Rereview Summaries

Dioscorea Villosa (Wild Yam) Root Extract
Polyamino Sugar Condensate
Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal

EXPERT PANEL MEETING

JUNE 12-13, 2023

DIOSCOREA VILLOSA (WILD YAM) ROOT EXTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report of the Amended Safety Assessment of Dioscorea Villosa (Wild Yam) Root Extract in 2004.[1] The Panel concluded that based on the chemical and animal data include in the safety assessment, Dioscorea Villosa (Wild Yam) Root Extract is safe for use in cosmetic products. In the Discussion of that report, the Panel further clarified that this conclusion is valid only for extracts prepared in a manner that produces a similar chemical profile as that described in the safety assessment, particularly in regard to diosgenin (i.e., an expected upper limit of 3.5%). Additionally, the Panel stated that extracts not prepared in a manner that produces a similar chemical profile would be considered safe if they have a similar safety test profile.

Because it has been at least 15 years since the final report was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel considered whether the safety assessment should be reopened. At the March 2023 meeting, the Panel reviewed 2022 information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[2] and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.[3] The frequency of use increased; Dioscorea Villosa (Wild Yam) Root Extract had 1 reported use in the original review and 43 reported uses in 2022[2]; total reported uses and use categories did not significantly change. However, the reported concentrations of use decreased; the maximum reported use concentration of Dioscorea Villosa (Wild Yam) Root Extract in 1999 was 15% (0.5% maximum solids from wild yam) in moisturizing formulations; in 2022, it is reported to be used at 0.3% in non-spray moisturizing products. The cumulative frequency and concentration of use data are presented in Table 1.

In January 2023, an extensive search of the world's literature was performed for studies dated 1999 forward, and new data were found.[4-9] Notable findings include two short-term oral toxicity studies and a 13-wk oral toxicity study in which the NOAEL for rat of both sexes was determined to be the maximum received dose of 5000 mg/kg/d. Additionally, studies demonstrating the potential cytotoxicity of *Dioscorea villosa* (wild yam) root extract against breast cancer cell lines, a study of anti-inflammatory effects, and a clinical study in which no significant side effects or metabolic/endocrinal changes were seen in healthy premenopausal women following 3 mo of topical application of wild yam cream, were found.

In summary, the Panel reviewed 2022 frequency and concentration of use data, in addition to any new, available, relevant safety data. Considering this information, as well as the information provided in the original safety assessment, the Panel reaffirmed the 2004 conclusion for Dioscorea Villosa (Wild Yam) Root Extract.

Table 1. Frequency (2022/1998) and concentration (2022/1999) of use according to likely duration and exposure by product category

	# of Uses		*Max Conc of Use (%)*	
	Dioscorea Villosa (Wild Yam) Root Extract			
	2022[2]	**1998[1]**	**2022[3]**	**1999[1]**
Totals*	**43**	**1**	**0.3**	**0.00001-15**
summarized by likely duration and exposure**				
Duration of Use				
Leave-On	*39*	*1*	*0.3*	*0.00001-15*
Rinse-Off	*4*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	2	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	25[a]; 10[b]	1[b]	NR	15[a]; 0.00001[b]
Incidental Inhalation-Powder	10[b]	1[b]	NR	0.00001[b]
Dermal Contact	42	1	0.3	0.00001-15
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	1	NR	NR	NR
Baby Products	NR	NR	NR	NR
as reported by product category				
Eye Makeup Preparations				
Eye Lotion	2	NR	NR	NR
Hair Preparations (non-coloring)				
Tonics, Dressings, and Other Hair Grooming Aids	1	NR	NR	NR
Personal Cleanliness Products				
Other Personal Cleanliness Products	1	NR	NR	NR
Skin Care Preparations				
Cleansing	2	NR	NR	NR
Face and Neck (exc shave)	6	NR	NR	NR
Body and Hand (exc shave)	4	1	NR	0.00001 (0.000002% maximum solids from wild yam)
Moisturizing	23	NR	0.3 (not spray)	15 (0.5% maximum solids from wild yam)
Night	1	NR	NR	NR
Paste Masks (mud packs)	1	NR	NR	NR
Other Skin Care Preparations	2	NR	NR	NR

NR – not reported

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

**likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

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

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

REFERENCES

1. Andersen FA (ed). Final report of the amended safety assessment of Dioscorea Villosa (Wild Yam) root extract. *Int J Toxicol.* 2004;23 Suppl 2:49-54.

2. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). 2022. Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients (VCRP). (Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2022; received January 11, 2022.)

3. Personal Care Products Council. 2022. Concentration of Use by FDA Product Category: Dioscorea Villosa (Wild Yam) Root Extract. (Unpublished data submitted by the Personal Care Products Council on October 31, 2022.)

4. Lima CM, Lima AK, Melo MG, et al. Bioassay-guided evaluation of Dioscorea villosa - an acute and subchronic toxicity, antinociceptive and anti-inflammatory approach. *BMC Complement Altern Med.* 2013;13:195.

5. Wojcikowski K, Wohlmuth H, Johnson DW, Gobe G. Dioscorea villosa (wild yam) induces chronic kidney injury via pro-fibrotic pathways. *Food and chemical toxicology.* 2008;46(9):3122-3131.

6. Cha SB, Kim HS, Bae JS, Song SW, Lim JO, Kim JC. A 13-week subchronic toxicity study of a Dioscorea Rhizome water extract in rats. *Regul Toxicol Pharmacol.* 2021;120:104844.

7. Mazzio E, Almalki A, Darling-Reed SF, Soliman KFA. Effects of Wild Yam Root (Dioscorea villosa) Extract on the Gene Expression Profile of Triple-negative Breast Cancer Cells. *Cancer Genomics Proteomics.* 2021;18(6):735-755.

8. Aumsuwan P, Khan SI, Khan IA, et al. Evaluation of wild yam (Dioscorea villosa) root extract as a potential epigenetic agent in breast cancer cells. *In Vitro Cellular & Developmental Biology-Animal.* 2015;51(1):59-71.

9. Komesaroff PA, Black CV, Cable V, Sudhir K. Effects of wild yam extract on menopausal symptoms, lipids and sex hormones in healthy menopausal women. *Climacteric.* 2001;4(2):144-150.

POLYAMINO SUGAR CONDENSATE

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report of the Safety Assessment of Polyamino Sugar Condensate in 1982.[1] The Panel concluded that in the present practices of use and concentration (described in the safety assessment), Polyamino Sugar Condensate is safe for topical application to humans. Upon re-review in 2002-2003, the Panel reaffirmed the original conclusion, as published in 2005.[2]

Because it has been at least 15 years since the prior review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel again considered whether the safety assessment should be reopened. At its March 2023 meeting, the Panel reviewed updated (2022) information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council (Council). Polyamino Sugar Condensate had 1 reported use in a body and hand formulations in 2022[3] At the time this ingredient was last considered for review, 25 uses were reported.[2] Concentration of use data were neither reported at the time the initial re-review was considered in 2002/2003 nor in response to a survey conducted by the Council in 2022.[2,4] The cumulative frequency and concentration of use data are presented in Table 1.

In January 2023, an extensive search of the world's literature was performed for studies dated 2000 forward. No relevant new data were found.

In summary, the Panel reviewed 2022 frequency and concentration of use data and noted the lack of any new, available, relevant safety data. Considering this information, as well as the information provided in the original safety assessment and the prior re-review document, the Panel once again reaffirmed the 1982 conclusion.

Table 1. Frequency and concentration of use (2022/2001) according to likely duration and exposure by product category

	Polyamino Sugar Condensate			
	# of Uses		*Max Conc of Use (%)*	
	2022[3]	**2001[2]**	**2022[4]**	**2001[2]**
Totals*	**1**	**25**	**NR**	**NR**
summarized by likely duration and exposure**				
Duration of Use				
Leave-On	*1*	*22*	*NR*	*NR*
Rinse-Off	*NR*	*3*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	NR	4	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]	5[a]; 11[b]	NR	NR
Incidental Inhalation-Powder	1[a]	5[a]	NR	NR
Dermal Contact	1	25	NR	NR
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR
as reported by product category				
Eye Makeup Preparations				
Other Eye Makeup Preparations	NR	4	NR	NR
Skin Care Preparations				
Cleansing	NR	2	NR	NR
Face and Neck (exc shave)	NR	1	NR	NR
Body and Hand (exc shave)	1	4	NR	NR
Moisturizing	NR	9	NR	NR
Night	NR	1	NR	NR
Paste Masks (mud packs)	NR	1	NR	NR
Other Skin Care Preparations	NR	2	NR	NR
Suntan Preparations				
Suntan Gels, Creams, and Liquids	NR	1	NR	NR

NR – not reported

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

**likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

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

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

REFERENCES

1. Anderson FA (ed). Final Report of the Safety Assessment of Polyamino Sugar Condensate. *Journal of the American College of Toxicology*. 1982;1(4):25-32.

2. Cosmetic Ingredient Review Expert Panel. Annual Review of Cosmetic Ingredient Safety Assessments--2002/2003. *Int J Toxicol.* 2005;24 Suppl 1:1-102.

3. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). 2022. Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients (VCRP). (Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2022; received January 11, 2022.)

4. Personal Care Products Council. 2022. Concentration of Use by FDA Product Category: Polyamino Sugar Condensate. (Unpublished data submitted by the Personal Care Products Council on October 24, 2022.)

PRUNUS AMYGDALUS DULCIS (SWEET ALMOND) SEED MEAL

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Sweet Almond Oil and Almond Meal in 1983.[1] On the basis of the available data and limited clinical experience presented in the report, the Panel concluded that Almond Meal (now named Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal) is safe for topical application to humans in the present practices of use and concentration (this ingredient was named Almond Meal in the original report). Upon re-review in November 2002, the Panel reaffirmed the original conclusion, as published in 2005.[2] Prunus Amygdalus Dulcis (Sweet Almond) Oil was not considered in this re-review because it was included in the safety assessment of plant-derived fatty acids, published in 2017.[3]

Because it has been at least 15 years since the prior re-review was published, in accordance with Cosmetic Ingredient Review (CIR) Procedures, the Panel considered whether the safety assessment should be reopened. At its March 2023 meeting, the Panel considered updated (2022) information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database[4] and maximum use concentrations provided in response to the survey conducted by the Personal Care Products Council.[5] Since the initial re-review was considered, the frequency of use for Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal has decreased slightly from 15 to 14 uses.[4] In 2002, the maximum concentration of use for this ingredient was reported to be 27% in leave-on products and 2% in rinse-off products.[2] No concentrations of use were reported in the 2022 survey for this ingredient.[5] The cumulative frequency and concentration of use data are presented in Table 1.

In January 2023, an extensive search of the world's literature was performed for studies dated 1997 forward. No new toxicological data were found.

In summary, the Panel reviewed 2022 frequency and concentration of use data and noted the lack of any new, available, relevant safety data. Considering this information, as well as the information provided in the original safety assessment and the prior re-review document, the Panel once again reaffirmed the 1983 conclusion.

Table 1. Frequency and concentration of use (2022/2002) according to likely duration and exposure and by product category

	# of Uses		*Max Conc of Use (%)*	
	2022[4]	**2002[2]**	**2022[5]**	**2002[2]**
	Prunus Amygdalus Dulcis (Sweet Almond) Seed Meal			
Totals*	**14ǂ**	**15**	**NR**	**0.5-27**
summarized by likely duration and exposure**				
Duration of Use				
Leave-On	*12*	*3*	*NR*	*0.5-27*
Rinse-Off	*2*	*12*	*NR*	*0.5-2*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	1	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	2[a]; 1[b]	1[b]	NR	0.5[b]
Incidental Inhalation-Powder	2; 1[b]	1[b]	NR	27; 0.5[b]
Dermal Contact	14	14	NR	0.5-27
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	1	NR	NR
Mucous Membrane	1	3	NR	0.5-2
Baby Products	NR	NR	NR	NR
as reported by product category				
Eye Makeup Preparations				
Other Eye Makeup Preparations	1	NR	NR	NR
Fragrance Preparations				
Powders (dusting/talcum, excl aftershave talc)	NR	NR	NR	27
Makeup Preparations				
Face Powders	2	NR	NR	NR
Makeup Bases	1	NR	NR	NR
Makeup Fixatives	2	NR	NR	NR
Other Makeup Preparations	1	NR	NR	NR
Manicuring Preparations (Nail)				
Cuticle Softeners	NR	1	NR	NR
Personal Cleanliness Products				
Bath Soaps and Detergents	NR	2	NR	0.5-2
Other Personal Cleanliness Products	1	1	NR	NR
Skin Care Preparations				
Cleansing	1	2	NR	NR
Body and Hand (exc. shave)	1	1	NR	0.5
Moisturizing	2	NR	NR	NR
Paste Masks (mud packs)	1	7	NR	2
Other Skin Care Preparations	1	1	NR	NR

NR – not reported

ǂ Reported as Prunus Dulcis (Sweet Almond) Seed Meal in the 2022 VCRP.

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

**likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

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

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

REFERENCES

1. Elder R, (ed),. Final report on the safety assessment of Sweet Almond Oil and Almond Meal. *J Am Coll Toxicol.* 1983;2(5):85-99.

2. Andersen FA (ed). Annual Review of Cosmetic Ingredient Safety Assessments - 2002/2003. Sweet Almond Oil and Almond Meal. *Int J Toxicol.* 2005;24(Suppl 1):98-101.

3. Burnett CL, Fiume MM, Bergfeld WF, et al. Safety Assessment of Plant-Derived Fatty Acid OIls. *Int J Toxicol.* 2017;36(Suppl 3):51S-129S.

4. US Food and Drug Administration (FDA) Center for Food Safety & Applied Nutrition (CFSAN). 2022. Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. (Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2022; received January 11, 2022). College Park, MD.

5. Personal Care Products Council. 2022. Concentration of use by FDA product category: Prunus Amygdalus Dulcis Seed Meal. Unpublished data submitted by Personal Care Products Council on October 28, 2022