---|---|---|
| Rosa Damascena (Damask Rose) Flower Water Extract | 12H - Paste Masks (Mud Packs) | 1 |

**Rosa Damascena (Damask Rose) Flower Wax**
**Total Uses: 7**

| | | |
|---|---|---|
| Rosa Damascena (Damask Rose) Flower Wax | 03F - Mascara | 1 |
| Rosa Damascena (Damask Rose) Flower Wax | 07E - Lipstick | 2 |
| Rosa Damascena (Damask Rose) Flower Wax | 10A - Bath Soaps And Detergents | 1 |
| Rosa Damascena (Damask Rose) Flower Wax | 12D - Body And Hand (Exc Shave) | 1 |
| Rosa Damascena (Damask Rose) Flower Wax | 12J - Other Skin Care Preps | 2 |