Safety Assessment of *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	August 18, 2017
Panel Meeting Date:	September 11-12, 2017

The 2017 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Interim Director is Bart Heldreth, Ph.D. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088
cirinfo@cir-safety.org

Cosmetic Ingredient Review

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MEMORANDUM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: August 18, 2017

Subject: *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients

Attached is the Draft Report of *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients as used in cosmetics. [*HamVir092017Rep*] These eight ingredients are all derived from part(s) of the *Hamamelis virginiana* (Witch Hazel) plant.

In July 2017, an SLR was issued with an invitation for data on these ingredients. Concentration of use data were submitted. [*HamVir092017Data_1,2*] Data on method of manufacture, impurities, in vitro dermal and ocular irritation on Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract and Hamamelis Virginiana (Witch Hazel) Extract, and an HRIPT of Hamamelis Virginiana (Witch Hazel) Water with negative results were also submitted. [*HamVir092017Data_3,4*] Council comments have been addressed. [*HamVir092017PCPC*]

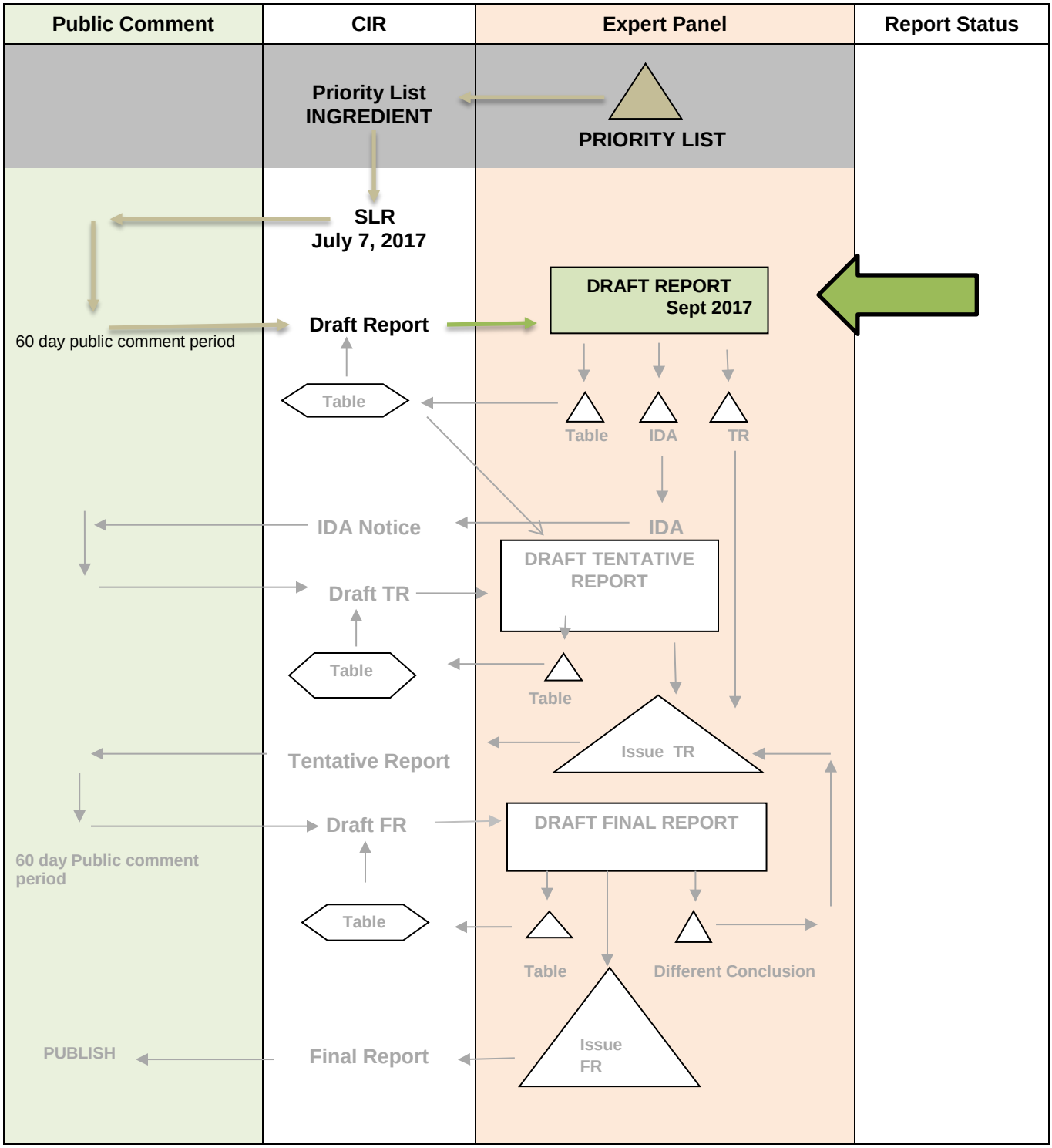
"Witch hazel" is a ubiquitous term and is used generically, along with other terms (e.g., "hamamelis water," "witch hazel extract," "witch hazel oil," and other variations) in the literature. Much of the information in the literature does not clarify the source plant part(s), the solvent(s), and/or the extraction method(s). This information is provided when known within the report. To add to the confusion, an additional CAS number has been found in the literature that is not used in the *Dictionary*. A letter has been sent to the Council asking for clarification on the INCI names and definitions.

If no further data are needed to formulate a conclusion of safety, the Panel should develop the basis for the Discussion and issue a Tentative Report. If more data are required, the Panel should list the data that are needed for a conclusion of safety, and issue an Insufficient Data Announcement.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY __*Hamamelis virginiana* (witch hazel)-derived ingredients_____

MEETING ___Sept 2017_____



History – *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients

2016 – Included in the priority list

June, 2017 – SLR posted with request for further information including:

- Constituent profiles for each of these ingredients
- Chemical and physical properties
- Method of manufacture
- Impurity data
- Dermal penetration
- Chronic dermal toxicity
- Inhalation toxicity
- Dermal irritation and sensitization

September, 2017 – Panel examines Draft Report.

Hamamelis virginiana (Witch Hazel)-derived ingredients Data Profile for ***DATE*, 2016**. Writer – Lillian Becker																				
		ADME		Acute toxicity			Repeated dose toxicity			Irritation					Sensitization						
	Use	Log K_{ow}	Dermal Penetration	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Animal	Ocular In Vitro	Dermal Animal	Dermal Human	Dermal In Vitro	Animal	Human	In Vitro	Repro/Devel	Genotoxicity	Carcinogenicity	Phototoxicity
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract																					
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract 84696-19-5											X			X							
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract													X								
Hamamelis Virginiana (Witch Hazel) Extract 84696-19-5											X			X							
Hamamelis Virginiana (Witch Hazel) Flower Water																X					
Hamamelis Virginiana (Witch Hazel) Leaf Extract																					
Hamamelis Virginiana (Witch Hazel) Leaf Water																					
Hamamelis Virginiana (Witch Hazel) Water																			X		
Undefined *Hamamelis virginiana* (Witch Hazel) Extract				X			X						X			X				X	

Ingredient Family Name

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	FEMA	Web
Hamamelis Virginiana (Witch Hazel) Water		Y	N	N	N	N	N	N	N	N	N	N	N	1	N	N	N	Y
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract		Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	84696-19-5	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract		Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Extract	84696-19-5	Y	N	86/8	Y	N	N	N	N	N	N	N	N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Flower Water		Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Leaf Extract		Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Leaf Water		Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Hamamelis virginiana (witch hazel) plant		N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
"Witch hazel"			N	N	N	Y	N	N	N	N	N	N	N	N	N	N	N	Y

Botanical and/or Fragrance Websites (if applicable)

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	IFRA	RIFM
Hamamelis Virginiana (Witch Hazel) Water		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Extract		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Flower Water		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Leaf Extract		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) Leaf Water		N	N	N	N	N	N
Hamamelis Virginiana (Witch Hazel) plant		Y	Y	Y	N	N	N

Search Terms

"witch hazel" OR CAS no.

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1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088
cirinfo@cir-safety.org

INTRODUCTION

This is a safety assessment of 8 *Hamamelis virginiana* (witch hazel)-derived ingredients as used in cosmetics (Table 1).

Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract	Hamamelis Virginiana (Witch Hazel) Flower Water
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Hamamelis Virginiana (Witch Hazel) Leaf Extract
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract	Hamamelis Virginiana (Witch Hazel) Leaf Water
Hamamelis Virginiana (Witch Hazel) Extract	Hamamelis Virginiana (Witch Hazel) Water

According to the *Web-Based Ingredient Dictionary* (wINCI), these ingredients mostly function in cosmetics as astringent and skin-conditioning agent - miscellaneous.[1] However, the only stated function therein for Hamamelis Virginiana (Witch Hazel) Flower Water is fragrance ingredient.

Drug astringent – skin protectant drug is also listed as a function of Hamamelis Virginiana (Witch Hazel) Water.[1] Drug astringent is not a cosmetic function, and the Cosmetic Ingredient Review (CIR) Expert Panel (Panel) does not evaluate non-cosmetic functions.

The names of the ingredients in this report are written in accordance with wINCI, as shown above, capitalized without italics and without abbreviations. When referring to the plant from which these ingredients are derived, the standard taxonomic practice of using *italics* will be followed (e.g., *Hamamelis virginiana*).

Often in the published literature, the information provided is not sufficient to determine how well the tested substance represents the cosmetic ingredient (e.g., "hamamelis water" with the CAS number 68916-39-2); the taxonomic name is used unless it is clear that the test substance is similar to a cosmetic ingredient. If the tested substance is a cosmetic ingredient, then the name from wINCI is used.

Botanicals, such as *Hamamelis virginiana* (witch hazel)-derived ingredients, may contain hundreds of constituents, some of which may have the potential to cause toxic effects. For example, geraniol and linalool are constituents of the *Hamamelis virginiana* (witch hazel) plant; geraniol is a potential dermal sensitizer as are the oxidation products of linalool.[2-4] In this assessment, CIR is reviewing the potential toxicity of each of the *Hamamelis virginiana* (witch hazel)-derived ingredients as a whole, complex mixture. CIR is not reviewing the potential toxicity of the individual constituents herein.

Pertinent data were discovered in other reports, including reports by the Committee on Herbal Medicinal Products (HMPC), the World Health Organization (WHO), and the European Agency for the Evaluation of Medicinal Products (EMEA), Veterinary Medicines Evaluation Unit.[5-7] Reports by these organizations are cited in this assessment to identify the source of the data obtained from these summaries.

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 CIR typically evaluates, is provided on the CIR website (http://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; http://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

CHEMISTRY

Definition

The definitions of the ingredients in this safety assessment are provided in Table 1.

Plant Identification

Hamamelis virginiana (witch hazel), a member of the family Hamadelidaceae, is indigenous to damp woods on the Atlantic coast of North America, regionally from Florida to Nova Scotia, and may be found as far west as Texas.[5,7-10] The appearance/structure of the plant and leaves vary widely with no consistent pattern of variation or geographic correlation. The plant may be a tall shrub with the branches coming from the base or small tree of up to 4.6 m tall. The leaves are 1 to 5 cm long and may alternate or stipulate, have short petioles, and may be unequilateral or rhomboid-ovate, with an oblique base and sinuate or sinuate-dentate margin. The flowers are golden-yellow and thread-like, and grow in axillary clusters. *Hamamelis virginiana* (witch hazel) likely reproduces through insect pollination instead of wind pollination. The leaves fall in autumn about the same time as fruits ripen from the flowers of the previous year. The fruit are a 2-beaked, 2-celled, woody capsule each cell containing a single black seed. This plant is unusual in that it has flowers and fruit at the same time.

Physical and Chemical Properties

Chemical and physical properties of for Hamamelis Virginiana (Witch Hazel) Leaf Water and Hamamelis Virginiana (Witch Hazel) Water at 84% to 85% in grain alcohol or ethanol are presented in Table 2.

Method of Manufacture

The definitions of several of the *Hamamelis virginiana* (witch hazel)-derived ingredients in this safety assessment give insight into possible methods of manufacture. For example, the definition for Hamamelis Virginiana (Witch Hazel)

Flower Water states that this ingredient is an aqueous solution of the steam distillates obtained from the flowers of *Hamamelis virginiana*.[1]

Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract

A manufacturer reported that the method of manufacture for a product mixture containing Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (10%) starts with the testing of the collected *Hamamelis virginiana* (witch hazel) plant material.[11] If the materials pass (criteria not specified), the plant matter is mechanically cleaned to remove unnecessary material. The twigs, bark, and leaves are then processed by grinding and milling. An aqueous extraction is performed at a specific pH and temperature for a specified duration (not provided). Phenoxyethanol, tetrasodium ethylenediaminetetraacetic acid (EDTA), methylparaben, ethylparaben, butylparaben, propylparaben, and isobutylparaben are added to the extract. The extract is filtered and the batch is sampled for quality control. Adjustments are made if needed. After the extract is packaged, it is sampled from microbes.

A similar method of manufacture was reported for a product mixture containing Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (20%).[11] The only difference is that the propylene glycol is added to dilute the mixture after the aqueous extraction is performed, and the EDTA is not added to the extract

Hamamelis Virginiana (Witch Hazel) Extract

A manufacturer reported that the method of manufacture for a product mixture containing Hamamelis Virginiana (Witch Hazel) Extract (5%) starts with grinding and milling the collected *Hamamelis virginiana* (witch hazel) plants.[12] The resulting material is extracted with cyclopentasiloxane at a specific pH and temperature for a specified duration (not provided). The extract is filtered and the batch is sampled for quality control. Adjustments are made if needed. After the extract is packaged, it is sampled for microbes.

Hamamelis Virginiana (Witch Hazel) Leaf Water

A manufacturer reported that one Hamamelis Virginiana (Witch Hazel) Leaf Water product is a distillate prepared from recently harvested and partially dried leaves of *Hamamelis virginiana* (witch hazel).[13] Alcohol is added to the final product at 14%.

Hamamelis Virginiana (Witch Hazel) Water

A manufacturer reports that a Hamamelis Virginiana (Witch Hazel) Water product is a distillate prepared from recently cut and partially dried dormant twigs of *Hamamelis virginiana* (witch hazel).[14] In this product, grain alcohol or ethanol is added to the final product at 14%.

Composition

Hamamelis virginiana (Witch Hazel) Plants

Constituents of the bark and leaves of *Hamamelis virginiana* (witch hazel) are presented in Table 3.

Polyphenols - The leaves contain up to, but not more than 3%, tannins.[7,15] The cortex/bark of the stems contains up to 12%, but not less than 4%, tannins. Both hydrolysable and condensed tannins are present, with the latter predominating.[7] Leaf tannins are a mixture of gallic acid (10%), hydrolysable hamamelitannin (1.5%) and condensed proanthocyanidins (88.5%). Bark tannins are similar qualitatively, but have a much greater hamamelitannin concentration (up to 65% of a hydroalcoholic extract). Polyphenols, other than tannins, include phenolic acids and flavonoids. At least 27 phenolic constituents have been identified.

Flavonoids – The leaves contain flavonoid galactosides and glucuronides and other flavonoids such as kaempherol, quercetin, quercitrin, and isoquercitrin.[5]

Catechins - Catechins include (+)-catechin, (+)-gallocatechin, (-)-epicatechin gallate(III), and (-)-epigallocatechin gallate(III). Oligomeric procyanidins are also present. [7,15]

Volatile oil – Both bark and leaves contain volatile oil (0.1% and 0.01% to 0.05%, respectively).[6] The composition of the volatile fraction obtained by water distillation from the leaves and bark of *Hamamelis virginiana* (witch hazel), determined by gas chromatography-mass spectrometry (GC-MS), consists of about 175 identified compounds in the leaves and 168 compounds in the bark.[2,5] The dominating substances were represented by a homologous series of alkanes, alkenes, aliphatic alcohols, related aldehydes, ketones, and fatty acid esters. The volatile oil contains hexane-2-ol, hexenol, α- and β-ionones, eugenol, safrole (maximum 0.2% of the volatile oil) and sesquiterpenes. Other constituents include gallic acid. The bark contains significantly higher levels of phenylpropanoids and sesquiterpenoids in the volatile fractions compared to the leaves, which contain higher amounts of monoterpenoids.[5] Other components include kaempferol, quercetin, chlorogenic acid isomers, and hydroxycinnamic acids.[7] The volatile oil contains small amounts of safrole and eugenol as well as numerous other minor components, such as resin, wax, and choline.

The constituents in the volatile fraction of water-distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using n-hexane as the collector solvent are listed in Table 4. The constituents were identified by GC-MS.[2]

Hamamelis virginiana (Witch Hazel)-Derived Ingredients

The methods of manufacture significantly impact the compositions of *Hamamelis virginiana* (witch hazel)-derived ingredients. For example, distilled ingredients have fewer astringent tannins than a water extract.[16]

Hamamelis Virginiana (Witch Hazel) Water is reported by a manufacturer to be supplied at 85% to 86% with 14% to 15% grain alcohol or ethanol.[17-19] The same manufacturer reports that Hamamelis Virginiana (Witch Hazel) Leaf Water is also supplied at 85% to 86% with 14% to 15% ethanol.[20]

Impurities/Constituents

Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract

One manufacturer reported that Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract is supplied in product mixtures.[21-24] Two product mixtures that include Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract at 10.00% or 20.00%, also contain tetrasodium EDTA or propylene glycol, respectively (Table 5). Both of these product mixtures also contain methylparaben, ethylparaben, butylparaben, propylparaben, and isobutylparaben. These product mixtures were certified to not include detectable allergens including amyl cinnamal, citral, courmarin, eugenol, germaniol, and linalool (Table 6). These product mixtures are also certified to not include detectable pesticides including alachlor, diazinon, heptachlor, dichlorodiphenyltrichloroethane (DDT), and parathion. These two product mixtures are also specified to contain < 20 ppm heavy metal, < 10 ppm lead, < 2 ppm arsenic, and < 1 ppm cadmium.[25,26] Microbial content is < 100 colony forming units (CFU)/g with no pathogens, < 100 CFU/g yeast and mold, and 0 CFU/g gram negative bacteria.

Hamamelis Virginiana (Witch Hazel) Extract

One manufacturer reported that Hamamelis Virginiana (Witch Hazel) Extract is supplied as a product mixture of 5.00% Hamamelis Virginiana (Witch Hazel) Extract and 95.00% cyclopentasiloxane.[27,28] This product mixture was certified to not include detectable allergens including amyl cinnamal, citral, courmarin, eugenol, germaniol, and linalool (Table 6). This product mixture was also certified to not include detectable pesticides including alachlor, diazinon, heptachlor, DDT, and parathion. These two product mixtures are also specified to contain < 20 ppm heavy metal, < 10 ppm lead, < 2 ppm arsenic, and < 1 ppm cadmium.[29] Microbial content is < 100 CFU/g with no pathogens, < 100 CFU/g yeast and mold, and 0 CFU/g gram negative bacteria.

Hamamelis Virginiana (Witch Hazel) Leaf Water

Specifications for Hamamelis Virginiana (Witch Hazel) Leaf Water (and 14% grain alcohol) state that this ingredient is to contain < 50 mg/100 mL nonvolatile residue, < 10 CFU/mL yeast and mold, a maximum of 1 CFU/mL gram negative bacteria, and is below the levels of detection for acetone, other ketones, isopropyl alcohol and *t*-butyl alcohol.[13]

Hamamelis Virginiana (Witch Hazel) Water

Specifications for Hamamelis Virginiana (Witch Hazel) Water (and 14% grain alcohol) state that this ingredient is to contain < 25 mg/100 mL nonvolatile residue, < 10 CFU/mL yeast and mold, a maximum of 1 CFU/mL bacteria, and is below the levels of detection for acetone, other ketones, isopropyl alcohol and t-butyl alcohol, and formaldehyde.[14,30,31] Tannins are limited to < 0.03 mg/mL.

Hamamelis virginiana (witch hazel)

Table 7 lists constituents of concerns of *Hamamelis virginiana* (witch hazel) plants. These plants are reported to contain linalool and quercetin.[2,32] Safrole was also found at a level of < 0.2% in *Hamamelis virginiana* (witch hazel) leaf oil.[5] Possible contaminants (e.g., tributylphosphate and dibutyl phthalate) from the volatile fraction of water-distilled leaves and bark are noted in Table 4.

The International Fragrance Association (IFRA) publishes restrictions for fragrance ingredients. Constituents of *Hamamelis virginiana* (witch hazel) that have restrictions established by the International Fragrance Association Standards are listed in Table 8.[33]

During harvest, *Hamamelis virginiana* (witch hazel) plants can be confused with *Coryllus avellana* (hazelnut), thus may be a source of impurities.[5] The two plants can be distinguished by anatomical and analytical examination.

UV Absorption

Hamamelis virginiana (Witch Hazel)

In ethanol extracts of dried *Hamamelis virginiana* (witch hazel) plant material (most likely leaves), the light absorbance curves peaked between 250 and 280 nm, depending on the method of extraction.[34] Extracts were prepared by reperculation and microwave assisted extraction, and tested at 3%, 10%, and 40%.

USE

Cosmetic

The safety of the cosmetic ingredients included in this assessment is evaluated based on data received from the U.S. Food and Drug Administration (FDA) and the cosmetic 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 FDA's Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentration by product category.

According to VCRP survey data received in 2017, Hamamelis Virginiana (Witch Hazel) Water is reported to be used in 386 formulations (255 in leave-on formulations, 122 in rinse-off formulations, and 9 in formulations that are diluted for the bath; Table 9).[35] Hamamelis Virginiana (Witch Hazel) Extract is reported to be used in 359 formulations (266 in leave-on formulations, 91 in rinse-off formulations, and 2 in formulations that are diluted for the bath) and Hamamelis Virginiana (Witch Hazel) Leaf Extract is reported to be used in 218 formulations (138 in leave-on formulations, 73 in rinse-off formulations, and 7 in formulations that are diluted for the bath). All other in-use ingredients are reported to be used in 128 or fewer formulations. The VCRP has entries for "Hamamelis Virginiana Flower Water," which is assumed to be Hamamelis Virginiana (Witch Hazel) Flower Water.

The results of the concentration of use survey conducted by the Council in 2017 indicate Hamamelis Virginiana (Witch Hazel) Extract has the highest reported maximum concentration of use; it is used at up to 86% (in skin fresheners).[36] Hamamelis Virginiana (Witch Hazel) Water is used at up to 43% (in the category of other skin care preparations). All other in-use ingredients are reported to be used at up to 5% or less.

In some cases, reports of uses were received in the VCRP, but concentration of use data were not provided. For example, Hamamelis Virginiana (Witch Hazel) Flower Water is reported to be used in 43 cosmetic formulations, but no use concentration data were reported. In other cases, no uses were reported in the VCRP, but concentration of use data were received from industry; Hamamelis Virginiana (Witch Hazel) Leaf Water had no reported uses in the VCRP, but use concentrations in paste masks and mud packs were provided in the industry survey. Therefore, it should be presumed there is at least one use in every category for which a concentration is reported.

There were no uses reported to the VCRP and the industry survey for Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Extract and Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract.

Several of these ingredients were reported to be used in formulations used near the eyes (up to 35.8% in eye lotions and other eye makeup preparations) and in formulations that come in contact with mucous membranes (up to 35.8% in lipsticks). Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract and Hamamelis Virginiana (Witch Hazel) Water are used in formulations that may be ingested (including lipsticks, mouth washes, and breathe fresheners) at up to 35.8% in lipsticks, and in formulations for use on babies (no concentrations of use reported).

Additionally, some of the *Hamamelis virginiana* (witch hazel)-derived ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Hamamelis Virginiana (Witch Hazel) Water and Hamamelis Virginiana (Witch Hazel) Extract are used in body and hand spray formulations at up to 25.8% and 5%, respectively. 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.[37,38] 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.[39,40] Hamamelis Virginiana (Witch Hazel) Extract and Hamamelis Virginiana (Witch Hazel) Water were reported to be used in face powders at concentrations up to 0.05% and 0.093%, respectively. Conservative estimates of inhalation exposures to respirable particles during the use of loose-powder cosmetic products are 400- to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[41-43]

Non-Cosmetic

Hamamelis virginiana (witch hazel), under the name "witch hazel" may be used as an active ingredient as an astringent in over-the-counter (OTC) anorectal drug products at 10% to 50% and OTC skin protectant drug products (as an astringent active ingredient with no limit specified). [21CFR346.18; 21CFR347.12]

Hamamelis virginiana (witch hazel) preparations are commonly used for dermatological conditions, including diaper-related dermatitis; however, clinical studies supporting these uses are generally lacking.[5] In Europe, extracts of *Hamamelis virginiana* (witch hazel) folium and/branches are used in teas/poultices (leaf), liquid and dry extracts (leaf 1:1 or 2 with 30% to 60% ethanol; bark 5 to 7:1 with 30% ethanol, respectively), distillates (1:1.12 to 2.08 with ethanol), ointments, creams, tinctures (1:10 with 45% ethanol), suppositories, and liquid extracts to treat hemorrhoids, fever, nose and gum bleeds, lesions, varicose veins, and other minor inflammations of the skin and mucosa. *Hamamelis virginiana* (witch hazel) folium is also used to make eye drops (10%) to treat irritation.

Hamamelis virginiana (witch hazel), 2.5% to 10.8% (w/w) of an extract of the leaves, is used in veterinary medicine as a topical solution, or as an ointment, combined with other herbal extracts, to promote wound-healing of minor injuries to the skin, treatment of skin inflammations, ulcerations, and dermatoses.[6]

TOXICOKINETIC STUDIES

Dermal Penetration

Obtaining data on the toxicokinetics of *Hamamelis virginiana* (witch hazel)-derived ingredients would not be practical because these ingredients are complex mixtures. Exposure to the components of these ingredients

in cosmetics is expected to be lower than that from dietary exposure because these ingredients are incorporated into cosmetic products only at very low concentrations.

A manufacturer reported that *Hamamelis virginiana* (witch hazel) extracts dermally applied in therapeutic amounts do not penetrate into the deeper layers of the skin because of the astringency of their ingredients, thus, they are not absorbed into the blood circulation.[5]

Absorption, Distribution, Metabolism, and Excretion (ADME)

No published ADME studies were discovered and no unpublished data were submitted.

TOXICOLOGICAL STUDIES

Acute Dose Toxicity

No published acute dermal or inhalation toxicity studies were discovered and no unpublished data were submitted.

Oral

The oral administration of a single dose of a *Hamamelis virginiana* (witch hazel) preparation (10 to 20 g; preparation was not specified) showed no toxic effect in mice and rats.[5] No further details were provided.

Mucosal

New Zealand White rabbits (n = 2/sex) were administered suppositories containing *Hamamelis virginiana* (witch hazel) ethanol extract (0, 20, 100, or 300 mg/kg).[44] The extract was characterized as having a minimum of 10% tannins and containing gallic acid. The suppository was comprised of hard fat, white beeswax, and colloidal anhydrous silica. The suppositories were melted and a single dose was administered with a graduated pipette with a plastic tip. The rabbits were observed for 7 h after dosing and then daily for 2 weeks. A local examination of the anorectal region was conducted on days 2, 7 and 14 post-dosing. Blood was sampled on the last day of the observation period. No rabbits died as the result of the experiment. There were no differences in body weights among test groups. There were no changes in liver and kidney functions. There was a non-dose-dependent increase in serum urea content in all treatment rabbits. There were no hematological effects observed. The no-observed-adverse-effects-level (NOAEL) was > 300 mg/kg.

Short-Term Toxicity Studies

No published short-term oral, dermal, or inhalation toxicity studies were discovered and no unpublished data were submitted.

Mucosal

Sprague Dawley rats (n = 5/sex) were administered suppositories containing *Hamamelis virginiana* (witch hazel) ethanol extract (0, 20, 100, or 300 mg/kg/day) for 28 days.[44] The extract was characterized as having a minimum of 10% tannins and containing gallic acid. The suppository was comprised of hard fat, white beeswax, and colloidal anhydrous silica. The suppositories were melted and administered with a graduated pipette with a plastic tip. The rats were observed for 1 h after dosing, and then observed and weighed daily. Feed and water consumption was assessed weekly. Blood was sampled by cardiac puncture on the last day of the observation period. The rats were killed and necropsied; the digestive tract was included in the examinations. The liver, kidney, and rectal biopsies were isolated from two rats/sex in the placebo and high-dose groups; these samples were fixed in formaldehyde and examined under light microscope. No rats died as the result of the experiment and no clinical signs were observed. There were no differences in body weight gains among test groups. The observed organs (liver, kidneys, spleen, submandibular salivary glands, heart, testis, and lungs) were similar among placebo and treatment groups. There were no changes in liver and kidney functions without changes in serum lipids and protein profiles. There were no hematological effects observed. The NOAEL was > 300 mg/kg/day.

Subchronic

No published dermal or inhalation subchronic toxicity studies were discovered and no unpublished data were submitted.

Oral

Hamamelis virginiana (witch hazel) at 100 mg/kg/day was orally administered to rats for three months. There were no abnormalities reported. No further information was provided.[5]

Chronic Toxicity Studies

No published chronic oral or inhalation toxicity studies were discovered and no unpublished data were submitted.

Dermal

In a National Toxicology Program (NTP) experiment, a 2-year skin painting study of a *Hamamelis virginiana* (witch hazel)-derived substance (50% in deionized water and at 100%; under the name "Hamamelis water" with the CAS number 68916-39-2) was conducted using male and female F344 rats and B6C3F$_1$ mice.[45-47] Further details are presented in the Carcinogenicity section.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No published reproductive or developmental toxicity studies were discovered and no unpublished data were submitted.

GENOTOXICITY STUDIES

In Vitro

Hamamelis Virginiana (Witch Hazel) Water

Hamamelis Virginiana (Witch Hazel) Water (concentration not specified) was not genotoxic in a *Salmonella* mammalian microsome assay (stains TA97, TA98, TA100, and TA1535), with and without metabolic activation.[5]

A sister chromatid exchange (SCE) and a chromosome aberration test were performed on Hamamelis Virginiana (Witch Hazel) Water.[48] The results of both assays were negative at up to 5000 µg/mL, with and without metabolic activation.

Hamamelis Virginiana (Witch Hazel) Water (up to 5000 µg/mL) was tested for mutagenic potential in the L5178Y tk+/- mouse lymphoma cell forward mutation assay, with and without metabolic activation.[5,49] Cultures were exposed to the test substance for 4 h, and cultured for 2 days before plating in soft agar with or without trifluorothymidine (TFT; 3 µg/mL). The negative control was distilled water; the positive controls were methyl methanesulphonate without metabolic activation and ethyl methanesulphonate with metabolic activation. The test substance was tested at least twice and was not identified as a mutagen.

Hamamelis virginiana (witch hazel)

Hamamelis virginiana (witch hazel) leaf oil (under the CAS number 68916-39-2) (100 to 10,000 µg/plate) was not genotoxic in an Ames assay (stains TA98, TA100, TA1535, and TA1537), with and without metabolic activation.[50]

In Vivo

No published in vivo genotoxicity studies were discovered and no unpublished data were submitted.

CARCINOGENICITY STUDIES

No published oral or inhalation carcinogenicity studies were discovered and no unpublished data were submitted.

Dermal

In a skin painting study, a *Hamamelis virginiana* (witch hazel)-derived substance (50% in deionized water and at 100%; under the name "Hamamelis water" with the CAS number 68916-39-2) was dermally administered to male and female F344 rats and B6C3F$_1$ mice, 5 days per week for 2 years, in a National Toxicology Program (NTP) experiment.[45-47] There was a trend for increased tumors, fibromas or fibrosarcomas noted in the male rats and alveolar/bronchiolar adenomas or carcinomas in female mice, but none of these observations were statistically-significant. There were no other signs of carcinogenicity in either species at either concentration. No further details were provided. A technical report number was assigned to the chronic study of this test article. The study was considered inadequate and no technical report was prepared.

Subcutaneous

An aqueous *Hamamelis virginiana* (witch hazel) leaf extract (10 mg in saline; 0.5 mL) was subcutaneously injected into the flanks of NIH Black rats once per week for up to 78 weeks.[51] Saline was the control. The extract was made from wild collected leaves that were powdered and extracted with hot water, and lyophilized. The dose was based on preliminary studies to find the amount of plant material that did not produce any systemic toxicity or local necrosis and sloughing (this dose did cause some swelling, which disappeared within 1 to 2 weeks). Injections were conducted for 78 weeks or until a tumor was detected. The detected tumor was allowed to grow to sufficient size, and then the rat was killed and necropsied. Rats that lived through treatment were observed for an addition 12-week period, and then they were killed and necropsied. Tumor tissue and organs (including regional lymph nodes, lungs, liver, spleen, and kidneys) were examined. No tumors were detected in the control group. Three males in the treatment group had tumors that were discovered in weeks 72 to 73. No tumors were observed in the female rats. Two males (weeks 24 and 57) and one female (week 59) died of lung infections. The number of treated rats with tumors was not significantly greater than that of the controls.

DERMAL IRRITATION AND SENSITIZATION STUDIES

In Vitro

EpiDerm™ assays of two product mixtures that contains Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) were negative (Table 10). [52,53] An EpiDerm™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5%) was negative for predicting dermal irritation.

Sensitization

A human repeated insult patch test (HRIPT; n = 105) was performed on a product containing Hamamelis Virginiana (Witch Hazel) Water (25.80%).[54] Induction patches were applied neat to the upper back three times per week for three weeks. The test sites were wiped with 70% isopropyl alcohol prior to placement of the patches. Patches were in place for 24 h. The test sites were examined prior to the application of the next patch. After approximately 2 weeks rest, the challenge patch was applied for 24 h. The challenge site was examined upon removal, and at 48 and 72 h. If there was a reaction, the challenge site was examined again at 96 h. There were no reactions at any time during this test demonstrating no potential for irritation or sensitization of this test material.

OCULAR IRRITATION STUDIES

No published in vivo ocular irritation studies were discovered and no unpublished data were submitted.

In Vitro

EpiOcular™ assays of two product mixtures that contains Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) were negative for predicting ocular irritation (Table 11). [52,53] An EpiOcular™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5%) was negative for predicting ocular irritation.

CLINICAL STUDIES

Retrospective and Multicenter Studies

In a multicenter, prospective pediatric cohort study, subjects of different age groups (27 days to 1 year; 1 to 5 years; 6 to 11 years of age) suffering from superficial skin lesions, diaper skin rash, or other local inflammations of skin and mucous membranes were treated in a randomized manner with either an ointment containing *Hamamelis virginiana* (witch hazel; concentration, composition, and source not specified; n = 231) or dexpanthenol, a documented therapy used for the control (n = 78).[5,55] The recommended individual observation periods were 7 to 10 days; dosage was based on the recommendations of the treating physician. Tolerability of the ointment containing *Hamamelis virginiana* (witch hazel) was assessed as excellent or good by 99.1% of the doctors and 98.2% of the parents (dexpanthenol: 97.4% and 92.3%, respectively). Twelve of 231 subjects experienced adverse events, which included confusion, head lice, cough/allergic reaction, fungal infection/deterioration, otitis, increase in erythema, rhinopharyngitis, burning sensation, super-infection, diaper candidiasis, and obstructive bronchitis. The authors considered only two adverse events as potentially *Hamamelis virginiana* (witch hazel)-related (i.e. erythema and burning sensation), which were resolved by the end of the treatment period.

Subjects (n = 12) that were confirmed to be sensitized to chamomile (thus, Compositae-sensitive) were administered patch tests for other plant-derived extracts, including an aqueous-alcoholic *Hamamelis virginiana* (witch hazel) distillate (concentration and method of extraction not specified).[56] One subject had a positive reaction the *Hamamelis virginiana* (witch hazel) distillate.

Subjects (n = 1032) that were in clinics to be patch tested for allergens were administered additional patch tests for ointments that contain botanical extracts, including one that contained *Hamamelis virginiana* (witch hazel) extract (25%).[57] A total of four subjects had positive results to the ointment containing *Hamamelis virginiana* (witch hazel) extract. Two of these subjects also had reactions to other ointments and to “wool fat,” one of the ingredients in the ointments.

Damaged Skin

Studies on the use of *Hamamelis virginiana* (witch hazel)-derived substances on damaged skin are summarized in Table 12.

There were no reported adverse effects when a cream containing Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract (10%) was applied to skin damaged by UVB light.[58]

There were no reported adverse effects from an oil/water (o/w) emulsion containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00256% *Hamamelis* ketone) applied to skin damaged by UVB light or tape stripping.[59] There were no reported adverse effects from three O/W emulsions containing *Hamamelis virginiana* (witch hazel) distillates (10% *Hamamelis* ketone) from different suppliers applied to skin damaged by UVB light.[60]

There were no adverse events attributed to a cream containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00064%) when applied to subjects with moderately severe atopic eczema for 14 days.[61]

Case Reports

A 31-year-old non-atopic woman started to use a new eye gel that contained "witch hazel distillate," after which edema developed around the eyes within 1 week.[62] At the same time, she was treated with 1% hydrocortisone-17-butyrate for dermatitis of the lower limbs. She stopped using the eye gel, but instead started to use alternative remedies (not specified). Over the following days, edema spread to the rest of the face and neck and then presented as eczema. She was treated systemically with corticosteroid and told not to use any cosmetics or other treatments. The dermatitis resolved and did not relapse. A patch test of the eye cream and its components was conducted. At the readings on day 3, the patch test had positive results for the eye cream (+) and for "witch hazel distillate" in a concentration-dependent manner (1%, -; 5%, +?; 10%, +; 50%, ++; 100%, ++).

SUMMARY

This is a safety assessment of 8 *Hamamelis virginiana* (witch hazel)-derived ingredients as used in cosmetics. According to wINCI, the functions of these ingredients include cosmetic astringent and skin-conditioning agent – miscellaneous.

Hamamelis virginiana (witch hazel), a member of the family Hamadelidaceae, is indigenous to damp woods on the Atlantic coast of North America ranging from Florida to Nova Scotia.

In ethanol extracts of dried *Hamamelis virginiana* (witch hazel) plant material (most likely leaves), the light absorbance curves peaked between 250 and 280 nm, depending on the method of extraction.

According to VCRP survey data received in 2017, Hamamelis Virginiana (Witch Hazel) Water is reported to be used in 386 formulations (255 in leave-on formulations, 122 in rinse-off formulations, and 9 in formulations that are diluted for the bath). Hamamelis Virginiana (Witch Hazel) Extract is reported to be used in 359 formulations and Hamamelis Virginiana (Witch Hazel) Leaf Extract is reported to be used in 218 formulations. All other in-use ingredients are reported to be used in 128 or fewer formulations.

The results of the concentration of use survey conducted by the Council in 2017 indicate Hamamelis Virginiana (Witch Hazel) Extract has the highest reported maximum concentration of use; it is used at up to 86% (in skin fresheners). Hamamelis Virginiana (Witch Hazel) Water is used at up to 43% (in the category of other skin care preparations). All other in-use ingredients are reported to be used at up to 5% or less.

In the United States, *Hamamelis virginiana* (witch hazel), under the name "witch hazel" may be used as an active ingredient as an astringent in OTC anorectal drug products at 10% to 50% and in OTC skin protectant drug products (no limit specified).

The oral administration of a single dose of a *Hamamelis virginiana* (witch hazel) preparation (10 to 20 g; preparation was not specified) showed no toxic effect in mice and rats.

In an experiment where *Hamamelis virginiana* (witch hazel) ethanol extract was administered to rabbits in a suppository in a single dose, no rabbits died as the result of the experiment. There were no differences in body weights among test groups. There were no changes in liver and kidney functions. There were no hematological effects observed. The NOAEL was > 300 mg/kg.

There were no abnormalities reported when *Hamamelis virginiana* (witch hazel) at 100 mg/kg/day was orally administered to rats for three month.

In an experiment where *Hamamelis virginiana* (witch hazel) ethanol extract was administered to rats in a suppository for 28 days, no rats died as the result of the experiment. There were no differences in body weights among test groups. There were no changes in liver and kidney functions. There were no hematological effects observed. The NOAEL was > 300 mg/kg.

Hamamelis Virginiana (Witch Hazel) Water was not genotoxic in SCE, chromosome aberration, and Ames tests. Hamamelis Virginiana (Witch Hazel) Water was not mutagenic to mouse lymphoma cells in a forward mutation assay.

In a skin painting study, a *Hamamelis virginiana* (witch hazel)-derived substance (50% in deionized water and at 100%) was dermally administered to male and female rats and mice for 2 years in a NTP study. There were no significant signs of carcinogenicity in either species at either concentration.

The number of treated rats with tumors was not significantly greater than that of the controls when an aqueous *Hamamelis virginiana* (witch hazel) leaf extract (10 mg in saline) was subcutaneously injected into the flanks of rats once per week for up to 78 weeks.

EpiDerm™ assays of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) were negative for predicting dermal irritation. An EpiDerm™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5%) was negative for predicting dermal irritation.

An HRIPT of a product containing Hamamelis Virginiana (Witch Hazel) Water (25.80%) demonstrated no potential for irritation or sensitization.

EpiOcular™ assays of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract (5% and 10%) were predictive of no ocular irritation. An EpiOcular™ assay of Hamamelis Virginiana (Witch Hazel) Extract (5%) was predictive of no ocular irritation.

In a multicenter, prospective pediatric cohort study, subjects suffering from superficial skin lesions, diaper skin rash, or other local inflammations of skin and mucous membranes were treated with either an ointment containing either *Hamamelis virginiana* (witch hazel; concentration, composition, and source not specified) or dexpanthenol (control). Only

two adverse events were potentially related to the *Hamamelis virginiana* (witch hazel; i.e.: erythema and burning sensation), which were resolved by the end of the treatment period.

One of 12 subjects that were confirmed to be sensitized to chamomile (thus, Compositae-sensitive) had a positive reaction to *Hamamelis virginiana* (witch hazel) distillate in a patch test. Four of 1032 subjects had positive results to an ointment containing *Hamamelis virginiana* (witch hazel) extract in a patch test.

There were no reported adverse effects when a cream containing Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract (10%) was applied to skin damaged by UVB light.

There were no reported adverse effects from an o/w emulsion containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00256% *Hamamelis* ketone) applied to skin damaged by UVB light or tape stripping. There were no reported adverse effects from o/w emulsions containing *Hamamelis virginiana* (witch hazel) distillates (10% *Hamamelis* ketone) from different suppliers applied to skin damaged by UVB light.

There were no adverse events attributed to a cream containing *Hamamelis virginiana* (witch hazel) distillate (up to 0.00064%) when applied to subjects with moderately severe atopic eczema for 14 days.

DISCUSSION

[*To be developed.]*

CONCLUSION

[To be developed.]

TABLES

Table 1. Definitions and functions of the *Hamamelis virginiana* (Witch Hazel)-derived ingredients.[1]

Ingredient	Definition	Functions
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract is the extract of the bark and leaves of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract 84696-19-5 [(generic)]	Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract is the extract of the bark, leaves and twigs of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract is the extract of the bark and twigs of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Extract 84696-19-5 [(generic)]	Hamamelis Virginiana (Witch Hazel) Extract is the extract of the whole plant, *Hamamelis virginiana*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Flower Water [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Flower Water is an aqueous solution of the steam distillate obtained from the flowers of *Hamamelis virginiana.*	Fragrance ingredient
Hamamelis Virginiana (Witch Hazel) Leaf Extract [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Leaf Extract is the extract of the leaves of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Leaf Water [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Leaf Water is an aqueous solution of the steam distillates obtained from the leaves of *Hamamelis virginiana.*	Cosmetic astringent; skin-conditioning agent – miscellaneous
Hamamelis Virginiana (Witch Hazel) Water [84696-19-5 (generic)]	Hamamelis Virginiana (Witch Hazel) Water is an aqueous solution containing natural volatile oils obtained by the distillation of twigs, bark and leaves of *Hamamelis virginiana.*	Drug astringent – skin protectant drugs; skin-conditioning agent - miscellaneous

Table 2. Chemical and physical properties of *Hamamelis virginiana* (witch hazel)-derived ingredients.

Property	Value	Reference
Hamamelis Virginiana (Witch Hazel) Leaf Water[a]		
Physical Form	Liquid	13,20
Color	Clear Colorless to slight yellow	20 13
Odor	Characteristic Characteristic with slight green note	20 13
Specific Gravity @ 20°C @ 25°C	0.976 - 0.982 0.979 - 0.983	13,20 13,20
Vapor pressure mmHg@ 20°C	18.75	20
Vapor Density mmHg	1.03	20
Melting Point °C	-8	20
Boiling Point °C	88	20
Water Solubility	Very soluble	20
Hamamelis Virginiana (Witch Hazel) Water[a]		
Physical Form	Liquid	14,17-19,30,31
Color	Clear	14,17-19,30,31
Odor	Characteristic Mild	14,17-19,30,31 31
Specific Gravity @ 20°C @ 25°C	0.976 - 0.982 0.979 - 0.983	17-19,30,31 17-19,30,31
Vapor pressure mmHg @ 20°C	18.75	18,19
Vapor Density mmHg	1.03	18,19
Melting Point °C	-8	18,19
Boiling Point °C	88	18,19
Water Solubility g/L	Very soluble	18,19

[a] These values are for Hamamelis Virginiana (Witch Hazel) Leaf Water and Hamamelis Virginiana (Witch Hazel) Water at 84%-85% in grain alcohol or ethanol.

Table 3. Constituents found in the bark and leaves of *Hamamelis virginiana* (witch hazel) plants.[32]

Chemical	Plant Part	Low PPM	High PPM
6-methylheptadien-3,5-dione	Leaf	-	25.0
Acetaldehyde	Leaf	-	160.0
Afzelin	Leaf	-	-
Alcohols	Leaf	-	2000.0
Alpha-Ionone	Leaf	-	175.0
Astragalin	Leaf	-	-
Beta-Ionone	Leaf	-	50.0
Catechin-3-gallate	Bark	-	-
Catechin-tannin	Leaf	-	-
Choline	Leaf	-	2000.0
D-Gallocatchein	Bark	-	-
Ellagitannin	Bark	-	-
EO	Leaf	-	5000.0
Esters	Leaf	-	750.0
Gallic-acid	Leaf	-	54400.0
Gallo-tannin	Leaf	-	-
Hamamelidine	Leaf	-	-
Hamamelin	Bark	-	160000.0
Hamamelin	Leaf	-	70000.0
Hamamelitannin	Leaf	-	80000.0
Hamamelitannin	Bark	10000.0	30000.0
Hamamelose	Leaf	-	-
Isoquercitrin	Leaf	-	-
Kaempferol	Leaf	-	-
L-Epicatechin	Bark	-	-
L-Epigallocatechin	Bark	-	-
Leucocyanidin	Leaf	-	-
Leucodelphinidin	Leaf	-	-
Myricetin	Leaf	-	-
Myricetin-3-glucoside	Leaf	-	-
N-hexen-2-al	Leaf	-	485.0
Phenol	Bark	-	-
Phlobaphene	Bark	-	-
Quercetin	Leaf	-	-
Quercitrin	Leaf	-	-
Quinic acid	Leaf	-	-
Safrole	Leaf	-	10.0
Saponins	Leaf	-	-
Spiraeoside	Leaf	-	-
Tannins	Leaf	10000.0	70000.0

Table 4. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Hydrocarbons		
Alkanes, alkenes		
Octane	0.59	1.47
Nonane	0.01	0.02
Decane	0.01	0.04
Undecane	-	0.02
4,8-Dimethyl-1,3,7-nonatriene	-	0.07
Dodecane	0.03	0.1
Tridecane	0.54	trace
Tetradecane	0.23	0.2
3-Methyltetradecane	0.27	-
Pentadecane	0.1	minor
4,8,12-Trimethyl-1,3,7-tridecatetraene	0.23	0.13
Hexadecane	0.07	0.39
Not identified	0.13	-
1-Hexadecyne	0.16	-
Heptadecadiene	-	0.78
1-Heptadecene	-	0.05
Heptadecane	0.31	0.5

Table 4. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
1-Octadecene	-	0.14
Octadecane	0.12	0.71
1-Nonadecene	-	0.31
Nonadecane	0.78	1.64
Eicosane	0.6	1.14
1-Heneicosene	-	0.14
Heneicosane	trace	4.78
2-Methylheneicosane	0.02	-
3-Methylheneicosane	0.01	-
1-Docosene	-	0.05
Docosane	1.27	0.87
Methyldocosane	0.05	0.04
2-Methyldocosane	0.02	0.04
Tricosane	10.38	3.14
Methyltricosane	0.02	-
Not identified	0.35	-
5-Methyltricosane	-	0.04
1-Tetracosene	0.08	0.06
Tetracosane	2.59	1,64
Methyltetracosane	0.03	-
Methyltetracosane	0.07	0.05
Methyltetracosane	0.01	-
4-Methyltetracosane	0.02	-
Methyltetracosane	0.07	-
Pentacosane	10.99	3.56
4-Methylpentacosane	0.05	-
2-Methylpentacosane	0.18	-
3-Methylpentacosane	0.15	-
1-Hexacosene	-	0.07
Hexacosane	2.27	1.92
Methylhexacosane	0.05	-
2-Methylhexacosane	0.22	0.15
3-Methylhexacosane	0.04	-
Heptacosane	16.12	5.45
3-Methylheptacosane	0.08	0.07
Ethyltetracosanoate	0.09	-
Octacosane	1.75	1.65
Methyloctacosane	0.03	-
2-Methylhexacosane	0.22	0.15
3-Methylhexacosane	0.04	-
Heptacosane	16.12	5.45
3-Methylheptacosane	0.08	0.07
Ethyltetracosanoate	0.09	-
Octacosane	1.75	1.65
Methyloctacosane	0.03	-
2-Methyloctacosane	0.07	-
3-Methyloctacosane	0.08	-
Nonacosane	7.12	6.86
Methylnonacosane	0.09	0.18
Triacontane	1.14	1.96
2-Methyltriacontane	0.13	-
3-Methyltriacontane	0.04	-
Hentriacontane	1.14	2.24
Methylhentriacontane	0.06	-
Dotriacontane	0.69	0.98
Triatriacontane	0.68	1.01
Tetratriacontane	0.3	0.76
Sum	62.85	45.42

Table 4. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Alcohols		
cis-3-Hexenol	0.19	0.1
1-Hexanol	0.13	1.33
1-Heptanol	-	0.32
1-Octen-3-ol	0.03	1.16
3-Octanol	-	0.11
1-Octanol	Minor	-
1-Nonanol	0.09	0.6
1-Pentadecanol	-	0.05
1-Hexadecanol	0.1	0.05
1-Octadecanol	Minor	0.34
Eicosanol	0.02	1.25
Not identified	0.09	-
1-Docosanol	0.21	-
Sum	0.86	5.31
Aldehydes		
Octanal	0.03	-
Nonanal	0.62	2.72
2,6-Nonadienal	-	0.05
2-Nonenal (*cis* or *trans*)	-	0.01
Decanal	0.03	0.67
Undecanal	0.42	0.36
trans-2-Undecenal	0.03	0.36
Dodecanal	0.2	0.14
Tridecanal	0.24	0.41
Tetradecanal	0.05	0.07
Pentadecanal	0.13	0.12
Hexadecanal	0.15	0.15
Nonadecanal	0.03	0.09
Eicosanal	Trace	0.1
Heneicosanal	-	0.02
Docosanal	0.28	0.3
Tetracosanal	0.39	0.28
Hexacosanal	0.91	0.17
Octacosanal	0.28	0.12
Sum	3.79	6.14
Ketones		
2-Undecanone	-	0.02
γ-Nonalactone	-	0.03
2-Tridecanone	0.04	0.01
6-Methyl-5-(3-methylphenyl)-2-hepanone	-	Minor
5,9-Dimethyl-2-decanone	-	0.03
2-Pentadecanone	0.04	0.02
2-Hexadecanone	-	0.03
6,10,14-Trimethylpentadecan-2-one	0.7	0.68
2-Heptadecanone	0.05	0.08
γ-Hexadecalactone	-	0.04
2-Octadecanone	-	0.05
2-Nonadecanone	-	0.19
2-Eicosanone	-	0.02
2-Heneicosanone	-	0.29
2-Tricosanone	-	0.06
Sum	0.83	1.55

Table 4. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Esters		
Methyl salicylate	-	0.02
cis-3-Hexenyl butyrate	Trace	-
trans-2-Hexenyl butyrate	0.14	-
cis-3-Hexenyl 2- or 3-methylbutyrate	0.15	0.24
cis-3-Hexenyl tiglate or angelate	0.06	0.02
Hexyl tiglate	Trace	0.02
Butyl benzoate	Trace	-
cis-3-Hexenyl hexanoate	0.23	-
trans-2-Hexenyl hexanoate	0.03	-
cis-3-Hexenyl *trans*-2-hexenoate	Trace	-
2-Methyl- or 3-methyl butylbenzoate	-	0.02
trans-2-Hexenyl *trans*-2-hexenoate	0.02	-
cis-3-Hexenyl benzoate	0.3	Trace
Hexyl benzoate	-	Trace
cis-3-Hexenyl octanoate	Trace	-
cis-3-Hexenyl salicylate	0.01	-
Benzyl benzoate	0.01	0.06
2-Phenylethyl benzoate	-	0.21
Sum	0.95	0.59
Terpenoids		
Monoterpenes		
cis-Linalool oxide (furanoid)	0.31	1.89
trans-Linalool oxide (furanoid)	0.12	0.5
Linalool	3.71	2.03
Hotrienol	Trace	Trace
Myrcenol	0.04	-
trans-Pinocarveol	-	0.06
Not identified	0.03	-
Nerol oxide	0.09	-
Not identified	0.12	-
Isoborneol	-	0.38
4-Terpineol	-	Minor
p-Cymen-8-ol	Trace	Trace
α-Terpineol	1.06	0.44
Myrtenol	-	0.3
Nerol	0.03	0.39
Isobornyl formate	-	Trace
Geraniol	1.74	1.21
Not identified	-	0.53
Geranyl formate	0.01	-
Geranylacetone	0.07	0.61
Sum	7.36	8.34

Table 4. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Sesquiterpene hydrocarbons		
Cyclosativene	0.07	Trace
α-Ylangene	-	11.1
Sesquiterpene hydrocarbon	-	0.8
Sesquiterpene hydrocarbon	0.07	-
β-Caryophyllene	0.21	-
Sesquiterpene hydrocarbon	-	Trace
cis-α-Bergamotene	-	0.18
α-Humulene	0.05	-
α-Himachalene	-	0.04
Sesquiterpene hydrocarbon	-	0.03
β-Santalene	0.03	-
(*E*)-β-Farnesene	-	0.06
α-Amorphene	-	2.02
α-Curcument	-	Minor
α-Fanesene	0.08	-
Germacrene-D	-	0.16
(*E*,*E*)-α-Farnesene	1.47	-
β-Bisabolene	-	Minor
(*Z*)-γ-Bisabolene	-	1.08
δ-Calacorene	-	0.25
β-Calacorene	-	Minor
Cadalene	0.05	0.35
Sum	2.07	15.35
Oxygenated sesquiterpenes		
Not identified	-	0.15
trans-Nerolidol	0.17	2.73
Oxygenated sesquiterpene	-	0.08
Viridiflorol or ledol	0.21	-
α-Eudesmol	0.05	1.32
γ-Eudesmol	0.02	-
Gossonorol	-	0.23
α-Turnerone	0.8	-
τ-Muurolol	-	0.16
Not identified	-	0.16
Not identified	-	Trace
Sum	1.25	4.83
Diterpenes		
Manoyl oxide	0.03	0.93
Geranyl linalool-isomer-4[a]	0.47	-
Kaurene	0.02	-
Manool	0.1	-
Sum	0.62	0.99
Compounds with 13 carbons		
Vitispirane (*cis* and *trans*)	0.09	0.29
Rieslingacetal	Trace	Trace
1,1,6-Trimethyl-1,2-dihydronaphthalene	0.21	-
1,1,6-Trimethyl-1,2,3,4-tetrahydronaphthalene	0.01	-
trans-β-Damascenone	Trace	-
Hydroxydihydroedulan-1[a]	Trace	0.19
Sum	0.31	0.48
Phenylpropanoids		
Estragol	-	1.63
trans-Anethole	-	3.3
Eugenol	-	2.41
Methyleugenol	-	0.12
trans-Methylisoeugenol	-	Minor
Sum	-	7.46

Table 4. The constituents in the volatile fraction of water distilled (4 h) leaves and bark from freshly harvested *Hamamelis virginiana* (witch hazel) using *n*-hexane as the collector solvent identified by GC-MS.[2]

Compound	Leaf (%)	Bark (%)
Fatty acids and fatty acid esters		
Nonanoic acid	0.11	0.09
Methyl tetradecanoate	0.03	0.01
Ethyl tetradecanoate	0.01	-
Isopropyl tetradecanoate	0.07	-
Methyl hexadecanoate	0.33	0.05
Hexadecanoic acid	1.62	0.03
Ethyl hexadecanoate	0.16	0.02
Methyl linolate	0.09	-
Methyl linolenate	0.47	Trace
Methyl oleate	0.13	-
Ethyl linolate	0.14	-
Ethyl linolenate	0.05	-
Methyl eicosanoate	0.04	-
Methyl docosanoate	0.11	-
Methyl tetracosanoate	0.15	-
Sum	3.57	0.20
Miscellaneous compounds		
2-Phenylacetaldehyde	-	0.02
1,4-Dimethyoxybenzene	-	Trace
Not identified	0.36	-
Not identified	0.02	0.45
Not identified	0.18	0.04
Dimethylnaphthalene[b]	-	0.06
Not identified	Trace	-
Butylhydroxytoulene[b]	-	0.04
β-ionone	0.08	0.07
Not identified	0.25	-
Not identified	0.26	-
Tribuylphosphate[b]	-	0.15
Phenanthrene[b]	0.01	0.19
Diisobutyl phthalate*	0.01	0.01
Methylanthracene or Methylphenanthrene[b]	-	0.01
Dibutyl phthalate[b]	0.07	0.33
Fluoranthene or Pyrene[b]	-	0.05
Isophytol	0.68	0.05
trans-Phytol	9.79	-
Not identified	0.34	0.03
Not identified	0.18	-
Not identified	0.06	-
Not identified	0.14	0.28
Dioctyl phthalate[b]	-	Trace
Not identified	0.23	-
Not identified	0.16	0.05
Not identified	0.71	-
Not identified	0.33	-
Squalene	0.09	0.31
Sum	14.03	2.14
Total	98.48	98.8

[a] No further information was provided on the chemical
[b] Compound is probably a contaminant.
GC-MS = Gas chromatography-mass spectrometry; Minor = minor component of a peak comprised of more than one compound as estimated by MS; Trace = < 0.01%

Table 5. The contents of two product mixtures that contain Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract.[21-24]

	A	B
Mixture constituent	%	%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	10.00	20.00
Water	89.40	31.50
Propylene glycol	0	48.00
Phenoxyethanol	0.362	0.362
Tetrasodium EDTA	0.10	0
Methylparaben	0.078	0.078
Ethylparaben	0.02	0.02
Butylparaben	0.02	0.02
Propylparaben	0.01	0.01
Isobutylparaben	0.01	0.01

Table 6. Allergens certified to not be present in product mixtures containing 10% or 20% Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig or 5.00% Hamamelis Virginiana (Witch Hazel) Extract. [21,23,27]

Allergen	**Limit of Detection (ppm)**
α-Isomethyl ionone	< 0.02
Amyl cinnamal	< 0.10
Amylcinnamyl alcohol	< 1.00
Anise alcohol	< 0.00
Benzyl alcohol	< 0.01
Benzyl benzoate	< 0.09
Benzyl cinnamate	< 0.30
Benzyl salicylate	< 0.06
Butylphenyl methylpropional	< 0.50
Cinnamal	< 0.01
Cinnamyl alcohol	< 0.30
Citral	< 1.00
Citronellol	< 1.00
Coumarin	< 0.00
Eugenol	< 0.70
Farnesol	< 0.04
Geraniol	< 0.08
Hexyl cinnamal	< 0.40
Hydroxycitronellal	< 1.00
Hydroxymethylpentyl 3-cyclohexene carboxaldehyde	< 0.30
Isoeugenol	< 0.06
Limonene	< 0.05
Linalool	< 0.00
Methyl 2 octynoate	< 0.02
Evernia furfuracea	< 0.00

Table 7. Constituents of concern found in *Hamamelis virginiana* (witch hazel)

Constituent	Concern	Reference
Afzelin	Cytotoxic, promoted death of neutrophils	[63]
Geraniol	Potential dermal sensitizer	[4]
Linalool	Hydroperoxides are potential dermal sensitizers. Safe at up to 4.3% (20% in a consumer fragrance)	[3]
Phenol	Toxic by ingestion, inhalation, and dermal absorption. Strong dermal irritant. May induce cardiac arrhythmia and is toxic to the liver and kidneys.	[64,65]
Quercetin	Positive genotoxic effect in an Ames assay Consistently genotoxic in in vitro tests and in some in vivo studies of i.p. exposures, but was consistently nongenotoxic in oral exposure studies	[66,67]
Safrole	Liver cancer (hepatocellular carcinoma, adenoma) in male mice; liver cancer and other tumors in rats.	[68]

Table 8. Constituents of *Hamamelis virginiana* (witch hazel) that have IFRA standards.[33]

Constituent	Standard Limits
2-Phenylacetaldehyde	Limited to 0.01% - 2.9%, depending on use category due to sensitization.*
Benzyl benzoate	Limited to 2% - 42.8%, depending on use category due to sensitization.*
trans-β-Damascenone	Limited to 0.2% in fragrances and Eau de Toilette; 0.01% in other leave-on and rinse-off products; and 0.2% in non-skin, and incidental skin contact products due to carcinogenicity.
Estragol	Limited to 0.2% - 4.3%, depending on use category due to sensitization.*
Eugenol	Limited to 0.2% - 4.3%, depending on use category due to sensitization.*
Geraniol	Limited to 0.03% - 8.6%, depending on use category due to sensitization.*
Ionone (mixed isomers)	Limited to 2% - 50.72%, depending on use category due to sensitization.*
Linalool	Limit peroxide level to 20 mmol/L due to sensitization. Linalool and natural products known to be rich in linalool, such as bois de rose, coriander or ho wood oil, should only be used when the level of peroxides is kept to the lowest practical level. It is recommended to add antioxidants at the time of production of the raw material. The addition of 0.1% BHT or alpha-tocopherol for example has shown great efficiency. The maximum peroxide level for products in use should be 20 mmol/L.
Phenylacetaldehyde	Limited to 0.02% - 3%, depending on use category due to sensitization.*
Safrole	Not to be used as a fragrance ingredient. Essential oils containing safrole are not to exceed 0.01% in consumer products.

IFRA - International Fragrance Association

* Use categories are based on types of skin contact (e.g., skin, lips), length of contact (e.g., leave-on, rinse-off), or type of use (e.g., mouthwash)

Table 9. Frequency of use according to duration and exposure of *Hamamelis virginiana* (witch hazel)-derived ingredients.[35,36]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract		Hamamelis Virginiana (Witch Hazel) Extract		Hamamelis Virginiana (Witch Hazel) Flower Water		Hamamelis Virginiana (Witch Hazel) Leaf Water	
Total/range	**128**	**0.00005-4.3**	**359**	**0.000013-86**	**43[e]**	**NR**	**NR**	**4.1-5**
Duration of use								
Leave-on	90	0.00005-4.3	266	0.00003-86	21	NR	NR	NR
Rinse-off	37	0.00005-0.072	91	0.000013-5	21	NR	NR	4.1-5
Diluted for (bath) use	1	NR	2	0.000013-0.5	1	NR	NR	NR
Exposure type								
Eye area	14	NR	12	0.1-35.8	3	NR	NR	NR
Incidental ingestion	1	NR	NR	35.8	NR	NR	NR	NR
Incidental Inhalation-sprays	23[a];26[b]	0.18[a]	2; 79[a]; 128[b]	0.00003-5; 0.0013-86[a]; 0.01[b]	6[a]; 6[b]	NR	NR	NR
Incidental inhalation-powders	26[b]	0.004-4.3[c]	1; 128[b]	0.05; 0.0001-5[c]; 0.01[b]	6[b]	NR	NR	NR
Dermal contact	122	0.00005-4.3	349	0.000013-86	43	NR	NR	4.1-5
Deodorant (underarm)	2[a]	NR	3[a]	0.0013[d]	NR	NR	NR	NR
Hair-noncoloring	3	NR	7	0.0001-0.3	NR	NR	NR	NR
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	2	NR	2	NR	NR	NR	NR	NR
Mucous Membrane	6	NR	13	0.000013-35.8	8	NR	NR	NR
Baby	1	NR	NR	NR	NR	NR	NR	NR

	Hamamelis Virginiana (Witch Hazel) Leaf Extract		Hamamelis Virginiana (Witch Hazel) Water	
Total/range	**218**	**0.00018-0.011**	**386**	**0.00008-43**
Duration of use				
Leave-on	138	0.00018-0.011	255	0.00008-43
Rinse-off	73	0.00035-0.01	122	0.00066-33.3
Diluted for (bath) use	7	NR	9	NR
Exposure type				
Eye area	9	NR	21	0.04-6.6
Incidental ingestion	NR	NR	5	0.1
Incidental Inhalation-sprays	1; 44[a]; 65[b]	0.00035[a]	92[a]; 81[b]	0.00008-25.8; 1[a]
Incidental inhalation-powders	1; 65[b]	0.0018-0.011[c]	2[c]; 81[b]	0.093; 0.00066-12.9[c]
Dermal contact	195	0.00018-0.011	354	0.00008-43
Deodorant (underarm)	6[a]	0.00018[d]	14[a]	6[d]
Hair-noncoloring	23	0.00035-0.00042	24	2.5
Hair-coloring	NR	NR	NR	NR
Nail	NR	NR	1	4.3
Mucous Membrane	24	NR	45	0.1-1.5
Baby	NR	NR	4	NR

NR = Not Reported; Total = Rinse-off + Leave-on + Diluted for Bath Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.
[a] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.
[c] It is possible these products may be powders, but it is not specified whether the reported uses are powders.
[d] Not spray.
[e] VCRP lists this ingredient as Hamamelis Virginiana Flower Water.

Table 10. In vitro dermal irritation assays of *Hamamelis virginiana* (Witch Hazel)-derived ingredients

Ingredient	Concentration	Assay	Results	Reference
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	10% (product mixture)	EpiDerm™	Not predicted to be a dermal irritant. Controls had the expected results.	52
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	20% (product mixture)	EpiDerm™	Not predicted to be a dermal irritant. Controls had the expected results.	53
Hamamelis Virginiana (Witch Hazel) Extract	5% in cyclopentasiloxane	EpiDerm™	Not predicted to be a dermal irritant. Controls had the expected results.	69

Table 11. In vitro ocular irritation assays of *Hamamelis virginiana* (Witch Hazel)-derived ingredients

Ingredient	Concentration	Assay	Results	Reference
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	10% (product mixture)	EpiOcular™	Not predicted to be an ocular irritant. Controls had the expected results.	52
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	20% (product mixture)	EpiOcular™	Not predicted to be an ocular irritant. Controls had the expected results.	53
Hamamelis Virginiana (Witch Hazel) Extract	5% in cyclopentasiloxane	EpiOcular™	Not predicted to be an ocular irritant. Controls had the expected results.	69

Table 12. *Hamamelis virginiana* (witch hazel)-derived ingredients administered to damaged skin.

Ingredient	Dose, vehicle	Procedure/notes	Results	Reference
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract	Creams with and without Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract (10%)	Skin on subjects' backs (n = 28; skin types I, II, or III) was exposed to 800 UV light (mainly in the UVB range with a small amount of UVA and visible light) at 1, 1.25, 1.6, and 2 MED. Test substances were administered using 18-mm Finn chambers immediately after and at 7 and 24 h after irradiation. Test sites were observed at 7, 24 and 48 h after irradiation.	There were no adverse events reported at any time during the experiment.	58
Hamamelis virginiana (witch hazel) distillate (plant parts not specified)	0.00064% (0.64 mg *Hamamelis* ketone/100 g; 75 µL applied) o/w emulsion with and without PC; 0.00256% (2.56 mg *Hamamelis* ketone/100 g; 75 µL applied). Controls were the vehicles and an untreated area.	Randomized, double-blind studies. EXPERIMENT 1: Skin on subjects' backs (n=24) was exposed to 800 UV light (mainly in the UVB range with a small amount of UVA and visible light) at 1.5 MED then test substances were applied. Test sites were observed at 24 and 48 h. EXPERIMENT 2: Skin subjects' backs (n=12) was tape stripped. The low-dose (0.00064% without PC) emulsion and the vehicle (control) were applied. Skin on another group of subjects backs (n=12) was tape stripped. The low- and high-dose (0.00064% and 0.00256% with PC) emulsions were applied. Vehicles were the controls. Test sites were observed at 4, 8 and 24 h.	There were no adverse effects observed in any group during the experiments.	59
Hamamelis virginiana (witch hazel) distillates (plant parts and composition not specified) from three different suppliers	O/W emulsions containing a *Hamamelis virginiana* (witch hazel) distillate (10%) from three different suppliers	Double-blind study. Skin on light-skinned subjects backs (n = 40) was exposed to a sun simulator (UVA:UVB, 16:1; 4 mW/cm^2 UVB) at 1.2, 1.4, and 1.7 MED. Test substances (250 µL) were administered using 18-cm Finn chambers immediately after and at 24 and 48 h after irradiation. Test sites were observed at 24, 48, and 72 h after irradiation.	There were no adverse events reported at any time during the experiment.	60
Hamamelis virginiana (witch hazel) distillate (plant parts not specified)	Creams containing *Hamamelis virginiana* (witch hazel) distillate (0.00064%; 0.64 mg *Hamamelis* ketone/100 g) with and without 0.5% hydrocortisone or just the vehicle	Randomized, double-blind study. Subjects (n = 72) with moderately severe atopic eczema applied a cream containing *Hamamelis virginiana* (witch hazel) distillate on one side of the body and either the same cream with hydrocortisone or the vehicle to lesions on the other side of the body twice per day for 14 days. Blood samples were collected before and after the experiment period at the discretion of a physician.	Self and physician scores of tolerability were similar to controls. Five subjects had itching, erythema, stinging, lichenification/dry skin from using the vehicle. One subject had signs of skin irritation from both the cream containing *Hamamelis virginiana* (witch hazel) distillate and the vehicle control. There were no adverse effects connected to the application of *Hamamelis virginiana* distillate.	61

MED = minimal erythema doses; o/w= oil/water; PC = phosphatidylcholine

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2017 VCRP Data – *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients

01A - Baby Shampoos	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
02B - Bubble Baths	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	7
03E - Eye Makeup Remover	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	6
05A - Hair Conditioner	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
05I - Other Hair Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
07C - Foundations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
07E - Lipstick	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
07F - Makeup Bases	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
07I - Other Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
08B - Cuticle Softeners	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
08G - Other Manicuring Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	2
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	4
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	2
11E - Shaving Cream	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	3
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	15
12B - Depilatories	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	23
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	3
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	11
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	2
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	11
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	7
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	17
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	3
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02C - Bath Capsules	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	2
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	6
03E - Eye Makeup Remover	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
03F - Mascara	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	4
04C - Powders (dusting and talcum, excluding aftershave talc)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
04E - Other Fragrance Preparation	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
05A - Hair Conditioner	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
05B - Hair Spray (aerosol fixatives)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
05F - Shampoos (non-coloring)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	2
07C - Foundations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	4
07F - Makeup Bases	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
07I - Other Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
08G - Other Manicuring Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	2
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	8
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	3
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	3
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	6
11E - Shaving Cream	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
11G - Other Shaving Preparation Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	4
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	47
12B - Depilatories	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	8
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	119
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	9
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	56
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	5
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	15
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	11
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	28
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	5
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02B - Bubble Baths	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	5
02D - Other Bath Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	2
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	5
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	4
05A - Hair Conditioner	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	8
05B - Hair Spray (aerosol fixatives)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	1
05F - Shampoos (non-coloring)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	12
05G - Tonics, Dressings, and Other Hair Grooming Aids	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	1
05I - Other Hair Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	1
07B - Face Powders	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	1
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	13
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	6
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	4
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	3
11E - Shaving Cream	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	4
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	23
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	48
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	17
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	21
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	3
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	5
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	16
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	12
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	3
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01A - Baby Shampoos	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
01B - Baby Lotions, Oils, Powders, and Creams	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
01C - Other Baby Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
02A - Bath Oils, Tablets, and Salts	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
02B - Bubble Baths	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	5
02D - Other Bath Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	3

03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	7
03E - Eye Makeup Remover	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	3
03F - Mascara	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	9
05A - Hair Conditioner	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	4
05C - Hair Straighteners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
05D - Permanent Waves	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
05F - Shampoos (non-coloring)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	9
05G - Tonics, Dressings, and Other Hair Grooming Aids	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	4
05I - Other Hair Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
07F - Makeup Bases	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
07H - Makeup Fixatives	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
07I - Other Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	3
08B - Cuticle Softeners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
09B - Mouthwashes and Breath Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	5
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	26
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	14
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	5
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	19
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	54
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	60
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	21
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	34
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	7
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	11
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	32
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	25
13A - Suntan Gels, Creams, and Liquids	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	7
13C - Other Suntan Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
		386

02A - Bath Oils, Tablets, and Salts	HAMAMELIS VIRGINIANA FLOWER WATER	1
03D - Eye Lotion	HAMAMELIS VIRGINIANA FLOWER WATER	2
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA FLOWER WATER	1
07A - Blushers (all types)	HAMAMELIS VIRGINIANA FLOWER WATER	1
07C - Foundations	HAMAMELIS VIRGINIANA FLOWER WATER	1
07I - Other Makeup Preparations	HAMAMELIS VIRGINIANA FLOWER WATER	1
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA FLOWER WATER	7
12A - Cleansing	HAMAMELIS VIRGINIANA FLOWER WATER	11
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA FLOWER WATER	3
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA FLOWER WATER	3
12F - Moisturizing	HAMAMELIS VIRGINIANA FLOWER WATER	5
12G - Night	HAMAMELIS VIRGINIANA FLOWER WATER	1
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA FLOWER WATER	3
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA FLOWER WATER	3
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There were no reported uses in the 2017 VCRP for:
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract
Hamamelis Virginiana (Witch Hazel) Bark Twig Extract
Hamamelis Virginiana (Witch Hazel) Leaf Water

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: February 2, 2017

SUBJECT: Concentration of Use by FDA Product Category: *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients

Concentration of Use by FDA Product Category – *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients*

Hamamelis Virginiana (Witch Hazel) Water
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract
Hamamelis Virginiana (Witch Hazel) Extract
Hamamelis Virginiana (Witch Hazel) Flower Water
Hamamelis Virginiana (Witch Hazel) Leaf Extract
Hamamelis Virginiana (Witch Hazel) Leaf Water

Ingredient	Product Category	Maximum Concentration of Use
Hamamelis Virginiana (Witch Hazel) Water	Eye lotions	1.4-6.6%
Hamamelis Virginiana (Witch Hazel) Water	Eye makeup removers	2%
Hamamelis Virginiana (Witch Hazel) Water	Other eye makeup preparations	0.04%
Hamamelis Virginiana (Witch Hazel) Water	Colognes and toilet waters	0.00008%
Hamamelis Virginiana (Witch Hazel) Water	Shampoos (noncoloring)	2.5%
Hamamelis Virginiana (Witch Hazel) Water	Face powders	0.093%
Hamamelis Virginiana (Witch Hazel) Water	Foundations	4.3%
Hamamelis Virginiana (Witch Hazel) Water	Lipstick	0.1%
Hamamelis Virginiana (Witch Hazel) Water	Other manicuring preparations	4.3%
Hamamelis Virginiana (Witch Hazel) Water	Bath soaps and detergents	0.1-0.89%
Hamamelis Virginiana (Witch Hazel) Water	Deodorants Not spray	 6%
Hamamelis Virginiana (Witch Hazel) Water	Other personal cleanliness products	1.5%
Hamamelis Virginiana (Witch Hazel) Water	Aftershave lotions	0.9-8%
Hamamelis Virginiana (Witch Hazel) Water	Shaving cream	0.0074-0.45%
Hamamelis Virginiana (Witch Hazel) Water	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.01-33.3%
Hamamelis Virginiana (Witch Hazel) Water	Face and neck products Not spray	 0.00066-12.9%
Hamamelis Virginiana (Witch Hazel) Water	Body and hand products Not spray Spray	 0.1-4.3% 25.8%
Hamamelis Virginiana (Witch Hazel) Water	Paste masks and mud packs	0.00066-5%
Hamamelis Virginiana (Witch Hazel) Water	Skin fresheners	1%
Hamamelis Virginiana (Witch Hazel) Water	Other skin care preparations	0.5-43%
Hamamelis Virginiana (Witch Hazel) Water	Suntan products Pump spray	 8.9%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Shaving cream	0.0035%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0005-0.072%

Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Face and neck products Not spray	 0.004-4.3%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Moisturizing products Not spray	 0.072%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Night products Not spray	 0.00005%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Paste masks and mud packs	0.00005%
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Skin fresheners	0.18%
Hamamelis Virginiana (Witch Hazel) Extract	Bath oils, tablets and salts	0.000013-0.0001%
Hamamelis Virginiana (Witch Hazel) Extract	Other bath preparations	0.5%
Hamamelis Virginiana (Witch Hazel) Extract	Eye lotions	0.1-35.8%
Hamamelis Virginiana (Witch Hazel) Extract	Other eye makeup preparations	35.8%
Hamamelis Virginiana (Witch Hazel) Extract	Colognes and toilet waters	0.00003-0.5%
Hamamelis Virginiana (Witch Hazel) Extract	Hair conditioners	0.3%
Hamamelis Virginiana (Witch Hazel) Extract	Hair sprays Pump spray	 0.0001%
Hamamelis Virginiana (Witch Hazel) Extract	Face powders	0.05%
Hamamelis Virginiana (Witch Hazel) Extract	Foundations	0.003-0.05%
Hamamelis Virginiana (Witch Hazel) Extract	Lipstick	35.8%
Hamamelis Virginiana (Witch Hazel) Extract	Bath soaps and detergents	0.2%
Hamamelis Virginiana (Witch Hazel) Extract	Deodorants Not spray	 0.0013%
Hamamelis Virginiana (Witch Hazel) Extract	Feminine hygiene deodorants	0.01%
Hamamelis Virginiana (Witch Hazel) Extract	Other personal cleanliness products	0.01%
Hamamelis Virginiana (Witch Hazel) Extract	Aftershave lotions	0.0027-0.3%
Hamamelis Virginiana (Witch Hazel) Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0001-5%
Hamamelis Virginiana (Witch Hazel) Extract	Depilatories	0.000013%
Hamamelis Virginiana (Witch Hazel) Extract	Face and neck products Not spray	 0.0001-1.8%
Hamamelis Virginiana (Witch Hazel) Extract	Body and hand products Not spray Spray	 0.0001-5% 0.03-5%
Hamamelis Virginiana (Witch Hazel) Extract	Moisturizing products Not spray	 0.0034%
Hamamelis Virginiana (Witch Hazel) Extract	Night products Not spray	 0.12%
Hamamelis Virginiana (Witch Hazel) Extract	Paste masks and mud packs	0.0034-0.1%
Hamamelis Virginiana (Witch Hazel) Extract	Skin fresheners	0.5-86%
Hamamelis Virginiana (Witch Hazel) Extract	Other skin care preparations	1.1%
Hamamelis Virginiana (Witch Hazel) Extract	Indoor tanning preparations	0.0013-6.1%
Hamamelis Virginiana (Witch Hazel) Leaf	Hair conditioners	0.00042%

Extract		
Hamamelis Virginiana (Witch Hazel) Leaf Extract	Shampoos (noncoloring)	0.00035%
Hamamelis Virginiana (Witch Hazel) Leaf Extract	Tonics, dressings and other hair grooming aids	0.00035%
Hamamelis Virginiana (Witch Hazel) Leaf Extract	Deodorants Not spray	 0.00018%
Hamamelis Virginiana (Witch Hazel) Leaf Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.00035-0.01%
Hamamelis Virginiana (Witch Hazel) Leaf Extract	Face and neck products Not spray	 0.0018%
Hamamelis Virginiana (Witch Hazel) Leaf Extract	Body and hand products Not spray	 0.011%
Hamamelis Virginiana (Witch Hazel) Leaf Water	Paste masks and mud packs	4.1-5%

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

Information collected in 2016-2017

Table prepared: February 1, 2017

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D., Interim Director
COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: July 25, 2017

SUBJECT: Hamamelis Virginiana (Witch Hazel) Water

Clinical Research Laboratories, Inc. 2011. Repeated insult patch test of a soothing spray containing 25.80% Hamamelis Virginiana (Witch Hazel) Water.

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

Clinical
Research
Laboratories, Inc.

Final Report

Repeated Insult Patch Test

CLIENT: [redacted]

ATTENTION: [redacted]
Senior Director, Product Testing

TEST MATERIAL: **SOOTHING SPRAY**
ENG048418-0.1.4.8, DEL3-68-2
contains 25.80% Hamamelis Virginiana (Witch Hazel) Wate.

CRL STUDY NUMBER: **CRL30811-1**

AUTHORIZED SIGNATURES:

Bruce E. Kanengiser, M.D.
President/Medical Director

Michael J. Muscatiello, Ph.D.
Executive Vice President/COO

Anita Lee Cham, M.D.
Dermatologist

REPORT DATE: **May 20, 2011**

371 Hoes Lane, Suite 100 • Piscataway, NJ 08854 • (732) 981-1616 • FAX (732) 981-0520

Clinical Research Laboratories, Inc.

Good Clinical Practice Quality Assurance Audit Statement

Clinical Study Number: CRL30811-1

Start Date: March 28, 2011

Completion Date: May 6, 2011

The clinical study listed above was conducted in accordance with Clinical Research Laboratories, Inc. Standard Operating Procedures, which incorporate the principles of Good Clinical Practice defined by applicable guidelines and regulations established by U.S. Regulatory Agencies. The conduct of the study was monitored for compliance, and the associated records, including source documents or raw data, were reviewed for documentation practices and accuracy by a Project Manager/Study Director and/or a Quality Assurance Representative. Standard Quality Assurance audit procedures for this final report and study related documents were conducted.

Karen Hayley
Signature of QA Auditor

May 20, 2011
Date

FINAL REPORT

REPEATED INSULT PATCH TEST

PURPOSE

The purpose of this study was to determine the dermal irritation and sensitization potential of a test material.

INVESTIGATIVE SITE

Clinical Research Laboratories, Inc.
371 Hoes Lane, Suite 100
Piscataway, New Jersey 08854
732-981-1616

TEST MATERIAL

The following test material was provided by [redacted] and was received by Clinical Research Laboratories, Inc. on March 11, 2011:

Test Material	Test Condition	Patch Type
SOOTHING SPRAY ENG048418-0.1.4.8, DEL3-68-2	Test as Received	Semi-occlusive*

The test material was coded with the following CRL identification number:

CRL30811-1

STUDY DATES

This study was initiated on March 28, 2011 and was completed on May 6, 2011.

* Semi-occlusive Strip (Brady Medical, Mesquite,TX)

PANEL SELECTION

Each subject was assigned a permanent CRL identification number. All subjects signed an Informed Consent Form in compliance with 21 CFR Part 50: "Protection of Human Subjects" and a HIPAA Authorization Form in compliance with 45 CFR Parts 160 and 164. All subjects completed a Subject Profile/Medical History Form provided by Clinical Research Laboratories, Inc. prior to the study (Subject Demographics - Appendix I). Subjects who met the following Inclusion Criteria and none of the Exclusion Criteria were impaneled:

Inclusion Criteria

a. Male and female subjects between the ages of 18 and 70 years;

b. Subjects who do not exhibit any skin diseases which might be confused with a skin reaction from the test material;

c. Subjects who agree to avoid exposure of the test sites to the sun and to refrain from visits to tanning salons during the course of this study;

d. Subjects willing to sign an Informed Consent in conformance with 21CFR Part 50: "Protection of Human Subjects;"

e. Subjects who have completed a HIPAA Authorization Form in conformance with 45CFR Parts 160 and 164;

f. Subjects in generally good health who have a current Subject Profile/Medical History on file;

g. Subjects who are dependable and able to follow directions as outlined in the protocol.

Exclusion Criteria

a. Female subjects who are pregnant or nursing;

b. Subjects who are currently using any systemic or topical corticosteroids, anti-inflammatory drugs, or antihistamines on a regular basis;

c. Subjects exhibiting any skin disorder, sunburn, scars, excessive tattoos, etc. in the test area.

TEST METHOD

Prior to the application of the patch, the test area was wiped with 70% isopropyl alcohol and allowed to dry. The test material, which was prepared as described in the Test Material section of the report, was applied to the upper back (between the scapulae) and was allowed to remain in direct skin contact for a period of 24 hours.

Patches were applied to the same site on Monday, Wednesday, and Friday for a total of 9 applications during the Induction Period. This schedule may have been modified to allow for missed visits or holidays. If a subject was unable to report on an assigned test date, the test material was applied on 2 consecutive days during the Induction Phase and/or a makeup day was added at the end of the Induction Phase.

The sites were graded by a CRL technician for dermal irritation 24 hours after removal of the patches by the subjects on Tuesday and Thursday and 48 hours after removal of the patches on Saturday, unless the patching schedule was altered as described above.

The sites were graded according to the following scoring system:

Dermal Scoring Scale

0 No visible skin reaction
± Barely perceptible erythema
1+ Mild erythema
2+ Well defined erythema
3+ Severe erythema and edema
4+ Erythema and edema with vesiculation

If a "2+" reaction or greater occurred, the test material was applied to an adjacent virgin site. If a "2+" reaction or greater occurred on the new site, the subject was not patched again during the Induction Phase but was challenged on the appropriate day of the study. At the discretion of the Study Director, patch sites with scores less than a "2+" may have been changed.

Following approximately a 2-week rest period, the challenge patches were applied to previously untreated test sites on the back. After 24 hours, the patches were removed by a CRL technician and the test sites were evaluated for dermal reactions. The test sites were re-evaluated at 48 and 72 hours. Subjects exhibiting reactions during the Challenge Phase of the study may have been asked to return for a 96-hour reading.

RESULTS

This study was initiated with 114 subjects. Nine subjects discontinued study participation for reasons unrelated to the test material. A total of 105 subjects completed the study.

Individual dermal scores recorded during the Induction and Challenge Phases appear in Table I.

CONCLUSION

Based on the test population of 105 subjects and under the conditions of this study, the test material identified as SOOTHING SPRAY ENG048418-0.1.4.8, DEL3-68-2 did not demonstrate a potential for eliciting dermal irritation or sensitization.

RETENTION

Test materials and all original forms of this study will be retained by Clinical Research Laboratories, Inc. as specified in CRL Standard Operating Procedures 30.6 and 30.6C, unless designated otherwise by the Sponsor.

TABLE I

Summary of Dermal Scores

Test Material:	SOOTHING SPRAY ENG048418-0.1.4.8, DEL3-68-2

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	X	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0

X = Subject Absent

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	SOOTHING SPRAY ENG048418-0.1.4.8, DEL3-68-2

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
26	0	0	0	0	0	Discontinued						
27	0	0	Discontinued									
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	Discontinued											
36R	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	Discontinued								
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0

R = Due to early discontinuation of subject, the number was re-assigned.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	SOOTHING SPRAY ENG048418-0.1.4.8, DEL3-68-2

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	Discontinued										
55	0	Discontinued										
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0	0
59	0	0	0	0	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0	0	0	0
61	0	0	0	0	0	0	0	0	0	0	0	0
62	0	0	0	0	0	0	0	0	0	0	0	0
63	0	0	0	0	0	0	0	0	0	0	0	0
64	0	0	0	0	0	0	0	0	0	0	0	0
65	0	0	0	0	0	0	0	0	0	0	0	0
66	0	0	0	0	0	0	0	0	0	0	0	0
67	0	0	0	0	0	0	0	0	0	0	0	0
68	0	0	0	0	0	0	0	0	0	0	0	0
69	0	0	0	0	0	0	0	0	0	0	0	0
70	0	0	0	0	0	0	0	0	0	0	0	0
71	0	0	0	0	0	0	0	0	0	0	0	0
72	0	0	0	0	0	0	0	0	0	0	0	0
73	0	0	0	0	0	0	0	Discontinued				
74	0	0	0	0	0	0	0	0	0	0	0	0
75	0	0	0	0	0	0	0	0	0	0	0	0

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	SOOTHING SPRAY ENG048418-0.1.4.8, DEL3-68-2

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
76	0	0	0	0	0	0	0	0	0	0	0	0
77	0	0	0	0	0	0	0	0	0	0	0	0
78	Discontinued											
78R	0	0	0	0	0	0	0	0	0	0	0	0
79	0	0	0	0	0	0	0	0	0	0	0	0
80	0	0	0	0	0	0	0	0	0	0	0	0
81	0	0	0	0	0	0	0	0	0	0	0	0
82	0	0	0	0	0	0	0	0	0	0	0	0
83	0	0	0	0	0	0	0	0	0	0	0	0
84	0	0	0	0	0	0	0	0	0	0	0	0
85	0	0	0	0	0	0	0	0	0	0	0	0
86	0	0	0	0	0	0	0	0	0	0	0	0
87	0	0	0	0	0	0	0	0	0	0	0	0
88	0	0	0	0	0	0	0	0	0	0	0	0
89	0	0	0	0	0	0	0	0	0	0	0	0
90	0	0	0	0	0	0	0	0	0	0	0	0
91	0	0	0	0	0	0	0	0	0	0	0	0
92	0	0	0	0	0	0	0	0	0	0	0	0
93	0	0	0	0	0	0	0	0	0	0	0	0
94	0	0	0	0	0	0	0	0	0	0	0	0
95	0	0	0	0	0	0	0	0	0	0	0	0
96	0	0	0	0	Discontinued							
97	0	0	0	0	0	0	0	0	0	0	0	0
98	0	0	0	0	0	0	0	0	0	0	0	0
99	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0

R = Due to early discontinuation of subject, the number was re-assigned.

TABLE I
(Continued)

Summary of Dermal Scores

Test Material:	SOOTHING SPRAY ENG048418-0.1.4.8, DEL3-68-2

Subject Number	Induction Scores									Challenge Scores		
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour
101	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0
106	0	0	0	0	0	0	0	0	0	0	0	0
107	0	0	0	0	0	0	0	0	0	0	0	0
108	0	0	0	0	0	0	0	0	0	0	0	0
109	0	0	0	0	0	0	0	0	0	0	0	0
110	0	0	0	0	0	0	0	0	0	0	0	0
111	0	0	0	0	0	0	0	0	0	0	0	0
112	0	0	0	0	0	0	0	0	0	0	0	0

Appendix I

Subject Demographics

Subject Number	Subject Initials	CRL ID #	Age	Sex
1	WJ	27415	50	F
2	IR	11242	57	F
3	DP	28173	26	F
4	ML	26552	52	F
5	LT	26553	51	F
6	DJ	27153	50	F
7	AT	14294	69	F
8	DD	19959	50	F
9	FR	24101	40	M
10	SK	24596	41	F
11	JM	28283	60	M
12	KW	19599	36	F
13	PG	13984	49	F
14	JB	24280	53	F
15	SG	23926	48	F
16	RB	01250	66	F
17	TH	20099	47	F
18	MH	26838	58	F
19	ES	08372	33	F
20	TH	17294	48	F
21	CL	26977	42	F
22	MR	27448	42	F
23	DD	18786	53	F
24	AA	09472	30	F
25	DT	28229	62	F
26	SG	24997	20	F
27	VM	27472	49	F
28	MD	28151	64	F

Subject Number	Subject Initials	CRL ID #	Age	Sex
29	BR	00658	67	F
30	MI	14669	67	F
31	CL	14668	67	F
32	MC	24420	49	F
33	PG	23644	39	F
34	NK	26532	66	F
35	DS	27844	39	M
36	MR	26769	62	F
36R	AM	21393	45	F
37	JB	12170	67	F
38	DR	27133	62	M
39	RA	23557	38	F
40	NW	21719	51	F
41	SP	16517	43	F
42	JD	26979	55	M
43	MS	13309	32	F
44	AC	19922	20	F
45	CP	26218	47	F
46	MM	23048	40	F
47	JB	27871	65	M
48	PD	22109	52	F
49	VB	01717	49	F
50	JZ	27182	52	F
51	TF	26326	46	F
52	SP	28224	60	F
53	LP	27319	53	F
54	KC	20662	38	F
55	LL	28161	47	M
56	DP	16953	53	F

Clinical Research Laboratories, Inc.

Appendix I (Continued)

Subject Demographics

Subject Number	Subject Initials	CRL ID #	Age	Sex
57	DS	24036	42	M
58	VC	23036	54	F
59	MO	19978	53	F
60	LM	27381	58	M
61	LH	19614	46	F
62	CB	24215	48	F
63	MS	14977	52	F
64	LL	09586	52	M
65	KB	03776	47	F
66	SL	18114	34	F
67	SB	14645	66	M
68	LL	21886	66	F
69	DJ	27946	41	F
70	MW	23452	69	F
71	LJ	23672	56	F
72	MS	18864	36	F
73	HH	26375	49	F
74	MM	20961	50	F
75	LB	14480	47	F
76	SS	24228	45	M
77	DH	25304	55	M
78	RM	27622	29	M
78R	DL	24237	52	F
79	FK	04033	62	M
80	DH	27284	46	F
81	MJ	24157	43	F
82	RD	23029	62	M
83	TS	26793	54	M
84	JH	19225	46	M

Subject Number	Subject Initials	CRL ID #	Age	Sex
85	LC	22990	36	F
86	YM	26938	58	F
87	HP	26924	56	M
88	MC	25723	44	F
89	SB	22825	49	F
90	MB	03505	53	F
91	KS	27584	46	F
92	SC	17212	53	F
93	TS	25541	69	M
94	TC	20058	55	M
95	SH	11427	41	F
96	LA	28103	49	F
97	KT	16885	21	M
98	AL	27824	36	M
99	DG	16950	53	F
100	KD	24313	45	F
101	AC	23736	42	F
102	LD	25080	52	F
103	RH	21877	49	F
104	PF	28140	59	F
105	JM	08335	51	F
106	BB	23603	47	F
107	JA	26992	30	F
108	BA	22252	64	F
109	AR	19479	27	F
110	LH	13288	67	F
111	AM	25676	35	F
112	EW	28381	46	F

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D., Interim Director
COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: July 25, 2017

SUBJECT: Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract and Hamamelis Virginiana (Witch Hazel) Extract

Active Concepts. 2017. Certificate of origin ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Compositional breakdown ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Dermal and ocular irritation tests ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Manufacturing flow chart ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Product specification ABS Witch Hazel Extract NS (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Certificate of origin ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/TwigExtract).

Active Concepts. 2017. Compositional breakdown ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Dermal and ocular irritation tests ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

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Active Concepts. 2017. Manufacturing flow chart ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Product specification ABS Witch Hazel Extract (Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract).

Active Concepts. 2017. Certificate of origin ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract).

Active Concepts. 2017. Compositional breakdown ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract).

Active Concepts. 2017. Dermal and ocular irritation tests ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract).

Active Concepts. 2017. Manufacturing flow chart ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract).

Active Concepts. 2017. Product specification ABS Witch Hazel Extract Sil (Hamamelis Virginiana (Witch Hazel) Extract).

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Certificate of Origin

ABS Witch Hazel Extract NS
Code: 10318

Active Concepts, LLC certifies that all raw material(s) used to manufacture the above listed ingredient originate in the United States of America.

Active Concepts, LLC certifies that all raw material(s) used to manufacture the above listed ingredient are prepared from non-GMO organisms and are BSE-Free.

Active Concepts, LLC certifies the below sources for each item listed in our INCI Name:

INCI Name	Source	Plant Part
Water	Water	-
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Plant (*Hamamelis virginiana*)	Bark/Leaf/Twig
Phenoxyethanol	Synthetic	-
Tetrasodium EDTA	Synthetic	-
Methylparaben	Synthetic	-
Ethylparaben	Synthetic	-
Butylparaben	Synthetic	-
Propylparaben	Synthetic	-
Isobutylparaben	Synthetic	

Active Concepts, LLC certifies that the above listed ingredient has never been tested on animals.

Active Concepts, LLC certifies that the above listed ingredient can be classified as Vegan Compliant.

Active Concepts, LLC certifies that all raw material(s) used to manufacture the above listed ingredient are not derived from plants such as Opium, Hashish and *Mitragyna speciosa.*

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Compositional Breakdown

ABS Witch Hazel Extract NS
Code: 10318

Compositional Breakdown:

Ingredient	%
Water	89.40
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	10.00
Phenoxyethanol	0.362
Tetrasodium EDTA	0.10
Methylparaben	0.078
Ethylparaben	0.02
Butylparaben	0.02
Propylparaben	0.01
Isobutylparaben	0.01

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Compositional Breakdown

This is to certify that ABS Witch Hazel Extract NS does not contain allergen levels exceeding the following (Gas Chromatography-Mass Spectrometer Coupled):

ALLERGENS Dir 2003 15 CEE		
INCI NAME	CAS NUMBER	Limit (ppm)
Alpha-IsoMethyl Ionone	127-51-5	< 0.02
Amyl Cinnamal	122-40-7	< 0.10
Anise Alcohol	105-13-5	< 0.00
Benzyl Alcohol	100-51-6	< 0.01
Benzyl Benzoate	120-51-4	< 0.09
Benzyl Cinnamate	103-41-3	< 0.30
Benzyl Salicylate	118-58-1	< 0.06
Butylphenyl Methylpropional	80-54-6	< 0.50
Cinnamal	104-55-2	< 0.01
Cinnamyl Alcohol	104-54-1	< 0.30
Citral	5392-40-5	< 1.00
Citronellol	106-22-9	< 1.00
Coumarin	91-64-5	< 0.00
Eugenol	97-53-0	< 0.70
Farnesol	4602-84-0	< 0.04
Geraniol	106-24-1	< 0.08
Hexyl Cinnamal	101-86-0	< 0.40
Hydroxycitronellal	107-75-5	< 1.00
Hydroxymethylpentyl 3-Cyclohexene carboxaldehyde	31906-04-4	< 0.30
Isoeugenol	97-54-1	< 0.06
Limonene	5989-27-5	< 0.05
Linalool	78-70-6	< 0.00
Methyl 2 Octynoate	111-12-6	< 0.20
Evernia prunastri	90028-68-5	< 0.02
Evernia furfuracea	90028-67-4	< 0.00
Amylcinnamyl Alcohol	101-85-9	< 1.00

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Compositional Breakdown

This is to certify that ABS Witch Hazel Extract NS does not contain pesticide levels exceeding the following (Reverse Phase High Performance Liquid Chromatography-Mass Spectrometer Coupled):

EPA Pesticide Levels	
NAME	LIMIT (mg/kg)
Alachlor	< 0.02
Aldrin and Dieldrin	< 0 .05
Azinphos-methyl	< 1. 00
Bromopropylate	< 3.0 0
Chlordane(cis and trans)	< 0.05
Chlorfenvinphos	< 0.50
Chlorpyrifos	< 0.20
Chlorpyrifos-methyl	< 0.10
Cypermethrin	< 1.00
DDT	< 1.00
Deltamethrin	< 0.50
Diazinon	< 0.50
Dichlorvos	< 1.00
Dithiocarbamates	< 2.00
Endosulfan	< 3.00
Endrin	< 0.05
Ethion	< 2.00
Fenitrothion	< 0.50
Fenvalerate	< 1.50
Fonofos	< 0.05
Heptachlor	< 0.05
Hexachlorobenzene	< 0.10
Hexachlorocyclohexane	< 0.30
Lindane	< 0.60
Malathion	< 1.00
Methidathion	< 0.20
Parathion	< 0.50
Parathion-methyl	< 0.20

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Compositional Breakdown

Permethrin	< 1.00
Phosalone	< 0.10
Piperonyl butoxide	< 3.00
Pirimiphos-methyl	< 4.00
Pyrethrins	< 3.00
Quintozene(sum of 3 items)	< 1.00

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Dermal and Ocular Irritation Tests

Sample: ABS Witch Hazel Extract NS

Code: 10318

CAS #: 7732-18-5 & 84696-19-5

Test Request Form/Submission #: 3526

Lot #: 54594P

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Maureen Danaher*
Principle Investigator: *Jennifer Goodman*

Test Performed:
In Vitro EpiDerm™ Dermal Irritation Test (EPI-200-SIT)
EpiOcular™ Eye Irritation Test (OCL-200-EIT)

SUMMARY

In vitro dermal and ocular irritation studies were conducted to evaluate whether **ABS Witch Hazel Extract NS** would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays.

The product was tested according to the manufacture's protocol. The test article solution was found to be **non-irritating**. Reconstructed human epidermis and cornea epithelial model were incubated in growth media overnight to allow for tissue equilibration after shipping from MatTek Corporation, Ashland, MA. Test substances were applied to the tissue inserts and incubated for 60 minutes for liquid and solid substances in the EpiDerm™ assay and 30 minutes for liquid substances and 90 minutes for solid substances in the EpiOcular™ assay at 37°C, 5% CO_2, and 95% relative humidity (RH). Tissue inserts were thoroughly washed and transferred to fresh plates with growth media. After post substance dosing incubation is complete, the cell viability test begins. Cell viability is measured by dehydrogenase conversion of MTT [(*3-4,5-dimethyl thiazole 2-yl*)], present in the cell mitochondria, into blue formazan salt that is measured after extraction from the tissue. The irritation potential of the test chemical is dictated by the reduction in tissue viability of exposed tissues compared to the negative control.

Under the conditions of this assay, the test article was considered to be **non-irritant**. The negative and positive controls performed as anticipated.

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Dermal and Ocular Irritation Tests

I. Introduction

A. Purpose

In vitro dermal and ocular irritation studies were conducted to evaluate whether a test article would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays. MatTek Corporation's reconstructed human epidermal and human ocular models are becoming a standard in determining the irritancy potential of test substances. They are able to discriminate between irritants and non-irritants. The EpiDerm™ assay has accuracy for the prediction of UN GHS R38 skin irritating and no-label (non-skin irritating) test substances. The EpiOcular™ assay can differentiate chemicals that have been classified as R36 or R41 from the EU classifications based on Dangerous Substances Directive (DSD) or between the UN GHS Cat 1 and Cat 2 classifications.

II. Materials

A. Incubation Conditions:	37°C at 5% CO_2 and 95% relative humidity
B. Equipment:	Forma humidified incubator, ESCO biosafety laminar flow hood, Synergy HT Microplate reader; Pipettes
C. Media/Buffers:	DMEM based medium; DPBS; sterile deionized H_2O
D. Preparation:	Pre-incubate (37°C) tissue inserts in assay medium; Place assay medium and MTT diluent at 4°C, MTT concentrate at -20°C, and record lot numbers of kit components
E. Tissue Culture Plates:	Falcon flat bottom 96-well, 24-well, 12-well, and 6-well tissue culture plates
F. Reagents:	MTT (1.0mg/mL); Extraction Solution (Isopropanol); SDS (5%); Methyl Acetate
G. Other:	Nylon Mesh Circles (EPI-MESH); Cotton tip swabs; 1mL tuberculin syringes; Ted Pella micro-spatula; 220mL specimen containers; sterile disposable pipette tips; Parafilm

III. Test Assay

A. Test System

The reconstructed human epidermal model, EpiDerm™, and comea epithelial model, EpiOcular™, consist of normal human-derived epidermal keratinocytes which have been cultured to form a multilayer, highly differentiated model of the human epidermis and comea epithelium. These models consist of organized basal, spinous, and granular layers, and the EpiDerm™ systems also contains a multilayer stratum comeum containing intercellular lamellar lipid layers that the EpiOcular™ system is lacking. Both the EpiDerm™ and EpiOcular™ tissues are cultured on specially prepared cell culture inserts.

B. Negative Control

Sterile DPBS and sterile deionized water are used as negative controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

C. Positive Control

Known dermal and eye irritants, 5% SDS solution and Methyl Acetate, were used as positive controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

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Dermal and Ocular Irritation Tests

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D. Data Interpretation Procedure

a. EpiDerm™

An irritant is predicted if the mean relative tissue viability of the 3 tissues exposed to the test substance is reduced by 50% of the mean viability of the negative controls and a non-irritant's viability is > 50%.

b. EpiOcular™

An irritant is predicted if the mean relative tissue viability of the 2 tissues exposed to the test substance is reduced by 60% of the mean viability of the negative controls and a non-irritant's viability is > 40%.

IV. Method

A. Tissue Conditioning

Upon MatTek kit arrival at Active Concepts, LLC the tissue inserts are removed from their shipping medium and transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for 60 minutes. After those 60 minutes the inserts are transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for an additional 18 to 21 hours.

B. Test Substance Exposure

a. EpiDerm™

30µL (liquid) or 25mg (solid) of the undiluted test substance is applied to 3 tissue inserts and allowed to incubate for 60 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

b. EpiOcular™

Each tissue is dosed with 20µL DPBS prior to test substance dosing. 50µL (liquid) or 50mg (solid) of the undiluted test substance is applied to 2 tissue inserts and allowed to incubate for 90 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

C. Tissue Washing and Post Incubation

a. EpiDerm™

All tissue inserts are washed with DPBS, dried with cotton tipped swab, and transferred to fresh media and culture plates. After 24 hours the inserts are again transferred into fresh media and culture plates for an additional 18 to 20 hours.

b. EpiOcular™

Tissue inserts are washed with DPBS and immediately transferred into 5mL of assay medium for 12 to 14 minutes. After this soak the inserts are transferred into fresh media and tissue culture plates for 120 minutes for liquid substances and 18 hours for solid substances.

D. MTT Assay

Tissue inserts are transferred into 300µL MTT media in pre-filled plates and incubated for 3 hours at 37°C, 5% CO_2, and 95% RH. Inserts are then removed from the MTT medium and placed in 2mL of the extraction solution. The plate is sealed and incubated at room temperature in the dark for 24 hours. After extraction is complete the tissue inserts are pierced with forceps and 2 x 200µL aliquots of the blue formazan solution is transferred into a 96 well plate for Optical Density reading. The spectrophotometer reads the 96-well plate using a wavelength of 570 nm.

V. Acceptance Criterion

A. Negative Control

The results of this assay are acceptable if the mean negative control Optical Density (OD_{570}) is ≥ 1.0 and ≤ 2.5 (EpiDerm™) or ≥ 1.0 and ≤ 2.3 (EpiOcular™).

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B. Positive Control

a. EpiDerm™

The assay meets the acceptance criterion if the mean viability of positive control tissues expressed as a % of the negative control is ≤ 20%.

b. EpiOcular™

The assay meets the acceptance criterion if the mean viability of positive control tissues is < 60% of control viability.

C. Standard Deviation

Since each irritancy potential is predicted from the mean viability of 3 tissues for EpiDerm™ and 2 tissues for EpiOcular™, the variability of the replicates should be < 18% for EpiDerm™ and < 20% EpiOcular™.

VI. Results

A. Tissue Characteristics

The tissue inserts included in the MatTek EpiDerm™ and EpiOcular™ assay kits were in good condition, intact, and viable.

B. Tissue Viability Assay

The results are summarized in Figure 1. In no case was the tissue viability ≤ 50% for EpiDerm™ or ≤ 60% for EpiOcular™ in the presence of the test substance. The negative control mean exhibited acceptable relative tissue viability while the positive control exhibited substantial loss of tissue viability and cell death.

C. Test Validity

The data obtained from this study met criteria for a valid assay.

VII. Conclusion

Under the conditions of this assay, the test article substance was considered to be **non-irritating**. The negative and positive controls performed as anticipated.

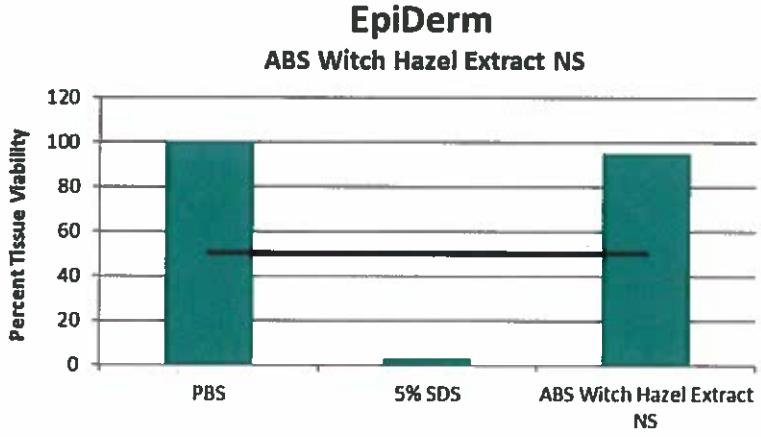

Figure 1: EpiDerm tissue viability

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Dermal and Ocular Irritation Tests

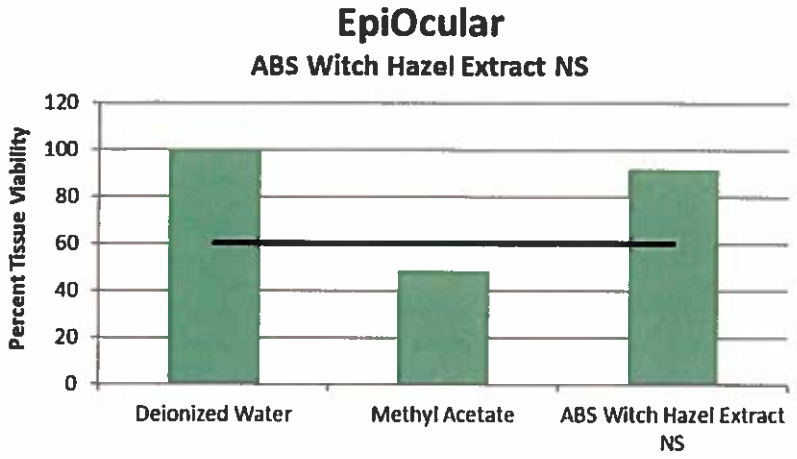

Figure 2: EpiOcular tissue viability

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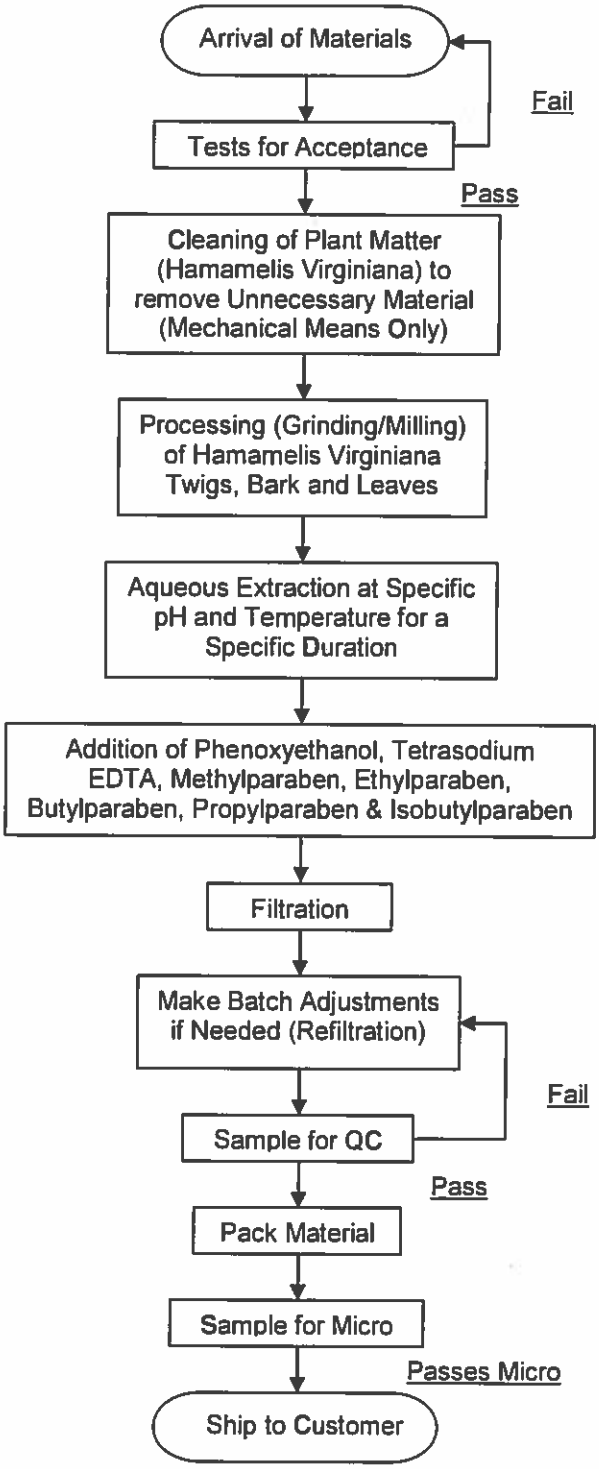
10318-ABS Witch Hazel Extract NS- Manufacturing Flow Chart



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Product Specification

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Product Name: ABS Witch Hazel Extract NS
Code Number: 10318
CAS #'s: 7732-18-5 & 84696-19-5
EINECS #'s: 231-791-2 & 283-637-9
INCI Name: Water & Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract
Status: Approved

Specification	Parameter
Appearance	Clear Colorless Liquid
Odor	Characteristic
pH	5.5 – 7.5
Refractive Index	1.3300 – 1.3380
Heavy Metals	< 20 ppm
Lead	< 10 ppm
Arsenic	< 2 ppm
Cadmium	< 1 ppm
Microbial Content Yeast & Mold Gram Negative Bacteria	< 100 CFU/g; No pathogens < 100 CFU/g 0 CFU/g

May Sediment upon Standing; Mix Well Prior to Use

**Note: Product may change appearance if exposed to cold temperatures during shipment or storage. If this happens, please gently warm to 45-50°C and mix until normal appearance is restored.

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Certificate of Origin

ABS Witch Hazel Extract
Code: 10278

Active Concepts, LLC certifies that all raw material(s) used to manufacture the above listed ingredient originate in the United States of America.

Active Concepts, LLC certifies that all raw material(s) used to manufacture the above listed ingredient are prepared from non-GMO organisms and are BSE-Free.

Active Concepts, LLC certifies the below sources for each item listed in our INCI Name:

INCI Name	Source	Plant Part
Propylene Glycol	Synthetic	-
Water	Water	-
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	Plant (*Hamamelis virginiana*)	Bark/Leaf/Twig
Phenoxyethanol	Synthetic	-
Methylparaben	Synthetic	-
Ethylparaben	Synthetic	-
Butylparaben	Synthetic	-
Propylparaben	Synthetic	-
Isobutylparaben	Synthetic	-

Active Concepts, LLC certifies that the above listed ingredient can be classified as Vegan Compliant.

Active Concepts, LLC certifies that the above listed ingredient has never been tested on animals.

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Compositional Breakdown

ABS Witch Hazel Extract
Code: 10278

Compositional Breakdown:

Ingredient	%
Propylene Glycol	48.00
Water	31.50
Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract	20.00
Phenoxyethanol	0.362
Methylparaben	0.078
Ethylparaben	0.02
Butylparaben	0.02
Propylparaben	0.01
Isobutylparaben	0.01

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Compositional Breakdown

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This is to certify that ABS Witch Hazel Extract does not contain allergen levels exceeding the following (Gas Chromatography-Mass Spectrometer Coupled):

ALLERGENS Dir 2003 15 CEE		
INCI NAME	CAS NUMBER	Limit (ppm)
Alpha-IsoMethyl Ionone	127-51-5	< 0.02
Amyl Cinnamal	122-40-7	< 0.10
Anise Alcohol	105-13-5	< 0.00
Benzyl Alcohol	100-51-6	< 0.01
Benzyl Benzoate	120-51-4	< 0.09
Benzyl Cinnamate	103-41-3	< 0.30
Benzyl Salicylate	118-58-1	< 0.06
Butylphenyl Methylpropional	80-54-6	< 0.50
Cinnamal	104-55-2	< 0.01
Cinnamyl Alcohol	104-54-1	< 0.30
Citral	5392-40-5	< 1.00
Citronellol	106-22-9	< 1.00
Coumarin	91-64-5	< 0.00
Eugenol	97-53-0	< 0.70
Farnesol	4602-84-0	< 0.04
Geraniol	106-24-1	< 0.08
Hexyl Cinnamal	101-86-0	< 0.40
Hydroxycitronellal	107-75-5	< 1.00
Hydroxymethylpentyl 3-Cyclohexene carboxaldehyde	31906-04-4	< 0.30
Isoeugenol	97-54-1	< 0.06
Limonene	5989-27-5	< 0.05
Linalool	78-70-6	< 0.00
Methyl 2 Octynoate	111-12-6	< 0.20
Evernia prunastri	90028-68-5	< 0.02
Evernia furfuracea	90028-67-4	< 0.00
Amylcinnamyl Alcohol	101-85-9	< 1.00

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Compositional Breakdown

This is to certify that ABS Witch Hazel Extract does not contain pesticide levels exceeding the following (Reverse Phase High Performance Liquid Chromatography-Mass Spectrometer Coupled):

EPA Pesticide Levels	
NAME	LIMIT (mg/kg)
Alachlor	< 0.02
Aldrin and Dieldrin	< 0 .05
Azinphos-methyl	< 1. 00
Bromopropylate	< 3.0 0
Chlordane(cis and trans)	< 0.05
Chlorfenvinphos	< 0.50
Chlorpyrifos	< 0.20
Chlorpyrifos-methyl	< 0.10
Cypermethrin	< 1.00
DDT	< 1.00
Deltamethrin	< 0.50
Diazinon	< 0.50
Dichlorvos	< 1.00
Dithiocarbamates	< 2.00
Endosulfan	< 3.00
Endrin	< 0.05
Ethion	< 2.00
Fenitrothion	< 0.50
Fenvalerate	< 1.50
Fonofos	< 0.05
Heptachlor	< 0.05
Hexachlorobenzene	< 0.10
Hexachlorocyclohexane	< 0.30
Lindane	< 0.60
Malathion	< 1.00
Methidathion	< 0.20
Parathion	< 0.50
Parathion-methyl	< 0.20

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Compositional Breakdown

Permethrin	< 1.00
Phosalone	< 0.10
Piperonyl butoxide	< 3.00
Pirimiphos-methyl	< 4.00
Pyrethrins	< 3.00
Quintozene(sum of 3 items)	< 1.00

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Dermal and Ocular Irritation Tests

Sample: ABS Witch Hazel Extract

Code: 10278

CAS #: 57-55-6 & 7732-18-5 & 84696-19-5

Test Request Form/Submission #: 3525

Lot #: 53339P

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Maureen Danaher*
Principle Investigator: *Jennifer Goodman*

Test Performed:
In Vitro EpiDerm™ Dermal Irritation Test (EPI-200-SIT)
EpiOcular™ Eye Irritation Test (OCL-200-EIT)

SUMMARY

In vitro dermal and ocular irritation studies were conducted to evaluate whether **ABS Witch Hazel Extract** would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays.

The product was tested according to the manufacture's protocol. The test article solution was found to be **non-irritating**. Reconstructed human epidermis and cornea epithelial model were incubated in growth media overnight to allow for tissue equilibration after shipping from MatTek Corporation, Ashland, MA. Test substances were applied to the tissue inserts and incubated for 60 minutes for liquid and solid substances in the EpiDerm™ assay and 30 minutes for liquid substances and 90 minutes for solid substances in the EpiOcular™ assay at 37°C, 5% CO_2, and 95% relative humidity (RH). Tissue inserts were thoroughly washed and transferred to fresh plates with growth media. After post substance dosing incubation is complete, the cell viability test begins. Cell viability is measured by dehydrogenase conversion of MTT [*(3-4,5-dimethyl thiazole 2-yl)*], present in the cell mitochondria, into blue formazan salt that is measured after extraction from the tissue. The irritation potential of the test chemical is dictated by the reduction in tissue viability of exposed tissues compared to the negative control.

Under the conditions of this assay, the test article was considered to be **non-irritant**. The negative and positive controls performed as anticipated.

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Dermal and Ocular Irritation Tests

I. Introduction

A. Purpose

In vitro dermal and ocular irritation studies were conducted to evaluate whether a test article would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays. MatTek Corporation's reconstructed human epidermal and human ocular models are becoming a standard in determining the irritancy potential of test substances. They are able to discriminate between irritants and non-irritants. The EpiDerm™ assay has accuracy for the prediction of UN GHS R38 skin irritating and no-label (non-skin irritating) test substances. The EpiOcular™ assay can differentiate chemicals that have been classified as R36 or R41 from the EU classifications based on Dangerous Substances Directive (DSD) or between the UN GHS Cat 1 and Cat 2 classifications.

II. Materials

A. Incubation Conditions:	37°C at 5% CO_2 and 95% relative humidity
B. Equipment:	Forma humidified incubator, ESCO biosafety laminar flow hood, Synergy HT Microplate reader; Pipettes
C. Media/Buffers:	DMEM based medium; DPBS; sterile deionized H_2O
D. Preparation:	Pre-incubate (37°C) tissue inserts in assay medium; Place assay medium and MTT diluent at 4°C, MTT concentrate at -20°C, and record lot numbers of kit components
E. Tissue Culture Plates:	Falcon flat bottom 96-well, 24-well, 12-well, and 6-well tissue culture plates
F. Reagents:	MTT (1.0mg/mL); Extraction Solution (Isopropanol); SDS (5%); Methyl Acetate
G. Other:	Nylon Mesh Circles (EPI-MESH); Cotton tip swabs; 1mL tuberculin syringes; Ted Pella micro-spatula; 220mL specimen containers; sterile disposable pipette tips; Parafilm

III. Test Assay

A. Test System

The reconstructed human epidermal model, EpiDerm™, and cornea epithelial model, EpiOcular™, consist of normal human-derived epidermal keratinocytes which have been cultured to form a multilayer, highly differentiated model of the human epidermis and cornea epithelium. These models consist of organized basal, spinous, and granular layers, and the EpiDerm™ systems also contains a multilayer stratum corneum containing intercellular lamellar lipid layers that the EpiOcular™ system is lacking. Both the EpiDerm™ and EpiOcular™ tissues are cultured on specially prepared cell culture inserts.

B. Negative Control

Sterile DPBS and sterile deionized water are used as negative controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

C. Positive Control

Known dermal and eye irritants, 5% SDS solution and Methyl Acetate, were used as positive controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

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D. Data Interpretation Procedure

a. EpiDerm™

An irritant is predicted if the mean relative tissue viability of the 3 tissues exposed to the test substance is reduced by 50% of the mean viability of the negative controls and a non-irritant's viability is > 50%.

b. EpiOcular™

An irritant is predicted if the mean relative tissue viability of the 2 tissues exposed to the test substance is reduced by 60% of the mean viability of the negative controls and a non-irritant's viability is > 40%.

IV. Method

A. Tissue Conditioning

Upon MatTek kit arrival at Active Concepts, LLC the tissue inserts are removed from their shipping medium and transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for 60 minutes. After those 60 minutes the inserts are transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for an additional 18 to 21 hours.

B. Test Substance Exposure

a. EpiDerm™

30µL (liquid) or 25mg (solid) of the undiluted test substance is applied to 3 tissue inserts and allowed to incubate for 60 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

b. EpiOcular™

Each tissue is dosed with 20µL DPBS prior to test substance dosing. 50µL (liquid) or 50mg (solid) of the undiluted test substance is applied to 2 tissue inserts and allowed to incubate for 90 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

C. Tissue Washing and Post Incubation

a. EpiDerm™

All tissue inserts are washed with DPBS, dried with cotton tipped swab, and transferred to fresh media and culture plates. After 24 hours the inserts are again transferred into fresh media and culture plates for an additional 18 to 20 hours.

b. EpiOcular™

Tissue inserts are washed with DPBS and immediately transferred into 5mL of assay medium for 12 to 14 minutes. After this soak the inserts are transferred into fresh media and tissue culture plates for 120 minutes for liquid substances and 18 hours for solid substances.

D. MTT Assay

Tissue inserts are transferred into 300µL MTT media in pre-filled plates and incubated for 3 hours at 37°C, 5% CO_2, and 95% RH. Inserts are then removed from the MTT medium and placed in 2mL of the extraction solution. The plate is sealed and incubated at room temperature in the dark for 24 hours. After extraction is complete the tissue inserts are pierced with forceps and 2 x 200µL aliquots of the blue formazan solution is transferred into a 96 well plate for Optical Density reading. The spectrophotometer reads the 96-well plate using a wavelength of 570 nm.

V. Acceptance Criterion

A. Negative Control

The results of this assay are acceptable if the mean negative control Optical Density (OD_{570}) is ≥ 1.0 and ≤ 2.5 (EpiDerm™) or ≥ 1.0 and ≤ 2.3 (EpiOcular™).

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B. **Positive Control**

a. EpiDerm™

The assay meets the acceptance criterion if the mean viability of positive control tissues expressed as a % of the negative control is ≤ 20%.

b. EpiOcular™

The assay meets the acceptance criterion if the mean viability of positive control tissues is < 60% of control viability.

C. Standard Deviation

Since each irritancy potential is predicted from the mean viability of 3 tissues for EpiDerm™ and 2 tissues for EpiOcular™, the variability of the replicates should be < 18% for EpiDerm™ and < 20% EpiOcular™.

VI. Results

A. Tissue Characteristics

The tissue inserts included in the MatTek EpiDerm™ and EpiOcular™ assay kits were in good condition, intact, and viable.

B. Tissue Viability Assay

The results are summarized in Figure 1. In no case was the tissue viability ≤ 50% for EpiDerm™ or ≤ 60% for EpiOcular™ in the presence of the test substance. The negative control mean exhibited acceptable relative tissue viability while the positive control exhibited substantial loss of tissue viability and cell death.

C. Test Validity

The data obtained from this study met criteria for a valid assay.

VII. Conclusion

Under the conditions of this assay, the test article substance was considered to be **non-irritating**. The negative and positive controls performed as anticipated.

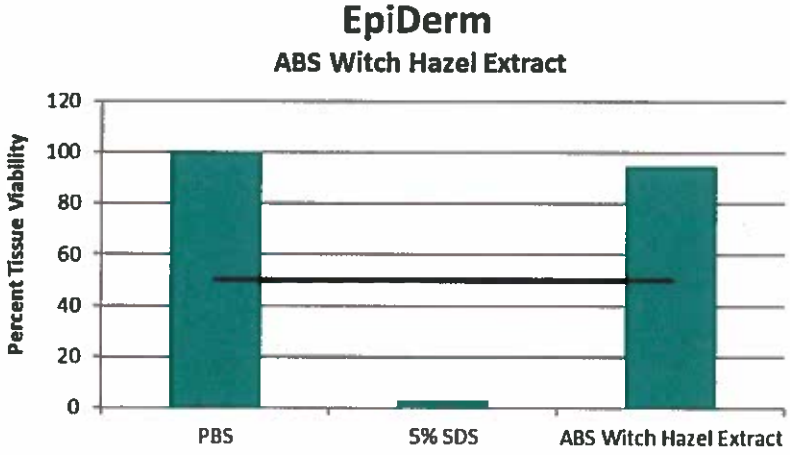

Figure 1: EpiDerm tissue viability

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Dermal and Ocular Irritation Tests

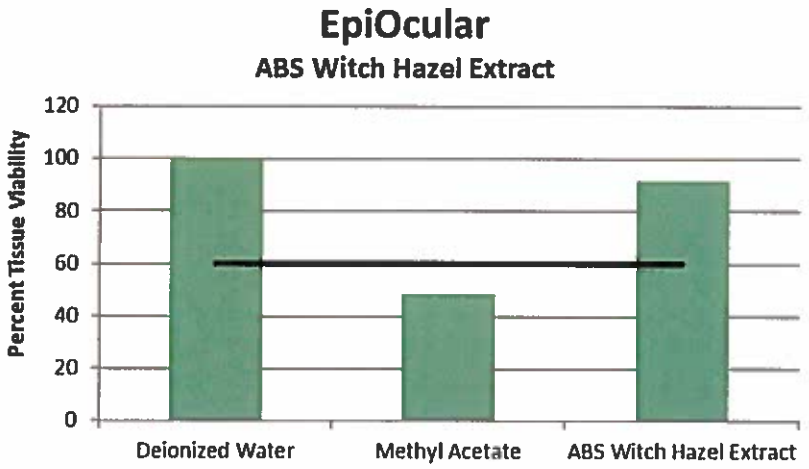

Figure 2: EpiOcular tissue viability

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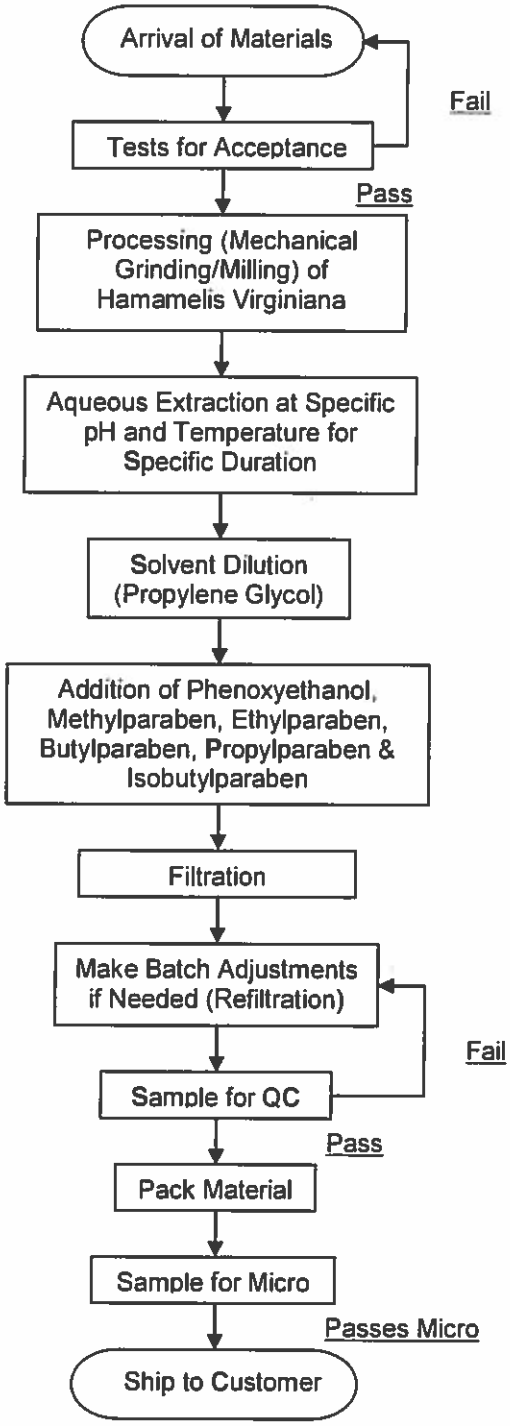
10278-ABS Witch Hazel Extract- Manufacturing Flow Chart



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Product Specification

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Product Name: ABS Witch Hazel Extract
Code Number: 10278
CAS #'s: 57-55-6 & 7732-18-5 & 84696-19-5
EINECS #'s: 200-338-0 & 231-791-2 & 283-637-9
INCI Name: Propylene Glycol & Water & Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract
Status: Approved

Specification	Parameter
Appearance	Amber Yellow Liquid
Odor	Characteristic
pH (direct)	4.5 – 5.5
Specific Gravity	1.038 – 1.055
Refractive Index	1.380 – 1.395
Propylene Glycol Content	47.5 – 52.5%
Heavy Metals	< 20 ppm
Lead	< 10 ppm
Arsenic	< 2 ppm
Cadmium	< 1 ppm
Microbial Content Yeast & Mold Gram Negative Bacteria	< 100 CFU/g; No pathogens < 100 CFU/g 0 CFU/g

May Sediment upon Standing; Mix Well Prior to Use

**Note: Product may change appearance if exposed to cold temperatures during shipment or storage. If this happens, please gently warm to 45-50°C and mix until normal appearance is restored.

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Certificate of Origin

ABS Witch Hazel Extract Sil
Code: 10128

Active Concepts, LLC certifies that all raw material(s) used to manufacture the above listed ingredient originate in the United States of America.

Active Concepts, LLC certifies that all raw material(s) used to manufacture the above listed ingredient are prepared from non-GMO organisms and are BSE-Free.

Active Concepts, LLC certifies the below sources for each item listed in our INCI Name:

INCI Name	Source	Plant Part
Cyclopentasiloxane	Synthetic	-
Hamamelis Virginiana (Witch Hazel) Extract	Plant (*Hamamelis virginiana*)	Whole Plant

Active Concepts, LLC certifies that the above listed ingredient can be classified as Vegan Compliant.

Active Concepts, LLC certifies that the above listed ingredient has never been tested on animals.

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Compositional Breakdown

ABS Witch Hazel Extract Sil
Code: 10128

Compositional Breakdown:

Ingredient	%
Cyclopentasiloxane	95.00
Hamamelis Virginiana (Witch Hazel) Extract	5.00

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Compositional Breakdown

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This is to certify that ABS Witch Hazel Extract Sil does not contain allergen levels exceeding the following (Gas Chromatography-Mass Spectrometer Coupled):

ALLERGENS Dir 2003 15 CEE		
INCI NAME	CAS NUMBER	Limit (ppm)
Alpha-IsoMethyl Ionone	127-51-5	< 0.02
Amyl Cinnamal	122-40-7	< 0.10
Anise Alcohol	105-13-5	< 0.00
Benzyl Alcohol	100-51-6	< 0.01
Benzyl Benzoate	120-51-4	< 0.09
Benzyl Cinnamate	103-41-3	< 0.30
Benzyl Salicylate	118-58-1	< 0.06
Butylphenyl Methylpropional	80-54-6	< 0.50
Cinnamal	104-55-2	< 0.01
Cinnamyl Alcohol	104-54-1	< 0.30
Citral	5392-40-5	< 1.00
Citronellol	106-22-9	< 1.00
Coumarin	91-64-5	< 0.00
Eugenol	97-53-0	< 0.70
Farnesol	4602-84-0	< 0.04
Geraniol	106-24-1	< 0.08
Hexyl Cinnamal	101-86-0	< 0.40
Hydroxycitronellal	107-75-5	< 1.00
Hydroxymethylpentyl 3-Cyclohexene carboxaldehyde	31906-04-4	< 0.30
Isoeugenol	97-54-1	< 0.06
Limonene	5989-27-5	< 0.05
Linalool	78-70-6	< 0.00
Methyl 2 Octynoate	111-12-6	< 0.20
Evernia prunastri	90028-68-5	< 0.02
Evernia furfuracea	90028-67-4	< 0.00
Amylcinnamyl Alcohol	101-85-9	< 1.00

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Compositional Breakdown

This is to certify that ABS Witch Hazel Extract Sil does not contain pesticide levels exceeding the following (Reverse Phase High Performance Liquid Chromatography-Mass Spectrometer Coupled):

EPA Pesticide Levels	
NAME	LIMIT (mg/kg)
Alachlor	< 0.02
Aldrin and Dieldrin	< 0 .05
Azinphos-methyl	< 1. 00
Bromopropylate	< 3.0 0
Chlordane(cis and trans)	< 0.05
Chlorfenvinphos	< 0.50
Chlorpyrifos	< 0.20
Chlorpyrifos-methyl	< 0.10
Cypermethrin	< 1.00
DDT	< 1.00
Deltamethrin	< 0.50
Diazinon	< 0.50
Dichlorvos	< 1.00
Dithiocarbamates	< 2.00
Endosulfan	< 3.00
Endrin	< 0.05
Ethion	< 2.00
Fenitrothion	< 0.50
Fenvalerate	< 1.50
Fonofos	< 0.05
Heptachlor	< 0.05
Hexachlorobenzene	< 0.10
Hexachlorocyclohexane	< 0.30
Lindane	< 0.60
Malathion	< 1.00
Methidathion	< 0.20
Parathion	< 0.50
Parathion-methyl	< 0.20

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Compositional Breakdown

Permethrin	< 1.00
Phosalone	< 0.10
Piperonyl butoxide	< 3.00
Pirimiphos-methyl	< 4.00
Pyrethrins	< 3.00
Quintozene(sum of 3 items)	< 1.00

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Dermal and Ocular Irritation Tests

Sample: ABS Witch Hazel Extract Sil

Code: 10128

CAS #: 541-02-6 & 84696-19-5

Test Request Form/Submission #: 3527

Lot #: NC170606-I

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Maureen Danaher*
Principle Investigator: *Jennifer Goodman*

Test Performed:
In Vitro EpiDerm™ Dermal Irritation Test (EPI-200-SIT)
EpiOcular™ Eye Irritation Test (OCL-200-EIT)

SUMMARY

In vitro dermal and ocular irritation studies were conducted to evaluate whether **ABS Witch Hazel Extract Sil** would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays.

The product was tested according to the manufacture's protocol. The test article solution was found to be **non-irritating**. Reconstructed human epidermis and cornea epithelial model were incubated in growth media overnight to allow for tissue equilibration after shipping from MatTek Corporation, Ashland, MA. Test substances were applied to the tissue inserts and incubated for 60 minutes for liquid and solid substances in the EpiDerm™ assay and 30 minutes for liquid substances and 90 minutes for solid substances in the EpiOcular™ assay at 37°C, 5% CO_2, and 95% relative humidity (RH). Tissue inserts were thoroughly washed and transferred to fresh plates with growth media. After post substance dosing incubation is complete, the cell viability test begins. Cell viability is measured by dehydrogenase conversion of MTT [(*3-4,5-dimethyl thiazole 2-yl*)], present in the cell mitochondria, into blue formazan salt that is measured after extraction from the tissue. The irritation potential of the test chemical is dictated by the reduction in tissue viability of exposed tissues compared to the negative control.

Under the conditions of this assay, the test article was considered to be **non-irritant**. The negative and positive controls performed as anticipated.

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Dermal and Ocular Irritation Tests

I. Introduction

A. Purpose

In vitro dermal and ocular irritation studies were conducted to evaluate whether a test article would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays. MatTek Corporation's reconstructed human epidermal and human ocular models are becoming a standard in determining the irritancy potential of test substances. They are able to discriminate between irritants and non-irritants. The EpiDerm™ assay has accuracy for the prediction of UN GHS R38 skin irritating and no-label (non-skin irritating) test substances. The EpiOcular™ assay can differentiate chemicals that have been classified as R36 or R41 from the EU classifications based on Dangerous Substances Directive (DSD) or between the UN GHS Cat 1 and Cat 2 classifications.

II. Materials

A. Incubation Conditions:	37°C at 5% CO_2 and 95% relative humidity
B. Equipment:	Forma humidified incubator, ESCO biosafety laminar flow hood, Synergy HT Microplate reader; Pipettes
C. Media/Buffers:	DMEM based medium; DPBS; sterile deionized H_2O
D. Preparation:	Pre-incubate (37°C) tissue inserts in assay medium; Place assay medium and MTT diluent at 4°C, MTT concentrate at -20°C, and record lot numbers of kit components
E. Tissue Culture Plates:	Falcon flat bottom 96-well, 24-well, 12-well, and 6-well tissue culture plates
F. Reagents:	MTT (1.0mg/mL); Extraction Solution (Isopropanol); SDS (5%); Methyl Acetate
G. Other:	Nylon Mesh Circles (EPI-MESH); Cotton tip swabs; 1mL tuberculin syringes; Ted Pella micro-spatula; 220mL specimen containers; sterile disposable pipette tips; Parafilm

III. Test Assay

A. Test System

The reconstructed human epidermal model, EpiDerm™, and comea epithelial model, EpiOcular™, consist of normal human-derived epidermal keratinocytes which have been cultured to form a multilayer, highly differentiated model of the human epidermis and cornea epithelium. These models consist of organized basal, spinous, and granular layers, and the EpiDerm™ systems also contains a multilayer stratum corneum containing intercellular lamellar lipid layers that the EpiOcular™ system is lacking. Both the EpiDerm™ and EpiOcular™ tissues are cultured on specially prepared cell culture inserts.

B. Negative Control

Sterile DPBS and sterile deionized water are used as negative controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

C. Positive Control

Known dermal and eye irritants, 5% SDS solution and Methyl Acetate, were used as positive controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

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D. Data Interpretation Procedure

a. EpiDerm™

An irritant is predicted if the mean relative tissue viability of the 3 tissues exposed to the test substance is reduced by 50% of the mean viability of the negative controls and a non-irritant's viability is > 50%.

b. EpiOcular™

An irritant is predicted if the mean relative tissue viability of the 2 tissues exposed to the test substance is reduced by 60% of the mean viability of the negative controls and a non-irritant's viability is > 40%.

IV. Method

A. Tissue Conditioning

Upon MatTek kit arrival at Active Concepts, LLC the tissue inserts are removed from their shipping medium and transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for 60 minutes. After those 60 minutes the inserts are transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for an additional 18 to 21 hours.

B. Test Substance Exposure

a. EpiDerm™

30µL (liquid) or 25mg (solid) of the undiluted test substance is applied to 3 tissue inserts and allowed to incubate for 60 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

b. EpiOcular™

Each tissue is dosed with 20µL DPBS prior to test substance dosing. 50µL (liquid) or 50mg (solid) of the undiluted test substance is applied to 2 tissue inserts and allowed to incubate for 90 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

C. Tissue Washing and Post Incubation

a. EpiDerm™

All tissue inserts are washed with DPBS, dried with cotton tipped swab, and transferred to fresh media and culture plates. After 24 hours the inserts are again transferred into fresh media and culture plates for an additional 18 to 20 hours.

b. EpiOcular™

Tissue inserts are washed with DPBS and immediately transferred into 5mL of assay medium for 12 to 14 minutes. After this soak the inserts are transferred into fresh media and tissue culture plates for 120 minutes for liquid substances and 18 hours for solid substances.

D. MTT Assay

Tissue inserts are transferred into 300µL MTT media in pre-filled plates and incubated for 3 hours at 37°C, 5% CO_2, and 95% RH. Inserts are then removed from the MTT medium and placed in 2mL of the extraction solution. The plate is sealed and incubated at room temperature in the dark for 24 hours. After extraction is complete the tissue inserts are pierced with forceps and 2 x 200µL aliquots of the blue formazan solution is transferred into a 96 well plate for Optical Density reading. The spectrophotometer reads the 96-well plate using a wavelength of 570 nm.

V. Acceptance Criterion

A. Negative Control

The results of this assay are acceptable if the mean negative control Optical Density (OD_{570}) is ≥ 1.0 and ≤ 2.5 (EpiDerm™) or ≥ 1.0 and ≤ 2.3 (EpiOcular™).

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B. Positive Control

a. EpiDerm™

The assay meets the acceptance criterion if the mean viability of positive control tissues expressed as a % of the negative control is ≤ 20%.

b. EpiOcular™

The assay meets the acceptance criterion if the mean viability of positive control tissues is < 60% of control viability.

C. Standard Deviation

Since each irritancy potential is predicted from the mean viability of 3 tissues for EpiDerm™ and 2 tissues for EpiOcular™, the variability of the replicates should be < 18% for EpiDerm™ and < 20% EpiOcular™.

VI. Results

A. Tissue Characteristics

The tissue inserts included in the MatTek EpiDerm™ and EpiOcular™ assay kits were in good condition, intact, and viable.

B. Tissue Viability Assay

The results are summarized in Figure 1. In no case was the tissue viability ≤ 50% for EpiDerm™ or ≤ 60% for EpiOcular™ in the presence of the test substance. The negative control mean exhibited acceptable relative tissue viability while the positive control exhibited substantial loss of tissue viability and cell death.

C. Test Validity

The data obtained from this study met criteria for a valid assay.

VII. Conclusion

Under the conditions of this assay, the test article substance was considered to be **non-irritating**. The negative and positive controls performed as anticipated.

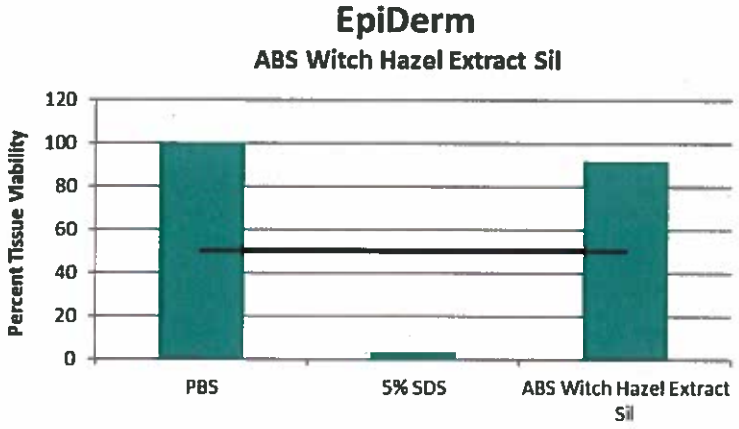

Figure 1: EpiDerm tissue viability

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Dermal and Ocular Irritation Tests

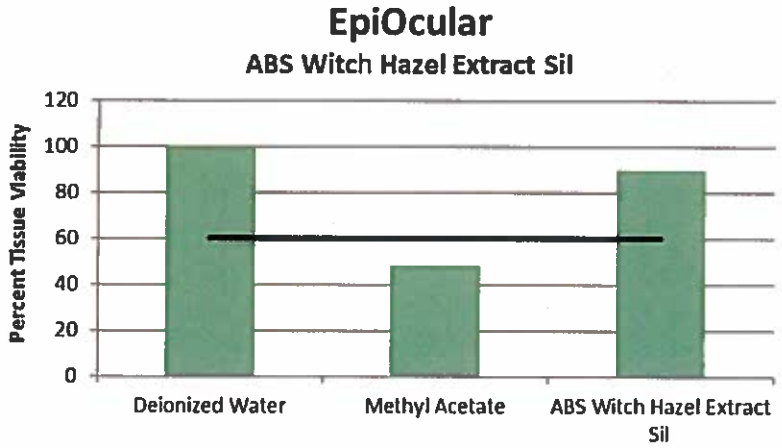

Figure 2: EpiOcular tissue viability

10128-ABS Witch Hazel Extract Sil-
Manufacturing Flow Chart

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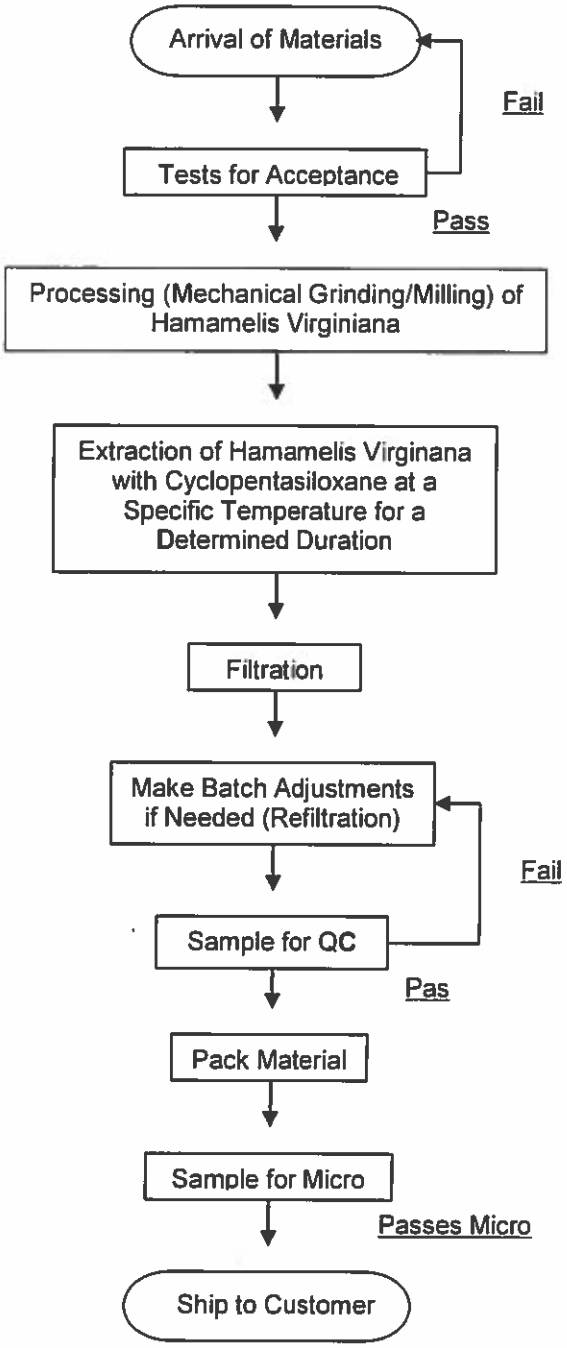

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Product Specification

Product Name: ABS Witch Hazel Extract Sil
Code Number: 10128
CAS #'s: 541-02-6 & 84696-19-5
EINECS #'s: 208-764-9 & 283-637-9
INCI Name: Cyclopentasiloxane & Hamamelis Virginiana (Witch Hazel) Extract
Status: Approved

Specification	Parameter
Appearance	Clear to Slightly Hazy Liquid
Color	Colorless to Light Yellow
Odor	Characteristic
Refractive Index (@ 25°C)	1.3930 – 1.4010
Specific Gravity (@ 25°C)	0.930 – 0.990
Heavy Metals	< 20 ppm
Lead	< 10 ppm
Arsenic	< 2 ppm
Cadmium	< 1 ppm
Microbial Content Yeast & Mold Gram Negative Bacteria	< 100 CFU/g; No pathogens < 100 CFU/g 0 CFU/g

May Sediment upon Standing; Mix Well Prior to Use

**Note: Product may change appearance if exposed to cold temperatures during shipment or storage. If this happens, please gently warm to 45-50°C and mix until normal appearance is restored.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D., Interim Director
COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: August 2, 2017

SUBJECT: Scientific Literature Review Safety Assessment of *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients as Used in Cosmetics (CIR report released July 7, 2017)

Introduction - It should be made clear that oxidation products of linalool, rather than linalool itself are responsible for the sensitization potential of this fragrance ingredient.

Cosmetic Use - When results of the Council's concentration of use survey are mentioned in the text, please include the reported maximum use concentrations, e.g., up to 5% Hamamelis Virginiana (Witch Hazel) Leaf Water in paste masks and mud packs, maximum use concentration in an eye area product 35.8% Hamamelis Virginiana (Witch Hazel) Extract in an eye lotion.

Non-Cosmetic Use - It should also be noted that in the skin protectant OTC drug regulations, witch hazel is listed as an astringent active ingredient (21CFR347.12).

Toxicokinetics - The first paragraph (especially the last sentence) in the Pharmacokinetics section of reference 2 is more useful than the statement that witch hazel extracts are not absorbed (unless there are data to support the lack of absorption statement). The first paragraph states: "According to the definition of HMP, the total preparation (e.g: Hamamelidis destillatum) must be regarded as the active substance. This involves a mixture of numerous constituents. The active constituents have not yet been clearly defined and many compounds are only contained in very small concentrations or defy analytical detection due to their chemical structure or their ubiquitous occurrence (polymeric phenols). No single constituent has been defined as therapeutically active marker and consequently, no appropriate pharmacokinetic studies are available."

Subchronic, Oral - Reference 2 cites the oral rat 3 month study to Bernard et al. 1972. The draft reference section at http://www.ema.europa.eu/docs/en_GB/document_library/Herbal_-_List_of_references_supporting_the_assessment_report/2010/01/WC500054054.pdf provides the following information about this reference:

Bernard P, Balansard P, Balansard G, Bovis A. [Venitonic pharmacodynamic value of galenic preparations with a base of hamamelis leaves]. Valeur pharmacodynamique toniveineuse des préparations galéniques à base de feuilles d'hamamélis. Journal De Pharmacie De Belgique [J Pharm Belg] 1972 Jul-Aug; Vol. 27 (4), 505-12.

Rather than just stating that: "No further information was provided." It would be helpful to state that there was no additional information in the secondary references and the primary reference was not readily available.

Chronic - When there is a two year NTP study, it is not appropriate to state that there are no chronic toxicity studies. The two year study should be mentioned in the chronic section with a statement that details about the study are presented in the Carcinogenicity section.

Genotoxicity - Was something in addition to Hamamelis Virginiana (Witch Hazel) Water tested in the mouse lymphoma cell forward mutation assay, as it says that cultures were "exposed to the chemicals"?

The NTP summary page for witch hazel https://ntp.niehs.nih.gov/testing/status/agents/ts-10183-p.html also indicates that there is a Drosophila study - Completed

Woodruff, R.C., Mason, J.M., Valencia, R., and Zimmering, S. Chemical mutagenesis testing in Drosophila: V. Results of 53 coded compounds tested for the National Toxicology Program. Environ. Mutagen. Vol. 7 (1985) 677-702

Results: Reciprocal Translocation/Sex-Linked Recessive Lethal Negative

The Ames assay listed on the NTP summary page is cited to (a reference not yet in the CIR report):

Mortelmans, K., Haworth, S., Lawlor, T., Speck, W., Tainer, B., and Zeiger, E. Salmonella mutagenicity tests. II. Results from the testing of 270 chemicals Environ. Mutagen. Vol. 8 (Suppl 7) (1986) 1-119.

Carcinogenicity - Although an NTP study was completed, the Carcinogenicity section should make it clear that: "A technical report number was assigned to the chronic study of this test article. The study was considered inadequate and no technical report was prepared." This statement is found on the NTP website at: https://ntp.niehs.nih.gov/results/pubs/longterm/reports/longterm/tr200299/abstracts/tr286/index.html

Table 5 - Please correct: "neutraphils"