Safety Assessment of Diatomaceous Earth as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	February 11, 2022
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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: Lisa A. Peterson, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Christina L. Burnett, Senior Scientific Analyst/Writer, CIR.

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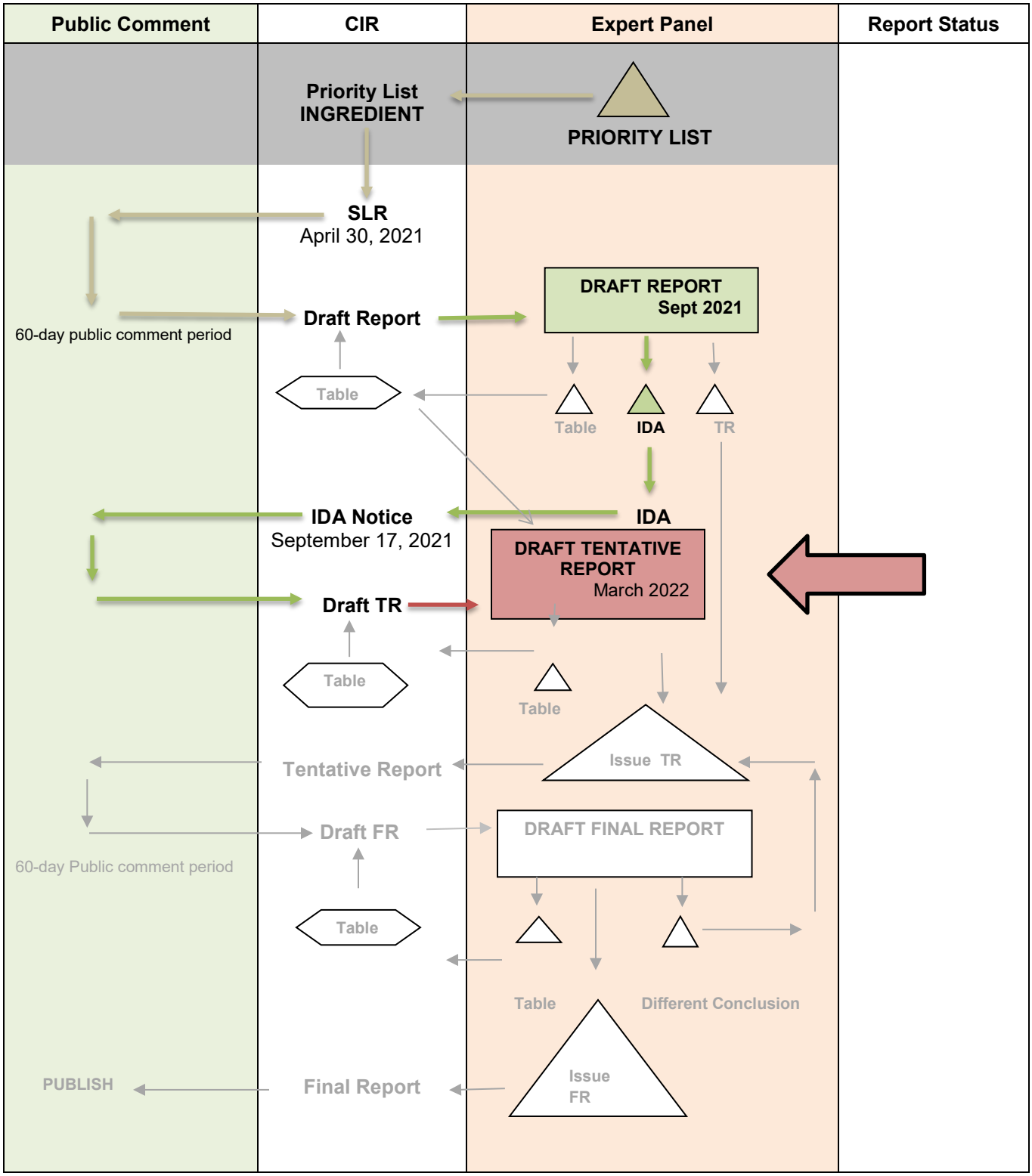
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Diatomaceous Earth

MEETING September 2021



Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: February 11, 2022
Subject: Safety Assessment of Diatomaceous Earth as Used in Cosmetics

Enclosed is the Draft Tentative Report of the Safety Assessment of Diatomaceous Earth as Used in Cosmetics. (It is identified as *report_DiatomaceousEarth_032022* in the pdf document.) At the September 2021 meeting, the Panel issued an Insufficient Data Announcement (IDA). The additional data needed to determine safety for this cosmetic ingredient are:

- Clarification on the type(s) of Diatomaceous Earth that is used in cosmetic products (i.e., natural, calcined, and/or flux-calcined)
- Method of manufacturing for the type(s) of Diatomaceous Earth that is used in cosmetic products
- Composition and impurities data (including crystalline silicate content) on the type(s) of Diatomaceous Earth that is used in cosmetic products

Since the issuance of the IDA, CIR has received information from a supplier providing information on the type of Diatomaceous Earth used in cosmetics (soda ash flux-calcined), method of manufacturing, and composition and impurities data (*data1_DiatomaceousEarth_032022*). CIR also received an in vitro ocular study on a formulation containing 9%-11% soda ash flux-calcined Diatomaceous Earth (diluted at 2%, 5%, and 10%), and information that clarified that some of the previous safety test data that are summarized in the report are on soda ash flux-calcined Diatomaceous Earth (*data2_DiatomaceousEarth_032022*). Additional data on the composition of Diatomaceous Earth from published literature have also been identified. All of these data have been incorporated into the report and are highlighted to aid in the Panel's review.

CIR also received comments and information from the International Diatomite Producers Association (IDPA) for the Panel's consideration (*IDPAcomments_DiatomaceousEarth_032022*). The comments were accompanied by a few published documents that can be furnished to the Panel, upon request. IDPA reports that its member companies only supply natural Diatomaceous Earth for use in cosmetics.

The Use Table has been updated with 2022 VCRP data and with new concentration of use data from the Council (*VCRP_DiatomaceousEarth_032022* and *data3_DiatomaceousEarth_032022*, respectively). Uses for Diatomaceous Earth increased from 116 to 135. The most notable change is that the number of uses in nail polish and enamel increased from 15 uses to 49. Currently, more than half of the uses for Diatomaceous Earth reported in the VCRP are in leave-on formulations. The results of the updated concentration of use survey conducted by the Council in 2021 indicate that Diatomaceous Earth is now used at up to 2% in rinse-off products (paste masks, which were previously reported to be used at up to 62.2%), and up to 0.01% in leave-on products (nail polish and enamel). Uses are reported in face powders in the VCRP, but no concentrations of use are reported. No other confirmed use in products which may be incidentally inhaled are reported.

Additional supporting documents for this report package include a flow chart (*flow_DiatomaceousEarth_032022*), report history (*history_DiatomaceousEarth_032022*, a search strategy (*search_DiatomaceousEarth_032022*), transcripts from the previous meeting (*transcripts_DiatomaceousEarth_032022*), and a data profile (*dataprofile_DiatomaceousEarth_032022)*.

A draft Abstract and Discussion have been included in this report version. The Panel should carefully consider and discuss the data (or lack thereof), and issue a Tentative Report with a safe, safe with qualifications, insufficient data, unsafe, or split conclusion, and identify any additional items for inclusion in the Discussion.

November 9, 2021

Carol Eisenmann, Ph.D.
Senior Toxicologist
Personal Care Products Council
1620 L Street, Suite 1200
Washington DC 20036

Re: IDPA Comments on the Draft Safety Assessment of Diatomaceous Earth as Used in Cosmetics and Other Matters

Submitted via E-Mail: eisenmannc@personalcarecouncil.org

Dear Dr. Eisenmann:

The International Diatomite Producers Association (IDPA) is a trade association representing major manufacturers of diatomaceous earth products worldwide. Founded in 1987, IDPA is committed to the safe use of diatomaceous earth products and to advancing research and maintaining a dialogue with industry, regulatory agencies and the scientific community in support of the safety of our employees and the communities we serve.

The Cosmetic Ingredient Review (CIR) Expert Panel for Cosmetic Ingredient Safety (Expert Panel) held a virtual two-day meeting on September 13 & 14, 2021, during which they considered a draft safety assessment of diatomaceous earth (DE) as used in cosmetics (https://www.cir-safety.org/sites/default/files/Diatomaceous%20Earth.pdf) (Draft Report). IDPA previously had submitted written comments to the CIR, dated June 29, 2021 (IDPA June 29, 2021 Comments)(Attachment 1.), which addressed the draft Scientific Literature Review (SLR) on DE prepared by CIR staff (https://cir-safety.org/sites/default/files/Diatomaceous%20Earth.pdf). IDPA representatives subsequently offered some oral comments at the September 13 meeting sessions consistent with, and expanding upon, those earlier written comments on the draft SLR.

At the conclusion of the plenary session on September 14, the Expert Panel approved an Insufficient Data Announcement (IDA) for the Draft Report on DE. As an industry liaison representative of the Personal Care Products Council (PCPC) to the CIR, you subsequently advised me that the following additional information was requested by the Expert Panel:

1. Clarification of the type of Diatomaceous Earth used in cosmetics (i.e., natural, calcined, and/or flux-calcined);

2. Method of manufacture for the type(s) of Diatomaceous Earth used in cosmetic products; and

3. Composition and impurities data (including crystalline silica content) on the type(s) of Diatomaceous Earth that is used in cosmetic products.

IDPA is pleased to submit the following comments to CIR, through you as the PCPC industry liaison representative, on the Draft Report on DE referenced above, on the additional information requested by the Expert Panel, and on other related matters. IDPA respectfully requests that a copy of these comments be shared with members of the Expert Panel, other liaison representatives, and CIR staff, as appropriate, so that all may better understand the suggested approach of IDPA on CIR's consideration of DE as used in cosmetics. A courtesy copy of these comments simultaneously has been provided to Dr. Bart Heldreth, Executive Director of the CIR, for his information.

1. Clarification of the type of Diatomaceous Earth used in cosmetics (i.e., natural, calcined, and/or flux-calcined)

IPDA once again has polled its member companies as to what type/grade of DE is used in cosmetics. Those IDPA member companies that directly supply DE to the cosmetics industry advise that they only supply natural DE, not calcined or flux-calcined DE for use in cosmetics. However, DE also is available to purchasers from distributors of DE products. Distributors of DE are advised against marketing any non-natural DE for use in cosmetics.

PCPC may be best positioned to solicit this information directly from the cosmetics industry.

2. Method of manufacture for the type(s) of Diatomaceous Earth used in cosmetic products

In the IDPA June 29, 2021 Comments, IDPA submitted the chapter on "Diatomite" from *Industrial Minerals & Rocks – Commodities, Markets, and Uses*, published by the Society for Mining, Metallurgy, and Exploration, Inc.[1] (See Attachment to Attachment 1.) Generally regarded as a standard reference on industrial minerals and their properties and uses, IDPA believes that much can be gleaned from the chapter to begin addressing the types of DE used in cosmetic products.

For its part, IDPA assumes that the only type of DE directly supplied to the cosmetics industry for use in cosmetics is natural DE.

> To produce natural DE an amorphous silica ore is minimally crushed, dried, milled and air classified to produce desired particle sizes. IDPA June 29, 2021 Comments at Page 2.
>
> The other two grades of DE are further thermally processed by calcining or flux-calcining. This additional thermal processing produces fundamental changes in the composition of the opaline silica frustule. Calcination and flux-calcination dehydrate the amorphous silica and initiate its conversion to crystalline cristobalite. Thermal processing also reduces the surface area of the diatoms by altering their physical form and thereby imparts certain desirable

[1] *Industrial Minerals & Rocks – Commodities, Markets, and Uses*, 7th Edition, edited by Jessica Elzea Kogel, et al., published by the Society for Mining, Metallurgy, and Exploration, Inc. (2006).

properties for a variety of commercial uses. However, the formation of crystalline silica produced by calcining and flux-calcining natural DE likely renders these grades inappropriate for use in cosmetics. IDPA June 29, 2021 Comments at Page 2.

Consequently, IDPA would like the SLR [and the Draft Report] on DE to be revised to focus exclusively on natural DE as the only form of DE IDPA deems appropriate for use in cosmetics. IDPA June 29, 2021 Comments at Page 2 (parenthetical added).

IDPA would draw the attention of the Expert Panel and CIR staff to related discussion of manufacturing DE in *Industrial Minerals & Rocks – Commodities, Markets, and Uses* found at Page 433 (top paragraph in right-hand column); at Page 435-6 (bottom paragraph in right-hand column); and at Page 437 (first full paragraph in right-hand column).

IDPA member companies are expert in the mining and processing of DE and should the Expert Panel have specific questions that go beyond the explanations and references offered here, IDPA stands ready to assist.

In reviewing the draft SLR [and Draft Report], IDPA notes that there are many references to calcined and flux-calcined DE. IDPA recommends that discussion of these two grades be deleted from the draft SLR [and Draft Report] as inappropriate for consideration. IDPA June 29, 2021 Comments at Page 2 (parenthetical added).

3. Composition and impurities data (including crystalline silica content) on the type(s) of Diatomaceous Earth that is used in cosmetic products

This request for information is more complicated than it appears at first blush (no pun intended). The challenge presented here is we are addressing DE, which is a natural mineral substance. It is not elemental or pure. Its chemical composition varies with the deposit from which the mineral is extracted. Its chemical composition may, or may not, be affected by mineral processing or thermal calcination, with or without a fluxing agent.

IDPA would draw the attention of the Expert Panel and CIR staff to Table 3 in *Industrial Minerals & Rocks – Commodities, Markets, and Uses* at Page 435, where the chemical composition of natural diatomites (oven–dried basis) is presented. While not exclusive, the table illustrates the variability present in the composition of natural DE.

Similarly, IDPA would draw the attention of the Expert Panel and CIR staff to Table 4 in *Industrial Minerals & Rocks – Commodities, Markets, and Uses* at Page 436, where typical trace element analysis of a particular DE product is offered. Note: Celatom FW-14 is a flux-calcined DE product.

The comments above lead to an area of discussion beyond the additional information requested by the Expert Panel. It appears that the CIR's definition of "chemical description" does not lend itself easily to DE as used in cosmetics.

(f) "Chemical description" means a concise definition of the chemical composition using

> standard chemical nomenclature so that the chemical structure or structures of the components of the ingredient would be clear to a practicing chemist. When the composition cannot be described chemically, the substance shall be described in terms of its source and processing. Part A. General, Section 1., Definitions., *Cosmetic Ingredient Review Procedures & Support to the Expert Panel for Cosmetic Ingredient Safety* (https://www.cir-safety.org/sites/default/files/CIR%20Procedures%20-%20September%202019.pdf).

IDPA maintains that natural DE, as opposed to calcined or flux-calcined DE is the appropriate chemical description for DE as used in cosmetics. However, in both the draft SRL and Draft Report, the definition from the *International Cosmetic Ingredient Dictionary and Handbook* appears to be the starting point for the evaluation of the safe use of DE in cosmetics. For the reasons stated in the IDPA June 29, 2021 Comments, oral statements made by IDPA representatives at the September 13 sessions of the Expert Panel meeting, and in these current comments, IDPA submits that the CIR Expert Panel should narrow the definition, and its evaluation, to the ingredient used in cosmetics . . . natural DE. The Chemical Abstract Service Registry Number for DE, 61790-53-2, equates to 100% diatomaceous earth, regardless of its crystalline silica content.

Without belaboring the point, other expert authoritative bodies have addressed DE and concluded that it is a Substance of Unknown or Variable Composition, Complex Reaction Products or Biological Material (UVCB). According to the Organization for Economic Co-Operation and Development (OECD):

> The concept of "impurities" typically does not apply to complex substances (UVCBs). Environmental Directorate, Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, ENV/JM/MONO(2014)4 (https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%282014%294&doclanguage=en) at Page 87. (Attachment 2.)

Moreover, the European Chemicals Agency (ECHA) has determined:

> Due to the lack of differentiation between constituents and impurities, the terms "main constituents" and "impurities" should not be regarded as relevant for UVCB substances. Guide for Identification and Naming of Substances under REACH and CLP, Version 2.1, May 2017 (https://echa.europa.eu/documents/10162/23036412/substance_id_en.pdf/ee696bad-49f6-4fec-b8b7-2c3706113c7d) at Page 38. (Attachment 3.)

IDPA recognizes that evaluating the safe use of mineral products as used in cosmetics typically is not pure or elemental. Their composition may, and likely does, vary. Natural DE comes from different deposits with different proportions of crystalline silica and other minerals. IDPA also recognizes that the Expert Panel currently is evaluating, contemporaneously with DE, several silicates and that the presence of crystalline silica is a topical issue. However, IDPA submits that mineral products containing crystalline silica can be, and are being, used safely, depending on the conditions of their intended use . . . including in cosmetics.

Most, if not all, cosmetic products containing DE are aqueous mixtures and applied wet. Even

when applied wet with the intention that the cosmetic will dry to perform its intended function, as in the case of facial masks, the dried mask is washed from the person's face with water. Even if allowed to dry and then intentionally allowed to disaggregate on someone's face, the respirable crystalline silica hypothetically generated would be *de minimis*. The disaggregated mask would not aerosolize into a respirable cloud in the person's breathing zone. The likelihood of repeated and prolonged exposure to respirable crystalline silica, sufficient to overcome the human body's natural defense mechanisms . . . resulting in lung overload . . . is extremely remote. It is unreasonable to assume that this hypothetical *de minimis* exposure would overcome the human body's natural defense mechanisms.

Analogous recognized examples of *de minimis* exposure to crystalline silica can be found in the State of California's Safe Use Determinations under Proposition 65. See: Issuance of Safe Use Determination for Exposures to Crystalline Silica From The Use of Four WOODWISE® Products; Issuance of a Safe Use Determination for Crystalline Silica in Interior Flat Latex Paint; Issuance of a Safe Use Determination for Crystalline Silica in Sorptive Mineral-based Pet Litter.

The dose makes the poison. Paracelsus is credited with expressing the classic toxicology maxim, "All things are poison, and nothing is without poison, the dosage alone makes it so a thing is not a poison." *Sola dosis facit venenum*. That maxim should be a touchstone in the current evaluation.

IDPA looks forward to continuing the dialogue on the safety of natural DE as used in cosmetics initiated by the draft SLR, the Draft Report, IDPA's comments and the Expert Panel's deliberations. Please do not hesitate to contact me with regard to suggestions you may have as to how IDPA and its member companies can best continue this exchange of views, information and data on the relevant science.

Respectfully submitted,

Mark G. Ellis
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IDPA Member Companies:

Chemviron, a Kuraray company
Dicalite Management Group, Inc.
EP Minerals, LLC, a U.S. Silica company
Imerys Performance Minerals

Showa Chemical Industry Company, Ltd.

Attachments:

Attachment 1: Letter to Dr. Bart Heldreth, dated June 29, 2021, with the attachment:

Attachment to Attachment 1: Chapter on "Diatomite", *Industrial Minerals & Rocks – Commodities, Markets, and Uses*, 7th Edition, edited by Jessica Elzea Kogel, et al., published by the Society for Mining, Metallurgy, and Exploration, Inc. (2006).

Attachment 2: Environmental Directorate, Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, ENV/JM/MONO(2014)4.

Attachment 3. Guide for Identification and Naming of Substances under REACH and CLP, Version 2.1, May 2017.

cc: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review

Diatomaceous Earth History

April 30, 2021 – Scientific Literature Review issued.

September 2021 - the Panel issued an IDA. The additional data needed to determine safety for this cosmetic ingredient are:

- Clarification on the type(s) of Diatomaceous Earth that is used in cosmetic products (i.e., natural, calcined, and/or flux-calcined)

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November - December 2021 – Unpublished data received by CIR staff.

Diatomaceous Earth Data Profile* – March 2022 – Christina Burnett																															
				Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	log P/log K_{ow}	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Diatomaceous Earth	X	X	X			X		X	X		X	X			X			X	X		X		X	X	X	X	X		X

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

Diatomaceous Earth

Ingredient	CAS #	PubMed	FDA	HPVIS	NIOSH	NTIS	NTP	FEMA	EU	ECHA	ECETOC	SIDS	SCCS	AICIS	FAO	WHO	Web
Diatomaceous Earth	61790-53-2; 68855-54-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	

Search Strategy

PubMed
Diatomaceous Earth = 938 hits, 73 relevant

Diatomaceous Earth toxicity = 75 hits, 30 relevant

Diatomaceous Earth cosmetics = 20 hits, 6 relevant

Diatomaceous Earth dermal = 0 hits

Diatomaceous Earth sensitization – 3 hits, 1 relevant

Search updated January 2022 - 0 new relevant hits.

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)

appropriate qualifiers are used as necessary
search results are reviewed to identify relevant documents

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://iaspub.epa.gov/oppthpv/public_search.html_page
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
  - technical reports search page: https://ntrl.ntis.gov/NTRL/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/

- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

SEPTEMBER 2021 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito's Team Meeting – September 13, 2021

DR. BELSITO: Boy, you got some good ones here, Christina.

MS. BURNETT: You know it.

DR. BELSITO: Okay. This is the first time we're looking at this. The SLR was released on April 30. Concentration of use survey, Council provided some dermal irritation, sensitization, and phototox. Comments from the Council were addressed. We also got some comments from the International Diatomite Producers Association, which are in here. And it's used in 116 formulations. Leave-on products and about a quarter of rinse-off paste masks. They have the 2019 concentration of use data to 5 percent face and neck, 20 percent hair, 62.2 in rinse offs. So that's what we got. So, under chemical properties, Christina, it just talks about the variety of shapes from which it's formed. Do we have any idea? I'm thinking in terms of inhalation issues.

MS. BURNETT: I'm sorry, can you repeat that again?

DR. BELSITO: So, under chemical properties for particle size distribution, medium and fine grade materials less than 90 microns. Do we have a lower limit? I mean, so --

MS. BURNETT: Right. Let me see if I can pull up that reference. Looking from ECHA data. It's going to take me a few minutes to figure that out.

DR. BELSITO: Okay, well, so the next thing is, on PDF page 11, we're going to get into the silica issue. It says in commercial products a large proportion of the amorphous silica in Diatomaceous Earth is converted into crystalline form during thermal processing, up to 40 to 60 percent.

MS. BURNETT: Correct.

DR. BELSITO: So, how are we going to deal with that, team members?

MS. BURNETT: We have a hand raised.

DR. BELSITO: Who has raised their hand?

MS. BURNETT: Mr. Ellis.

DR. BELSITO: Okay, can we allow him in?

MS. FIUME: He should be able to unmute his mic and speak. He is the person that sent us the IDPA information.

DR. BELSITO: Okay.

MR. ELLIS: Okay, can you hear me?

DR. BELSITO: Yes.

MS. BURNETT: Yes.

MR. ELLIS: Okay, great. Well, thank you, I realize that you're typically operating as the Expert Panel, but I had some communications with the CIR staff prior to this meeting to try to add some clarification that may be helpful to you as you evaluate Diatomaceous Earth.

I'm Mark Ellis, I am the executive director of the International Diatomite Producers Association, or IDPA, and we represent the major global manufacturers of Diatomaceous Earth. We became aware of what the Expert Panel and CIR were doing through our due diligence and learned about the scientific literature review. We discussed positions and we developed the comments that were filed that were shared with you.

And part of that due diligence looked at your consideration of the silicates because crystalline silica is an issue for Diatomaceous Earth, but part of what you need to appreciate is that there are different grades of Diatomaceous Earth. There's a natural form that's basically just dried and then there are calcined and flux-calcined grades that are thermally treated and in that thermal treatment the amorphous silica is converted to crystalline silica. And there are higher concentrations of crystalline silica in both calcined and flux-calcined Diatomaceous Earth.

The issue really comes down to how the CIR approaches some evaluations of chemical substances used in cosmetics. My understanding is that part of what staff refers to initially is the International Cosmetic Ingredient Dictionary and Handbook. And that staff is pretty much restricted to address what is in that dictionary and handbook.

And CIR staff shared with me the excerpt for Diatomaceous Earth, and it lists two chemical abstract service registry numbers. One is for natural Diatomaceous Earth, and the other one is for flux-calcined Diatomaceous Earth. And the general description also raises a question of calcined versus non-calcined, but they are wholly different animals in terms of their crystalline silica

content. And our members would prefer that CIR focus its scientific literature review, its draft report, or any tentative report moving forward solely on natural DE because it's essentially amorphous silica with very low, if any, crystalline silica content.

I'm going to offer another observation too because I think it's somewhat relevant to the discussion that you've had on the silicates. I'm a lawyer, but I've worked in the area of industrial minerals for about 40 years in a variety of settings. And a lot of it has focused in on occupational safety and health, so I have a lawyer's appreciation for toxicology.

One of the things that is difficult to appreciate is that these are not reagent-grade chemicals that you're dealing with. They have impurities in them because they are natural, so you may look at a chemical abstract service number and say that's what it is, but in reality what you have to look at in the evaluations you potentially are doing are, what is in the -- I used to call it the Material Safety Datasheet. It's the safety datasheet that lists the components in the product that the manufacturer of the cosmetic is using.

So, let's just say, if they list DE on there, and they have a chemical abstract service number for flux-calcined, it is going to have a much higher silica content than the natural DE. But there will also be other contaminates, potentially clays, and those aren't accounted for in the chemical abstract service number. They're only going to be revealed in the safety datasheet.

And I think that's part of what the issue you're dealing with here on the silicates, is that you're looking at one-tenth of one percent, which we know is the limit for listing a carcinogen on a safety datasheet. But it gets into limits of detections, limits of quantification as opposed to what's actually in the substance.

So, our sense of it is, is if you can depart from the strictures of that Cosmetic Ingredient Dictionary and Handbook and focus exclusively on natural DE, that your evaluation of the safety of DE in cosmetics will be tremendously improved. So I'll stop there.

DR. LIEBLER: Well, Mark, this is very helpful and your memo, which we reviewed when we received this draft report was also very helpful, particularly your offer to provide us additional information on the characterization of the Diatomaceous Earth ingredients that may be used in cosmetics. And I think that that would be very helpful to us. Some more information, more data would be really helpful to us.

MR. ELLIS: Well, we're interested in maintaining this dialogue with CIR to try to get a safe use determination for natural DE. I think part of it is that we're coming to you as outsiders without an appreciation for your procedures and policies. You know, I know enough to jump in and try to read what's there and respond to it, but much of the data, as I understand it, is coming from the manufacturers of the cosmetics themselves. And it's difficult for us to parse out from our members how much goes into cosmetics. I could tell you it's a small amount.

The principle use of Diatomaceous Earth is used in filtration and all of the processing that we do typically is geared towards making sure that beer that goes through it, wine that goes through it, oils that go through it are filtered appropriately. But it has many other uses because of its unique micro and macro characteristics as being the skeletal remains of these diatoms. We're happy to do what we can, but it's not a chief part of what we do, so I can't promise that we'll do everything that you want.

DR. LIEBLER: Well, Mark, we normally get nothing. We always get almost nothing from industry, so what you're offering to us is much more than that. And I realize there's some uncertainties about specifically defining which of these go into cosmetics.

On the other hand, if you can provide us information on the -- you know, if the overwhelming bulk of the production goes to DEs that are used in filtration for food and beverage, that's relevant to our thinking about this, even if you don't have hard numbers on what are the steps for cosmetic ingredients.

And the most useful thing, as I see it, is going to be a definition of the differences between the manufacturing processes that are used, the flux-calcined and the, sort of, natural that you mentioned, is briefly mentioned in our current draft report, but I think we'd benefit from better characterization that we can get from you and your team.

So, normally, the Expert Panel doesn't directly communicate with industry. It's CIR and the Council, or the Council communicates with industry, gathers data, passes it on to the CIR, and then the Expert Panel evaluates that. So that's the normal process. And what you're offering will be very helpful in that process.

MR. ELLIS: Okay, and we can work through Council to provide that information to CIR, and through CIR to the Expert Panel. Part of it is just determining what information you seek and what we are able to provide. But we do have a board meeting coming up in November, which is before your December meeting. Hopefully we'll be able to turn some of that information around and get it to you.

I plan on making a similar statement into the other breakout session. That was one of the things that was suggested because of how you're approaching your evaluation of these different chemical substances. So I hopefully will share this same kind of discussion with Dr. Cohen's group.

DR. LIEBLER: Don, you're muted.

DR. BELSITO: So I guess the major issue, from what I'm hearing, is the naturally sourced we're really not worried about crystalline silica, but with calcined and calcined flux that could be an issue, but we don't know what kind of Diatomaceous Earth is used as a cosmetic ingredient.

MR. ELLIS: Right, and I'm assuming that the only reason that flux-calcined and natural are in the same report is that somebody reported using that chemical abstract service number for flux-calcined, and we would counsel that that probably is not appropriate. We would suggest that they use natural DE.

DR. LIEBLER: At the time the definition was created in the dictionary, the flux-calcined got in there through whatever, you know, whatever source. That and the natural were the two that were in the dictionary. That's what we're bound to pursue because it's in the dictionary. So that's our starting point.

MR. ELLIS: Right.

DR. LIEBLER: If --

MR. ELLIS: And as I understand it, Dr. Heldreth said that, you know, you have some latitude as to what you consider and where staff is -- I'm going to use the word -- bound to address what's in the dictionary in the first instance that you can limit your evaluations to part of that if you feel is appropriate.

DR. LIEBLER: That's correct.

DR. BELSITO: Or a mixed conclusion.

DR. LIEBLER: Right, if need be, that's also correct. We get into these mixed conclusion situations, Mark, when we just don't have enough data to exclude. For example, if we have a significant amount of information that all leans towards natural, not flux-calcined in cosmetic products, then we can, in the discussion of our report, explain why we focused on the naturals, and that's what our conclusion is based on.

But, if we had insufficient information, then no. Then we kind of have to consider both as possibilities, and then we have to craft our conclusions accordingly based on the data. So more information helps us make a more informed assessment.

MR. ELLIS: Yep, I understand. Thank you.

DR. SNYDER: Mark, I have one question. So you mentioned the one-tenth of one percent as a requirement for listing as a potential carcinogen on any product. Where does that apply across? Would that apply to cosmetics?

MR. ELLIS: Well, it's part of the globally harmonized system of hazard communication. And I typically operate in the occupational realm rather than in the consumer product realm. But, typically, in a safety datasheet that would be required by OSHA, you would have to list as a carcinogen anything that has one-tenth of one percent of something that's been identified by IRAC in their monographs.

But, for instance, crystalline silica is identified as a group one carcinogen, which is a known human carcinogen. And natural DE is identified as a group three, which is unable to classify, and that's because there's limited evidence in humans, limited evidence in animals.

So, you know, that one-tenth of one percent is an artificial cut point, if you will. It's probably not toxicologically related.

I mean, I work with much higher concentrations of crystalline silica in an occupational setting and people that mine, people that work on construction sites, people that work in foundries, lifeguards on beaches, we all have crystalline silica in our lungs. And that's just because it's ubiquitous in the environment. But it probably has no toxicological effect because the body, over time, has developed mechanisms to deal with it, where the macrophages attack the crystalline silica and prevent fibrosis from happening. It's only when those biological responses are overwhelmed that you start to see the toxicological effects.

DR. ANSELL: The tenth of a percent is a threshold for disclosure.

MR. ELLIS: Yes.

DR. ANSELL: It isn't tied to --

MR. ELLIS: That's exactly it.

DR. ANSELL: -- any toxic event. Anything over one percent has to be disclosed, except for carcinogens, where the threshold is one-tenth of a percent.

DR. LIEBLER: Don, you're muted again.

DR. BELSITO: We also have the repeated dose toxicity study for inhalation on PDF page 12, specifically looking at flux-calcined Diatomaceous Earth.

DR. SNYDER: Yeah, that's all tabulated on Table 3, Don, on pages 18 to 21. And I read through all of those, and, to Mark's point, in many of those studies the only finding was aggregates sub-alveloar macrophages. Which would suggest that that is

reaching the lungs and it's being dealt with. It's just a matter of what levels exceed the capacity of the macrophages to engulf it and not let it drive any toxicity.

MR. ELLIS: Yeah, you mentioned read across earlier on in your discussion, and this is not a situation where a read across between flux-calcined DE and natural DE is appropriate.

DR. LIEBLER: We do not use read across for anything inorganic, Mark.

MR. ELLIS: Oh, okay. Thank you. That's something I didn't know.

DR. LIEBLER: Yeah. Sure.

DR. BELSITO: So, Mike, and to get back to the repeated dose tox study, would that clear the use of calcined Diatomaceous Earth and flux-calcined Diatomaceous Earth in respirable cosmetic products?

MR. ELLIS: I think that would be relevant. Again, I'm a lawyer, I'm not a toxicologist. But, you know, it seems to me that if you're looking at a repeat exposure type situation, that's something that ECHA, for instance, has evaluated and has it as a (inaudible) for inhalation. That's for the flux-calcined, so I just don't think it's appropriate to take that same moniker and attach it to natural DE.

DR. LIEBLER: So, Mark, just to be clear, if I was operating Ajax Cosmetic Company and I wanted to make a product that I wanted to use Diatomaceous Earth in, I could go to order Diatomaceous Earth and I would be presented with options of flux-calcined and natural and so forth, is that correct?

MR. ELLIS: That's true and it depends on who you buy it from because, if you buy it from a manufacturer, a manufacturer will typically work with a customer to try to meet a product that serves their specification. But, if they're buying it through a distributor, that product's already in commerce, and they may not have that same technical expertise that the manufacturer themselves might have.

DR. LIEBLER: Yeah, so in other words, there is the opportunity to have a selection based on properties, whether you customize it or wherever you get it, at least it's defined.

MR. ELLIS: Yes. I mean, you have a choice.

DR. LIEBLER: And the reason, where I'm going with this, I think if there's a substantial difference in the composition of flux-calcined versus natural and we can establish the degree to which natural versus flux-calcined is probably used in cosmetic ingredients, then I think we can deal with this. If the flux-calcined is not really used, then we don't need to be trying to assess the toxicity of flux-calcined.

MR. ELLIS: I think that's correct. The consultations that we've had with our members seems to be uniformly that they're only providing natural DE for cosmetic applications.

DR. LIEBLER: Yeah. I mean, anything we could get that documents that would be very helpful.

MR. ELLIS: Okay. Very good. I'm making a note there. Well, thank you again. I appreciate it.

DR. LIEBLER: Yeah, this is a big help. We appreciate it too, Mark, thank you.

DR. BELSITO: Thank you, Mark. Okay. I think that was really very helpful. To go back to the document, just --

MS. BURNETT: I was able to find the different particle size distribution information if you'd still like that.

DR. BELSITO: Yeah, sure, I think that should be incorporated too, obviously, but what was it, Christina?

MS. BURNETT: Okay. So you would like it for under ten microns?

DR. BELSITO: Yes.

MS. BURNETT: Coarse, approximately four percent or below is at ten microns. For the fine grade, it would be about 50 percent or less.

DR. LIEBLER: Yeah.

MS. BURNETT: I can type that up and put it in a table to help show that.

DR. BELSITO: But I still think that the repeat dose inhalation covers that, do we not?

DR. LIEBLER: What do you mean by that, Don?

DR. BELSITO: Well, I mean, so when Christina incorporates that, there's obviously going to be respirable particles.

DR. LIEBLER: Right.

DR. BELSITO: We know that the flux-calcined Diatomaceous Earth is going to contain a larger amount of crystalline silica, and we have that repeat inhalation dose toxicity study where there was no fibrosis over 2.5 years, so I think that covers the inhalation, correct?

DR. LIEBLER: I think so.

DR. BELSITO: Okay. Paul, do you agree?

DR. LIEBLER: Paul's muted.

DR. SNYDER: Sorry. The one study there, the hundred percent flux-calcined, where there was no observable effect concentration could not be determined. I do agree that one big study where they went out two and a half years and there was nothing, but I was trying to see at what concentration that was at. There's a one and a half year (audio gap).

DR. BELSITO: Well, they have a guinea pig study that was 1.5 years and --

DR. SNYDER: The dog study was two and a half years.

DR. BELSITO: Right.

DR. SNYDER: Yeah.

DR. BELSITO: And the particle range in the guinea pig study was 0.45 microns to greater than 10 microns, which I think is pretty good. I mean, you have multiple different species. Okay. And then the repro study, we don't have any developmental or repro --

DR. SNYDER: No, no DART. We have no DART, yeah.

DR. BELSITO: So do we need a 28-day dermal for absorption? I mean, we really can't go with GRAS status, can we? We don't know that all Diatomaceous Earth is used to filter wine, beer, et cetera.

DR. LIEBLER: I don't think we have any information that would suggest that these are absorbed. I mean, the little toxicokinetics suggests no absorption in the -- and that's in a dietary study. Livers, kidneys, spleens. Analyzed for residual silica, no difference between treated and controls. I can't imagine that the constituents of Diatomaceous Earth would be dermally absorbed.

DR. BELSITO: Right. So no oral absorption.

DR. LIEBLER: Yeah, no oral absorption, which would be easier.

DR. BELSITO: Right.

DR. LIEBLER: You know, we don't even have that. I mean, there's none of that. So I don't think a 28-day dermal is a reasonable request.

DR. BELSITO: Okay. So, in the discussion, we should point out that we don't have DART data, but there's no oral absorption making dermal absorption unlikely, or something to that affect?

DR. LIEBLER: Correct.

DR. BELSITO: Okay. And, then, just address, well, the subcutaneous exposure is really not pertinent to cosmetic use, so do we need to discuss that, the intraperitoneal too?

DR. SNYDER: No, those aren't relevant to cosmetic use.

DR. LIEBLER: Yeah. And I would point out under the non-cosmetic use, it says Diatomaceous Earth is GRAS as a filtering aid in food and beverages, and it's also, GRAS is the substance migrating to food from paper and paperboard products. In other words, if I read that correctly, it's understood that that could get into food from paper and paperboard products, and it's considered GRAS in that context. So I think that mitigates the systemic toxicity concerns.

DR. BELSITO: Right, okay, so then I can go into the discussion and -- then I just had a question, Christina, on the dermal irritation and sensitization studies. It says a cosmetic product containing 9 to 11 percent Diatomaceous Earth was not sensitizing in HRIPT, nor was it phototoxic in a human single application study, but, per our concentration of use table, I thought it was 0.9 to 1.1 percent.

MS. BURNETT: Yes, this data that was presented to us was a little tricky. Let me see if I can find the -- we were given a statement saying that this one trade name contains 9 to 11 percent and then they presented data afterwards using that trade name. Whether they reported it to the Council is how they use it. I know it doesn't match up with what the Council provided us in the survey, but I'm not sure how I can rectify that.

But on PDF page 33 is where we're giving a statement saying what these two trade names contain. So it could be from that they get diluted down into the formulation, but I don't know.

DR. BELSITO: Okay, and the max leave-on is 20 percent, but, I mean, I'm okay with the HRIPT at 9 to 11 percent. So we're going to have to have the heavy metals boilerplate and the discussion concerning calcined and flux-calcined and crystalline contaminants, but the chronic respiratory tox studies clear that. No repro or developmental, but no oral absorption, dermal absorption, not likely. Do not have the highest, or don't have data on sensitization at the highest, but I don't think we need it. So, for a conclusion, I would say safe as used, but, Dan, Paul?

DR. LIEBLER: I agree.

DR. SNYDER: I agree.

DR. BELSITO: Okay. Any other comments?

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DR. COHEN: Okay. May I move on to Diatomaceous Earth?

MS. BURNETT: Sure.

DR. COHEN: Okay. This is a draft report. This assessment is for a single ingredient, Diatomaceous Earth. It's the first time we're reviewing it. It's used as an abrasive absorbent, anti-caking agent, bulking agent, and opacifying agent in cosmetics.

We have frequency of use reported at 116 products and a max use of 5 percent on face and neck, and up to 20 percent in hair tonics and dressing at 62 percent in rinse off products, a paste mask.

It's also GRAS, as a substance, migrating to food from paper and paper board products. There's a discussion of crystalline silica content of 0.1 to 4 percent. We have some irritancy data on it, as well, and an HRIPT up to 11 percent.

I just had one question on PDF 24. It said, "A cosmetic formulation containing 0.9 to 1.1 percent Diatomaceous Earth." And it referenced 44 on PDF 29 which said 9 to 11 percent. I just wasn't sure if I was reading that wrong.

MS. BURNETT: I'm sorry. You broke up from me there.

DR. COHEN: On PDF 24, it said, "A cosmetic formulation containing 0.9 to 1.1 percent Diatomaceous Earth."

MS. BURNETT: Yes.

DR. COHEN: And it referenced 44 on PDF 29 that said 9 to 11 percent. And I wasn't sure if they were two separate things or the same thing off by a decimal point.

MS. BURNETT: I believe there's a dilution there.

DR. COHEN: Oh. Okay.

MS. BURNETT: Let me look which one that is, though.

DR. COHEN: So the question also here is, are we going to have a silicate discussion with this?

DR. PETERSON: Yeah, I think we have to because the silicate can be pretty high in some of these. If you look at the composition --

DR. SHANK: Yeah.

DR. PETERSON: -- it's the presence of the crystal and silica can be pretty high in some of the products. So I didn't have any data needs. That was the highlight is that there was a possible presence -- there is presence of crystalline silica which is going to be a concern for some of the products that are inhaled.

And that the inhalation studies, when they were done inhalation, they didn't see fibrosis, but when there was the intratracheal installation, there was evidence of lung issues. So I think we need to have a statement about considerations.

MS. BURNETT: We do have a hand raised. Before that, though, Dr. Cohen, that was a ten percent dilution on that in that table.

DR. COHEN: So it's one-tenth. Okay.

MS. BURNETT: Yes.

DR. COHEN: Thank you. Thank you.

MS. BURNETT: No problem. And Mark Ellis has his hand raised.

DR. HELDRETH: Yes, Mark is the executive director of the International Diatomite Producers Association, so he may have some insight about these ingredients.

DR. COHEN: Please proceed.

MR. ELLIS: Okay. Great. Thank you, Dr. Cohen. Let me please introduce myself. I'm Mark Ellis, I'm the Executive Director of the International Diatomite Producers Association or IDPA. We represent the major global manufacturers of Diatomaceous Earth products.

When we were made aware that the CIR was considering Diatomaceous Earth, we brought our members together doing due diligence, and we discussed difference positions and filed comments on this. And those have been part of the material that have been shared with you.

One of the things that we were aware of in that due diligence, was that CIR has been looking at silicates and the question of crystalline silica. And that really is an issue with Diatomaceous Earth because Diatomaceous Earth is more than just one thing. It is not a chemical reagent. It is a naturally occurring product that, in processing, is done in three different grades.

Natural DE is just lightly dried, but there's no thermal properties really attached to it, whereas calcine DE and flux-calcined DE purposely are calcined at higher temperatures. And, in the process of doing that, the amorphous silica is converted to crystalline silica. And it's done for a variety of reasons mostly linked to the principle purpose of Diatomaceous Earth which is as a filtration product.

But when we filed our comments on the scientific literature review, we made the point that we felt that the CIR should focus exclusively on natural DE because of its amorphous silica content rather than the calcined or flux-calcined.

In subsequent communications with Dr. Heldreth, we learned that, when the CIR staff approaches a chemical substance, they make reference to the *International Cosmetic Ingredient Dictionary and Handbook.* And that as they present the scientific literature reviewed view and the draft report, they have to address what's listed in that dictionary and handbook.

And that dictionary and handbook, Dr. Heldreth shared with me the excerpt there. And it spoke to not only natural DE with a chemical abstract service registry number, but to flux-calcined DE with a chemical abstract registry number. And then there's also in the definition a discussion of natural versus calcined.

And we think that this is an important point because it really confuses the issue to talk about Diatomaceous Earth as one substance. And, particularly, if we're going to be talking about the safe use of DE in cosmetic products, our members believe that you need to be focused in on natural DE and not on the higher silica content products.

And, from what I understand from your procedures, you have the ability to address these separate grades as opposed to dealing with them collectively. And I think that might facilitate you moving forward with a draft tentative report on the natural DE, whereas, it may be more problematic for the calcined or flux-calcined.

DR. PETERSON: Do we know which one is used in -- is it primarily the natural one that's used in cosmetics? I mean, is there some statement somewhere?

MR. ELLIS: Apparently, there's not. But what I received anecdotally from my members is that it is the natural DE that's used. And we had some discussion about that in Dr. Belsito's working group, and we'd be happy to talk to you about it, as well.

DR. COHEN: There's a comment in Composition and Impurities, that the crystalline silica content of un-calcined Diatomaceous Earth, is 0.1 to 4 percent. So is uncalcined DE the same as natural DE?

MR. ELLIS: Yes.

DR. COHEN: So is that specific sentence in there inaccurate?

MR. ELLIS: No, it's not. The problem that we're -- it's not a problem; it's a fact. The fact that we're dealing with is that this is a natural product. And a Chemical Abstract Registry number identifies it as being natural Diatomaceous Earth. But that assumes that it's basically a hundred percent pure, and it isn't.

And where you see that differentiation of what really is in the product is not in the Chemical Abstract Service number, but in a safety data sheet that might be produced by a manufacturer that discloses that it's 98 percent natural Diatomaceous Earth and lists the Chemical Abstract Service number. And it may have two percent crystalline silica and so it would list that Chemical Abstract Registry number for the amount of crystalline silica that might be in there.

But there also could be clays and other material that are in that natural deposit.

DR. BERGFELD: Is it forthcoming that something could be generated from your group to officially be included in our documentation?

MR. ELLIS: Yes, we talked about that. And I think a big part of it is determining what is most relevant to your deliberations. I think that part of what would help is to know what Diatomaceous Earth products are being used in cosmetics. And I know that the data that apparently goes into that dictionary and handbook is based on surveys done by the Personal Care Products Council.

I don't know whether we can trace, as producers, what material may be going in to cosmetics, but that would be potentially one thing we could do. If we could demonstrate that the bulk of Diatomaceous Earth going into cosmetics is natural DE, then you may be able to focus on what's really being used as opposed to what's out there as an alternative.

DR. COHEN: So it sounds like the crystalline content of natural DE is going to be the lowest of the three forms you've described, right?

MR. ELLIS: Yes.

DR. COHEN: But even in that situation, it could be up to four percent crystalline silica?

MR. ELLIS: Right. But I'm a lawyer; I'm not a toxicologist. I work in the occupational realm, and I do understand toxicology and epidemiology. You have to think about what the delivered dose is. It really doesn't matter what the percentage might be, although the percentage might cause you to believe that a higher-delivered dose might be there.

But we all have crystalline silica in our lungs. I mean, it's an ubiquitous thing. It's in dirt. It's in sand and dust. And our bodies over millennia have learned to adjust to that. We have different clearance mechanisms. Our macrophages can take that. It's only when the body's defense mechanisms get overwhelmed that we see indications of disease, most typically, silicosis.

But looking at a consumer product, from my perspective as a lawyer working occupationally, the exposures in a consumer product are going to be much less. I mean, California has done safe-use determinations on kitty litter or on flat latex paint. And the amount of silica that consumers might be exposed to in those instances is relatively small. And I might tentatively offer that it probably would be the same in cosmetics.

DR. COHEN: I think our dilemma stems from our silicate discussion, as a whole, right?. I mean, this is an off-shoot of that which is this quandary of taking PELs or occupational exposures or lifetime exposures and producing advice or our opinion on the manufacturing of a product. How do you take lifetime exposures, or exposures that have a time variable in there as they do in occupational medicine. It's over a number of hours per day, per year worked. How do you take that and say, this is how much you could put in a cosmetic agent for personal use? I personally have a hard time figuring that.

MR. ELLIS: Well, you should. And my guess is that there probably has not been a lot of transcription between what is a safe occupational -- or take it conversely -- a hazardous occupational exposure and how that translate to a safe consumer exposure.

There's scaling, obviously, involved. And, in the occupational setting, it's typically safe to work for a 40-hour work week for a 40-year working lifetime. So people like miners, people that work in foundries, those kind of people are exposed to crystalline silica at much higher rates than any consumer would be. And those occupational exposure limits tend to be protective.

DR. COHEN: Can I ask your opinion? Were you attending to the meeting when we spoke about silicates and our conclusion about the detection about crystalline silicates?

MR. ELLIS: I didn't attend the last meeting, but I did review the material on silicates. And I mentioned this point to the other working group. I think that you're confronted with talking about apples and oranges in many contexts here. This notion of one-tenth of one percent or one percent, those typically are related to the presence of a carcinogen.

Let's just take the case of crystalline silica. The International Agency for Research on Cancer has identified that as a Group 1 carcinogen, a known human carcinogen. But IARC also has looked at natural Diatomaceous Earth and it rates it as a Group 3, insufficient evidence in animals and insufficient evidence in humans. So it's not classifiable.

I think that what everybody focuses on -- and we do, too. If you look at those one-tenth percent or one percent numbers, they relate to specifically addressing the presence of a carcinogen and inhalation route of exposure.

And, again, a working lifetime because that's what the globally harmonized system classification deals with. But as you're dealing with consumer products, how do you get to what the delivered dose is and whether or not the body's mechanisms are sufficiently active to overcome that insult?

DR. COHEN: Yes, you've summarized the issues we've gone through on the silicates and how we're trying to understand Diatomaceous Earth.

DR. BERGFELD: Well, it sounds to me like we've been directed to using only the natural Diatomaceous, which has the lowest silicon. And discussing the other two as probably should not be included in cosmetic products until further evidence is presented.

DR. COHEN: So I think for purposes of having aligned messages. Two chemicals ago, we were talking about crystalline silica, and now we're talking about crystalline silica again. We don't quite have evidence that just uncalcined DE is used in cosmetics. We think maybe that's possible, but we don't know that for sure. And I think, Wilma, your comment about having that in the discussion is important.

And we have max use of 5 percent in a face and neck product, 20 percent in a hair tonic and dressing. And then we have this rinse off face paste. So that's a very interesting issue of 62 percent DE applied to the face to dry, right, perhaps, and then being in close proximity to the nose and mouth as it's drying. And then you rinse it off which is probably perhaps a lower risk.

Where do we align the level of detection of crystalline silica into this assessment?

MR. ELLIS: Well, I think that IARC specifically looks at crystalline silica as a Group 1 lung carcinogen. So inhalation is really the route of exposure that you would have to work with. But, obviously, something that's wet is not biologically available in that situation, so you probably can move away from concerns there.

I do think that the pursing out of this 0.1 percent and 1 percent is problematic because it doesn't get to the issue of delivered doses. It's more a limit of quantification or a limit of detection as opposed to a determination of what the dose is.

I think that one of the things that I will try to do -- because we are interested in working with CIR to get a safe-use determination from natural DE. I will try to work with our members to determine, sales into the cosmetic market, to what extent are they natural DE, to what extent are they calcined and to what extent they are flux-calcined?

And what I would propose to do is to communicate this information to the Personal Care Products Council, and I'll copy Dr. Heldreth on this. But the notion would be then that PCPC would share that information with CIR and CIR would share with the expert panel.

DR. COHEN: Tom, thoughts?

DR. SLAGA: Should we wait for that? Table this? Or what are we --

DR. COHEN: I'm a little stuck on -- let's say it comes back and it's natural DE -- it's all natural DE in cosmetics, right?

DR. SLAGA: Right.

DR. COHEN: We have a sentence in composition and impurities that the uncalcined is up to four percent crystalline silica, right?

Now, that's just the uncalcined DE. It gets diluted down once it's in products, you know, down 20 times. But, in this face mask, it's two-thirds DE. It's basically a DE mask. That's applied and then I don't know if it's dried or rinsed off before it dries. I just don't know.

How do we deal with that four percent crystalline silica issue even under the best of circumstances? And we don't have to make a final decision, here, but where are we generally going to work with this?

DR. PETERSON: So the problem is inhalation. So if you put a mask on, it's wet, you dry it off. There's not that much that you would necessarily inhale from putting on a mask unless it's sprayed on, but mostly you don't spray on a mask. I think you have to worry about the products that are inhaled.

DR. HELDRETH: There's also a 20 percent max concentration of use incidental inhalation sprays.

DR. COHEN: So that would get us down to 1 percent crystalline if we use the max of 4.8 percent. If we use the max of 4 percent crystalline.

MS. BURNETT: It looks like we have another hand raised.

DR. COHEN: I can't see who it is. Can you see, Christina?

DR. BERGFELD: Shripal Sharma.

MS. BURNETT: Shripal Sharma?

MR. SHARMA: Yeah. Good afternoon, everyone. My name is Shripal Sharma, and I work with Imerys as Director of Product Stewardship. And we are one of the suppliers of Diatomaceous Earth that Mark Ellis just mentioned. So I'd like to clarify a couple of issues here for the benefit of this expert panel.

One is that, based on our industry knowledge, we are not aware that any calcined DE or flux-calcined DE are used in cosmetics. We are only aware that only natural DE are used in cosmetics. Again, this is the knowledge -- that's the information that we have based on our own understanding of the market and based on the survey that Mark carried out with ITP companies.

The second point I would like to make is that, even though natural DE may contain some level of natural quartz as crystalline silica up to four percent, not all of those natural DE products are suitable for cosmetics. So, in general information, we produce and sell into various markets natural DE.

And only a fraction, maybe less than one percent of that natural DE goes into cosmetics. And even natural DE, as you say, from zero percent crystalline silica to four percent, based on our understanding, the natural DE going into cosmetics are relatively very low on crystalline silica, not in the range of the four percent, rather, on the lower side.

DR. BERGFELD: How can you document that?

MR. SHARMA: We document that based on the work that we do with our customers who are cosmetic customers, as an example. We work with them to provide them with samples they determine what the specification of the product will be. And, so, we document based on our own testing and the product that goes to the customer.

DR. BERGFELD: So you have a product line that is only cosmetic, is that right? And has certain classifications?

MR. SHARMA: No, we have hundreds of product lines for natural DE. And based on the specification that a customer is looking for, we sell one of those hundred products to those customers. And, based on our testing regime in our plant, we know what that product is and what its composition looks like.

DR. SLAGA: Well, we should be able to get that documentation then. Right?

MR. SHARMA: Yeah, the testing that we carry out in our lab, that's our documentation.

DR. BERGFELD: But the problem I see is who purchases it? Is it the cosmetic industry or others? We're interested in the cosmetic.

MR. SHARMA: Yeah, so, what I'm saying if we know which products are used in cosmetics. And we have the test results for those.

DR. BERGFELD: I'd like to see that.

MR. SHARMA: Okay.

DR. COHEN: Yeah, that would be useful.

DR. HELDRETH: Would that be something we could cite from the document?

MR. ELLIS: I think that there might be an issue there of confidential business information, and I can't speak for Imerys which is one of our member companies, but I know that others might have that concern.

If PCPC or CIR has provisions for receiving data that's confidential business information, we probably can get that information to you.

DR. HELDRETH: Yeah, CIR procedures don't allow for us to receive confidential information. Everything that we receive and the Panel relies on gets published on our website for anybody to see.

Now, you can submit information to the Personal Care Products Council. In the past, I've seen them scrub out company details, but the data needs to still be completely visible so the Panel can make their evaluation.

DR. BERGFELD: Bart, could we get a letter of summary? Just a general summary that is sent to us by the company who is the supplier based on their information without sharing in great detail?

DR. HELDRETH: Yeah, if the Panel feels comfortable with that I see no issue with that, if they're willing to provide such.

DR. COHEN: I think it will be helpful. I still think we need to harmonize our silicate manuscript with this one. So I agree. The method by which it's applied really will speak to risk. So, with the silicates we have, I think, a notation when there's a respiratory risk. When there's a risk of respiratory exposure, this is what we ask for. If there wasn't a respiratory exposure, we didn't really comment on the amount of crystalline silicate. Did I remember that correctly?

DR. BERGFELD: Yes.

DR. HELDRETH: Yeah.

DR. COHEN: So for DE, many of these exposures are -- some of them are not respiratory; some are. And when they are, wouldn't we ask for the level of crystalline silica in the final product? Not the DE itself, but the final product would be less than 0.1 percent crystalline silica.

DR. BERGFELD: That can be done.

MS. BURNETT: Yes, this is a draft report, so this is the first stage. You may issue an insufficient data notice with whatever needs you would like. So, if that is a need -- if you would like the Council, you know, you can ask the Council to ask their members about the calcined versus non-calcined. You know, what they use in their products. You can do that, too.

DR. COHEN: Yes, that was one of the IDA questions, the use of uncalcined versus calcined or flux-calcined DE in cosmetics.

DR. SHANK: The silicate report puts the limit on the silicate as less than 0.1 percent in raw material, not in the final formulation. Or it says, "Or if there is repeat dose inhalation data, but there is no adverse effect."

DR. COHEN: Right, but the silicate is the target chemical of that report. This is a contaminant or a component of a different thing, right? So the silicates are a component of the DE. That other report is purely for silicates.

DR. SHANK: But, as a raw material not as an ingredient.

DR. BERGFELD: Final formulation.

DR. SHANK: What the conclusion says that's a raw material not in the formula.

DR. COHEN: So, Ron, you're suggesting this raw material should have less than 0.1 percent crystalline silica in it?

DR. SHANK: Yes, that's what we said. But, the silicate report, the 0.1 percent is based on limited detection.

DR. BERGFELD: That's a good route to go.

DR. COHEN: It's the logical route to go, right, because it's the same day we're talking about this issue, right?

DR. BERGFELD: I guess so. Yeah, consistency.

DR. COHEN: From the industry, could you comment on that kind of conclusion just so we have some perspective?

MR. ELLIS: I'll take a shot at it. One of the things that I did most recently was I served as president of the Industrial Minerals Association North America, and I did that for 17 years. And I'm moving towards retirement, which is not coming soon enough. But, again, I have a 4-year career working as a lawyer but working principally in the area of occupational safety and health.

And I've worked with toxicologists and epidemiologists. And I'm convinced that you can use any product safely including nuclear radiation or coal if you use it wisely and use it prudently and you take precautions in how you use it. And I think that's part of the problem that we're dealing with here with crystalline silicate. I don't know how you deal with anything else that's been identified by IARC as a carcinogen. Because now you're translating to a strict number which is -- I hate to say it -- I believe it's arbitrary. One-tenth of one percent? It's something, as someone else mentioned, you can quantitate.

But as a toxicologist or medical doctors, you know the doses that poison, so how much is likely to cause an adverse reaction in a human? Not symptomatic, but I'm saying disease. And I think that the numbers we're talking about here are infinitesimally small compared with what you deal with in the occupational setting.

And I know that there's a precautionary principle, and that you're dealing with a consumer product. There may be certain reservations about what may be a safe exposure, but I do think that the literature on occupational exposure is a guide to take a look at what consumer exposures might be.

Again, translating is another issue I can't touch, but I think that when we're dealing with this one-tenth of one percent or one percent, those are really arbitrary numbers that don't relate to a delivered dose that may have anything to do with an adverse effect.

DR. COHEN: I fundamentally agree and understand regarding your comments. And, again, with occupational exposure limits, they're contextualized with time, right, time and place of exposure. We don't have that here. And one other thing that sort of resonates with me -- and I'm not sure -- but I don't recall ever seeing a safe dose of crystalline silica. So we're stuck between a dose that doesn't cause any demonstrative clinical disease and some other dose.

I'd ask our team, Tom, Ron, what's the safe exposure to crystalline silica?

DR. SHANK: We don't know.

DR. SLAGA: That's right. We don't know.

DR. SHANK: That's the problem.

MR. ELLIS: So take hydrogen fluoride as an example. That is a chemical that I would not want to play with. And small amounts can be fatal. You don't find that with crystalline silica. You have a long latency period. The body has clearance mechanisms that address most exposures that you have every day. But hydrogen fluoride is a whole difference animal.

DR. COHEN: I think it's a lot for us to contemplate. I think we're issuing an IDA at this point. And, Ron, I don't think we have sensitization data on max use or anything close to that, right? Christina, it was about 1 percent, 0.9 to 1.1 percent in the HRIPT? Because it was a dilution in there? Or is it 11 percent? Table 5 --

MS. BURNETT: It's a dilution. It was 10 percent up to 11 percent.

DR. COHEN: So --

MS. BURNETT: So then that would be 1.1 percent.

DR. COHEN: Yeah, so we're at 1.1 percent for the HRIPT, and we have max uses of 20 to 60 percent.

DR. SHANK: Twenty.

DR. COHEN: Well, there's a max with 60 percent, Ron.

MS. BURNETT: That's a rinse off. Do you want the max rinse off use or the max leave on use?

DR. COHEN: What's the max leave on use again?

DR. SHANK: Twenty percent.

DR. COHEN: Twenty percent.

MS. BURNETT: Right.

DR. COHEN: You know what's interesting? What then constitutes a max? So it's sort of in between. I look at rinse off products as shampoos, conditioners, soaps that go on and go off. What if you leave a mask on for three hours? Or six hours? Or overnight? Is that a rinse off product or a leave on product? I'm not quite sure, right? It's a provocative question, but at least -- all right, say 20 percent. We're off by a factor of 20 on that. So we need sensitization on max use, right.

DR. SHANK: Yes.

DR. COHEN: What else do we need?

DR. SHANK: Should we drop the calcined Diatomaceous Earth from the report?

DR. COHEN: There's only one ingredient in the safety assessment. But, apparently, there's methods of manufacturing that are different. So would we not put that in a discussion?

MS. BURNETT: Do you want industry to clarify?

DR. PETERSON: Yes.

MS. BURNETT: You want something like a memo or something that details what their suppliers use? Their members?

DR. BERGFELD: Very important, yes.

DR. PETERSON: And then I think in the discussion we can say that we wouldn't support the use of these other -- the natural one is going to be the safest.

MS. BURNETT: Would you like them to detail their impurities? Or do you think what we have is sufficient based on what I found?

DR. COHEN: If this data that is different from this, it would be very helpful.

MR. ELLIS: Okay. Dr. Cohen, I just want to thank you and the expert panel for allowing me to make those remarks.

DR. COHEN: We appreciate them. They were very valuable in helping us get through this. Thank you.

From the team, any further comments? Wilma, any?

DR. BERGFELD: I didn't hear. Is it Mike? Did he say he would give us that memo? Mark. It's Mark Ellis. Yeah, Mark.

MR. ELLIS: I think that I'm a little uncertain as to what that memo might say, so perhaps, doctor, after the discussion tomorrow in the plenary session, that could be narrowed down.

DR. BERGFELD: Thank you.

DR. SHANK: Okay.

DR. COHEN: Any further comments from the team before we move on? Okay.

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DR. COHEN: Yes, this was a source of considerable time and effort and discussion. So this is Diatomaceous Earth, which is a draft report, and it's the first time we're reviewing it, and the assessment is for this one ingredient. It's used as an abrasive, absorbent, anticaking agent, bulking agent, and opacifying agent in cosmetics. We have max use of five percent in face and neck care products, 20 percent in haircare products, and 62 percent in a rinse-off paste mask. And we have frequency of use reported. Diatomaceous Earth is also GRAS, as a substance migrating to food from paper and paperboard products.

Our group issued an insufficient data announcement with the request for clarification of the method of manufacturing for the three major types of DE, namely natural DE calcine and flux-calcine. Particularly since their crystalline silica content are different, we'd also like further information about the disposition of those three types as they relate to use in cosmetics.

We have irritation data but we wanted sensitization data at max use for a leave-on product. We also are faced with the information that even the uncalcined Diatomaceous Earth has a crystalline silica content of up to four percent. So, we couldn't help but interlace the conversation we had about silica earlier. That's the motion right now.

DR. BERGFELD: And it's an insufficient data announcement motion, correct?

DR. COHEN: It is.

DR. BERGFELD: Okay. Don?

DR. BELSITO: Yeah, so we had a slightly different take on this. And, we certainly appreciate, you know, the Cohen team's approach. We thought that we could potentially go with a safe as used conclusion and in the discussion limit heavy metals, crystalline contaminants, and that its GRAS status cleared systemic toxicity endpoints. We recognize that we didn't have sensitization at the highest leave-on of 20 percent, but again there's nothing in these ingredients that really would be sensitizers.

DR. LIEBLER: Well, Don, the only thing that didn't get highlighted in our discussion yesterday is this issue of the uncalcined Diatomaceous Earth having up to four percent crystalline silica. You know, it was right there in front of me and I didn't really flag it. That becomes then the same issue for incidental inhalation as with the silicates. And that's the only problem, other than that Diatomaceous Earth is devoid of systemic tox. So, I agree with David and his team that that's an issue we need to address.

DR. BELSITO: Okay.

DR. SNYDER: But I thought we learned yesterday that only natural Diatomaceous Earth is used. Those other two forms are not used in cosmetics so this would be a little bit like the silicates and we would say this report is only dealing with the natural Diatomaceous Earth. And it would have a similar type of discussion regarding the crystalline silica. And it would be expected that the flux and the calcinate would not be used in cosmetics and because of the presence of crystalline silica.

DR. LIEBLER: Well, but they --

DR. PETERSON: And I would add something similar to what's in the silicate that, you know, the expectation is -- because the conversation we had with industry was that they have some ability to manipulate the crystalline silicate that's in the Diatomaceous Earth. And, so, it seems like we could put a similar caveat to this one that we put in the silicate where it has to be formulated such that the crystalline silicate is below -- I forget how we worded it in the silicate, but that seems like it would be appropriate here.

DR. LIEBLER: The thing is with the silicates we came around to not being able to define a safe level of crystalline.

DR. PETERSON: Right, right, and so you come to the same thing here because, you know, you basically have another source of crystalline silicate, so the conclusion should be similar to what it is in the silicates in that there is no safe level of the crystalline silicates that we know of for inhalation. So (audio skip) that caveat.

DR. LIEBLER: Correct. Right.

DR. COHEN: We didn't have certitude that only natural DE was going into cosmetics. We had an assumption, I don't know, did we have that in a report that that was the case? We were sort of reassured, but we wanted more clarification from industry on that. That was part of our IDA.

DR. BERGFELD: I think we asked for a memo.

DR. COHEN: Yeah.

DR. LIEBLER: Yeah, I think that Diatomaceous Earth is only naturally sourced. It's not synthetically generated. And then it's maybe processed by this flux-calcination process for some applications. But it all comes from natural sources. So the unflux-calcined Diatomaceous Earth may have crystalline silica between .1 percent and four percent as it says in our report, and there's the rub.

DR. COHEN: That's exactly the rub, because our last iteration of silica had a .1 percent because that was the level of detection. And, I'm recalling that I think one of the manufacturers reported something like .11 percent. So, if we stick strictly to the last version of the silicate document, then it looks like we're knocking Diatomaceous Earth out of cosmetic use.

DR. LIEBLER: For inhalation?

DR. COHEN: For incidental inhalation.

DR. LIEBLER: Incidental inhalation, yeah.

DR. SNYDER: We're saying the data is insufficient to support safety, yeah.

DR. LIEBLER: Yep.

DR. COHEN: Well, we thought we would get further clarification about method of manufacturing, assurances about where each type of DE processing went where and specifically which one were in the cosmetic industry. And, I agree with Don. I think using that expert interpretation, the risk of sensitization would be low and we have irritation data. So, I would reiterate the IDA for further information on that and see what we get back from the industry.

DR. LIEBLER: This report is in an early stage and we've got the industry trade group very motivated to work with us to help us with our data needs. So I think that's a good place to be for now. So, that'll help us as we go forward.

DR. BERGFELD: So, what is the Belsito group doing now? Dan's going with the suggested conclusion. Don? Paul?

DR. BELSITO: I'm fine.

DR. BERGFELD: Paul?

DR. SNYDER: I'm fine. It's early stage, we're fine.

DR. BERGFELD: Okay. So, we're considering that a second to the Cohen conclusion, correct? It's an IDA.

DR. COHEN: It's an IDA, but I'd like to just restate that the IDA did not include sensitization at max use.

DR. BERGFELD: Okay. Did you want to add that?

DR. COHEN: No, we had it originally and then I think Don's comments and his team were provocative enough to change that motion.

DR. BERGFELD: You can put it in the discussion, though, if need be.

DR. COHEN: Yeah.

DR. BERGFELD: Okay, any other discussion regarding this particular ingredient? Lisa?

MS. BURNETT: Just to clarify for me.

DR. BERGFELD: Okay, Christina?

MS. BURNETT: The data needs are clarification on the method of manufacturing for the three types. And clarification from industry as to what type might be used in cosmetics, and any composition and impurities that can be gathered from that.

DR. COHEN: Yes.

DR. BERGFELD: I think the concentration on crystalline silica is there, need to know.

DR. COHEN: During the conversation asked if there was any additional composition and impurities data that might be brought into the report, if it was available.

MS. BURNETT: Thank you.

DR. BERGFELD: Okay. All right, any other comments, or, Christina, do we need anything else for clarification?

MS. BURNETT: I believe I have the two points that are needed. Thank you.

DR. BERGFELD: Okay. All right, I'll call the question. All those opposed? Abstaining? Unanimous approval of an IDA with the stated needs.

Safety Assessment of Diatomaceous Earth as Used in Cosmetics

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ABBREVIATIONS

BAL	bronchoalveolar lavage
CIR	Cosmetic Ingredient Review
CHO	Chinese hamster ovary
Council	Personal Care Products Council
DART	developmental and reproductive toxicity
Dictionary	*International Cosmetic Ingredient Dictionary and Handbook*
ECHA	European Chemicals Agency
FDA	Food and Drug Administration
GRAS	generally recognized as safe
HET-CAM	chorioallantoic membrane of a fertilized hen's egg
HRIPT	human repeated insult patch test
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life or health
ILO	Intentional Labor Office
LLNA	local lymph node assay
mppcf	million particles per cubic foot
NIOSH	National Institute for Occupational Safety and Health
NMRD	non-malignant respiratory disease
NOAEC	no-observable-adverse-effect-concentration
NR	not reported/none reported
OECD	Organization for Economic Co-operation and Development
OSHA	Occupational Safety and Health Administration
Panel	Expert Panel for Cosmetic Ingredient Safety
PEL	permissible exposure limit
ppm	parts per million
REL	recommended exposure limit
SCOGS	Select Committee on GRAS Substances
SHE	Syrian hamster embryos
SI	stimulation index
SMR	standardized mortality ratio
SWeRF	size-weighted relevant fine fraction
TG	test guideline
TWA	time weighted average
UICC	Union for International Cancer Control
US	United States
VCRP	Voluntary Cosmetic Registration Program

DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of Diatomaceous Earth. It is reported to function as an abrasive, absorbent, anticaking agent, bulking agent, and opacifying agent in cosmetic products. The Panel reviewed the available data to determine the safety of this ingredient. The Panel concluded that…[to be determined].

INTRODUCTION

This assessment reviews the safety of Diatomaceous Earth as used in cosmetic formulations. Diatomaceous Earth is reported to function as an abrasive, absorbent, anticaking agent, bulking agent, and opacifying agent in cosmetics, according to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*).[1]

The Expert Panel for Cosmetic Ingredient Safety (Panel) has reviewed related ingredients. In a report that was finalized in 2019, the Panel concluded that synthetically-manufactured amorphous silica and hydrated silica are safe in the present practices of use and concentration when formulated to be non-irritating.[2] Diatomaceous Earth is considered a natural amorphous form of silica. Synthetically-manufactured amorphous silica and hydrated silica are neither part of this safety assessment, nor are data from those reports included in this assessment; however, the reports on these ingredients are available on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients).

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

Some chemical and toxicological data on Diatomaceous Earth included in this safety assessment were obtained from assessments by the International Agency for Research on Cancer (IARC)[3] and the Agency for Toxic Substances and Disease Registry (ATSDR),[4] as well as from robust summaries of data submitted to the European Chemical Agency (ECHA; listed as Kieselguhr)[5] by companies as part of the REACH chemical registration process. These data summaries are available on the IARC, ATSDR, and ECHA websites, respectively, and when deemed appropriate, information from the summaries has been included in this report.

CHEMISTRY

Definition

Diatomaceous Earth (CAS No.61790-53-2 or 68855-54-9) is defined by the *Dictionary* as a mineral material consisting chiefly of the siliceous frustules and fragments of various species of diatoms, which may or may not be calcined.[1] [A frustule is the cell wall of a diatom]. Natural calcined and uncalcined forms are associated with the CAS No. 61790-53-2 and the flux-calcined form is associated with the CAS No. 68855-54-9.[3,6] The "calcined" form is processed Diatomaceous Earth that is heated to 800 - 1000 ºC to eliminate organic and carbonaceous material.[7] The "flux-calcined" form is Diatomaceous Earth that is heated with the addition of sodium carbonate as a fluxing agent that results in a coarser material. Diatomaceous Earth is considered a natural amorphous form of silica.[3,8]

Diatomaceous Earth is a polymorph of silica, or silicon dioxide.[3,4] Silica may exist in amorphous or crystalline structures. While both forms are made up of silicon-oxygen tetrahedra, crystalline silica is determined by a regular, repeating arrangement of the silicon and oxygen tetrahedra, while the arrangement of bonds in amorphous silica is highly disordered and randomly linked. Silica can be sourced naturally as a mineral, biogenically through diatoms, or it can be synthetically produced. Natural and biogenic forms of amorphous silica include opal, Diatomaceous Earth, silicates and volcanic glass; while natural forms of crystalline silica include quartz, cristobalite, flint, and sandstone.

Chemical Properties

Available chemical properties for Diatomaceous Earth are provided in Table 1. Particle size distributions for Diatomaceous Earth (flux-calcined) for coarse, medium, and fine-grade materials were 59.5%, 81.6%, and 99.6% less than 90 µm, respectively, and 4.56%, 14.7%, and 58.7% less than 10 µm, respectively (Table 2).[5] Diatomaceous Earth has an infinite variety of shapes, due to its origins in the living matter (diatoms) from which it formed.[3]

Method of Manufacture

Diatomaceous Earth is obtained by strip mining, commonly from the western portion of the United States (US).[9] Diatomaceous Earth is also mined in western Canada, France, Denmark, Spain, Iceland, Romania, the Czech Republic, Algeria, Kenya, Morocco, Japan, South Korea, China, Australia, New Zealand, Mexico, Peru, Argentina, Costa Rica, Chile, Brazil, Colombia, and Peru.[10] Following extraction from a mine, the raw material is crushed, dried, ground, purified and

alimented.[7] The resulting material may be used as-is (natural or milled product), or can be further process by heating (800 - 1000 ºC) in one of two ways to produce a "calcined" product or a "flux-calcined" product.[7,10] After heating, the material is then cooled and further ground before packaging. In commercial products, a large proportion of the amorphous silica in Diatomaceous Earth is converted into a crystalline form (cristobalite, up to 40% to 60%) during thermal processing.[3,10]

The International Diatomite Producers Association has reported that its member companies only supply natural Diatomaceous Earth for use in cosmetics;[11] however, a supplier has reported that Diatomaceous Earth used in cosmetics can be flux-calcined.[12] The flux-calcined material is produced through the following steps: harvesting, calcination, milling, sieving, quality control, packaging, and quality control. [12]

Composition and Impurities

The composition of Diatomaceous Earth varies depending on where it is mined and how it is processed.[13] Silica content in Diatomaceous Earth can vary between 68% to 96%.[3,10,13-16] Other components may include aluminum (III) oxide (~4 - 7%), iron (III) oxide (~1 - 4%), titanium (IV) oxide; ions of calcium, magnesium, sodium, and potassium; and phosphates.[3,10,13,15,16] Many elements are present in trace amounts, and co-deposited and secondary minerals can include clays, quartz, gypsum, mica, calcite, feldspars, salt, pyrite, sulfur, manganese nodules, and phosphates.[10] Diatomaceous Earth usually contains 0.1% to 4% quartz.[3] Chert and volcanic ash can be abundant constituents of the sediment, and common biogenic constituents include the siliceous remains of sponges, silicoflagellates, radiolaria, carbonized fossil leaves, and fossilized fish bones.[10] Chemical and mineral impurities can affect the properties of the final Diatomaceous Earth product, including pH, solubles present, density, and abrasiveness: commercial uses can be adversely affected unless contaminants can be removed or made insoluble through processing.

Crystalline silica content of Diatomaceous Earth is dependent on the degree of exposure to high temperatures and pressures; surface chemistry of an individual Diatomaceous Earth sample may vary, depending upon production method and degree of hydration.[4] The crystalline silica content of uncalcined Diatomaceous Earth is 0.1% to 4.0%. Cristobalite content of straight-calcined flux products is between 10% to 20%, and between 40% to 60% in flux-calcined products.[3,17]

A supplier has reported that a product containing 100% Diatomaceous Earth has < 1% respirable crystalline silica.[18] Another product containing 9-11% Diatomaceous Earth was reported to have < 0.11% respirable crystalline silica. This product also contained 57% - 61% *Lithothamnion calcareum* powder, 29% - 31% mannitol, and 0.7% - 1.5% zinc sulfate.[19] This supplier has reported that flux-calcined Diatomaceous Earth is used in the finished products at concentrations below 10% and has a respirable crystalline silica content of < 1% (cristobalite) based on the size-weighted relevant fine fraction (SWeRF) method of analysis.[12]

According to international standards for food additives, Diatomaceous Earth should not contain more than 10 mg/kg arsenic or lead.[6]

USE

Cosmetic

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

According to 2022 VCRP survey data, Diatomaceous Earth is used in a total of 135 formulations (Table 3).[20] Of these reported uses, the majority are in leave-on products, with over a third of the uses (50) reported to be in nail products. Twenty-five uses are reported to be in rinse-off paste masks (mud packs). While uses were reported in a number of categories in the VCRP, the results of the concentration of use survey conducted by the Council in 2021 reported uses for Diatomaceous Earth in only 3 categories: at 0.001% in hair dyes and colors, up to 0.01% in nail polish and enamel, and at 2% in rinse-off products (paste masks).[21]

Diatomaceous Earth may be used in products that can come into contact with the eyes or mucous membranes; for example, it is reported to be used in eye shadow, eye lotion, bath soaps and detergents, and other personal cleanliness products (concentrations not reported).[20,21] It is also reported to be used in products which maybe incidentally ingested, such as lipsticks and dentifrices (concentrations not reported). Additionally, Diatomaceous Earth is reported to be used in face powders (concentration not reported), and could possibly be inhaled. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[22-24]

Diatomaceous Earth is not restricted from use in any way under the rules governing cosmetic products in the European Union.[25]

Non-Cosmetic Use

Diatomaceous Earth has uses in food and beverages, including anticaking material foodstuffs and clarifier in wine and beer.[26] In 1979, the Select Committee on GRAS (generally recognized as safe) Substances (SCOGS) opined that Diatomaceous Earth is GRAS as a filtering aid in such food and beverages as apple cider, beer, beet and cane sugar, vinegar, and wine in natural, calcined, or flux-calcined forms.[27] Diatomaceous Earth is also GRAS as a substance migrating to food from paper and paperboard products (21CFR§182.90). Diatomaceous Earth is approved for use as a coating (21CFR§175.300), polymer (21 CFR§177.1680; §177.2260; §177.2410), and as a component of paper and paperboard (21CFR 176.170) and adjuvants (21CFR§178.3297) in indirect food additives. It is an approved food additive in animal feed with the restrictions that it cannot contain more than 15 ppm lead, 20 ppm arsenic, and 600 ppm fluorine (21 CFR§573.340).

The use of Diatomaceous Earth as a drug carrier is being investigated.[28,29] Diatomaceous Earth is an approved inactive ingredient in approved drug products, including capsules and tablets taken orally and in topical soaps.[30]

Diatomaceous Earth is used in refractory and insultation bricks, filtration media, fertilizers, abrasives, insulation materials, lubricants, paints, rubbers, absorbents, bulking agents, and as carriers for catalysts.[9,10,17,26] It is also widely used in pesticide formulations.[10,14,17,26,31,32]

TOXICOKINETIC STUDIES

No toxicokinetic studies were discovered in the published literature and no unpublished data were submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

In an oral study in accordance with Organization for Economic Co-operation and Development (OECD) test guideline (TG) 401, female Wistar rats received 300 mg/kg (1 rat) or 2000 mg/kg (5 rats) flux-calcined Diatomaceous Earth in arachis oil by gavage. [5] The purity of the test material was not stated. Clinical observations were made at 0.5, 1, 2, and 4 h post-dosing, and then daily for 14 d. Morbidity and mortality were checked twice daily and body weights were recorded on days 0, 7, and 14. No mortalities were observed at either dose level. No signs of systemic toxicity were observed at 300 mg/kg; however, at 2000 mg/kg, clinical signs of toxicity included hunched posture in all animals and ataxia in one animal. All animals had expected body weights gains, and no abnormalities were observed at necropsy. The LD_{50} for Diatomaceous Earth in this study was greater than 2000 mg/kg.

Inhalation

In a dust aerosol study in accordance with OECD TG 403, 5 male and 5 female Wistar rats received 2.7 mg/l flux-calcined Diatomaceous Earth (100%; target particle size 1 to 4 µm). [5] The rats were exposed to the test material nose-only for 24 h. Clinical observations were made during exposure, immediately after exposure, and 1 h after exposure, and then once daily for 14 d. Body weights were recorded on test days 1 (before exposure), 2, 4, 8, and 15 (before necropsy). No mortalities were observed. Clinical signs of toxicity included moderately-ruffled fur in all animals on test day 1 that persisted until day 2, and slight nose scabbing on day 1 in all animals. Marginal to slight body weight loss was noted in all males and 4 females on day 1 and 2 but returned to expected gains thereafter. No abnormalities were observed at necropsy. The LC_{50} for Diatomaceous Earth in this study was greater than 2.7 mg/l.

Short-Term, Subchronic, and Chronic Dose Toxicity Studies

Repeated dose oral and inhalation studies summarized here are described in Table 4. In 13-wk dietary studies, rats that received up to 5% natural or flux-calcined Diatomaceous Earth did not exhibit effects outside of increased body weight gains in one study.[5,33]

In inhalation studies, a no-observable-adverse-effect-concentration (NOAEC) could not be determined in a 28-d inhalation rat study of 100% pure flux-calcined Diatomaceous Earth (particle size range 1 to 3 µm) at up to 0.7 mg/l.[5] In a 2-yr rat inhalation study of a flux-calcined Diatomaceous Earth at up to 5 million particles per cubic foot (mppcf) per day plus 50 mppcf for 1 h three times per week (5 + 50 mppcf), no fibrosis was observed.[15] Perivascular and peribronchiolar localization of dust-laden macrophages were observed in both the 2 and 5 mppcf dose groups, and nodular lesions and reactions of the nodes were greater in the 5 mppcf dose group. A similar study of the same test material in guinea pigs also found no fibrosis after 1.5 yr, and a light increase in intra-alveolar macrophages with peribronchiolar localization in the 5 mppcf group. In another guinea pig study of unheated and heated Diatomaceous Earth (particle size range ~0.45 µm to > 10 µm), no fibrosis was noted during observations made at 2-3 mo intervals until study end at 2 yr.[34] No fibrosis was observed in mongrel dogs exposed to up to 5 mppcf flux-calcined Diatomaceous Earth for up to 2.5 yr.[15]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No DART studies were discovered in the published literature, and no unpublished data were submitted.

GENOTOXICITY STUDIES

In vitro genotoxicity studies summarized here are described in Table 5. Diatomaceous Earth (100% pure flux-calcined) was not mutagenic in an Ames test (up to 5000 µg/plate) or a mouse lymphoma cell gene mutation test (up to 40 µg/ml), and was not clastogenic in a human lymphocyte chromosome aberration test (up to 40 µg/ml).[5] Abnormal cell proliferation, colony-forming efficiency, and nuclei formation was observed in Chinese hamster ovary (CHO) cells in assays with unprocessed and flux-calcined Diatomaceous Earth (1.3 µm and 2.1 µm, respectively; concentrations tested not reported).[16] In studies with Syrian hamster embryo (SHE) cells treated with high temperature calcined and flux-calcined Diatomaceous Earth, concentration-dependent increases in cell division aberrations and cell transformations were observed; the induction of transforming potency was correlated with the amount of hydroxyl radicals generated.[35-37] Cell transformation was decreased or not observed in SHE cells exposed to uncalcined Diatomaceous Earth samples where the likelihood of radical generation was decreased or non-existent .

CARCINOGENICITY STUDIES

The International Agency for Research on Cancer (IARC) has determined that "there is *inadequate evidence* in experimental animals for the carcinogenicity of uncalcined Diatomaceous Earth." Overall, amorphous silica is not classifiable as to its carcinogenicity to humans (Group 3).[3]

Oral

In a feeding study, a group of 30 weanling Sprague-Dawley rats (sex not reported) received 20 mg/d Diatomaceous Earth (particle size not reported) mixed with cottage cheese at a concentration of 5 mg/g cheese.[38] The rats also received commercial rat chow and filtered tap-water ad libitum. A control group of 27 rats was only fed commercial rat chow. The animals were observed for their life span (mean survival following the start of treatment for treated rats was 840 d, and for control rats was 690 d). Complete gross and microscopic thoracic and abdominal necropsies were performed on each animal upon expiration, with special attention given to the gastrointestinal tract. During the course of the study, 5 malignant tumors (1 salivary gland carcinoma, 1 skin carcinoma, 2 sarcomas of the uterus, and 1peritoneal mesothelioma) and 13 benign tumors (9 mammary fibroadenomas, 1adrenal pheochromocytoma, and 3 pancreatic adenomas) were observed in the treated animals. The control group had 3 carcinomas (1 each in the lung, forestomach and ovary) and 5 mammary fibroadenomas. The authors determined that the difference in tumor incidence between treated and control rats was not statistically significant ($0.25 < p < 0.5$, χ^2-test).

Subcutaneous

A group of 36 female Marsh mice, 3-mo-old, received a subcutaneous injection of 20 mg Diatomaceous Earth (uncalcined, particle size, 3 - 9 µm, with some crystalline materia1 of larger size) suspended as a 10% slurry in isotonic saline (volume unspecified).[3] Another group of 36 female littermates received an injection of 0.2 ml saline only. The numbers of mice still alive at 19 mo were 19/36 in the treated group and 20/36 in the control group. The treated group showed an extensive reactive granulomatous and fibroplastic reaction at the site of injection, but no malignant tumors. No further details were available.

Intraperitoneal

In another study by the same researchers, a group of 29 female Marsh mice, 3-mo-old, received an intraperitoneal injection of 20 mg Diatomaceous Earth suspended as a 10% slurry in isotonic saline.[3] A group of 32 female littermates received an injection of the same volume of saline only (volume unspecified). The numbers of mice still alive at 19 mo were 1l/29 in the treated group and 19/32 in the control group. Lymphosarcomas at the injection site in the abdominal cavity were reported in 6/17 treated animals and 1/20 controls ($p = 0.02$; method of statistical analysis unspecified). No further details were available.

OTHER RELEVANT STUDIES

Pulmonary Response

The following summaries demonstrate the physiological changes to the pulmonary system when Diatomaceous Earth enters the lung. In an intratracheal study, groups of 6 male Sprague-Dawley rats received a single instillation of Diatomaceous Earth (90% amorphous silica; particle size < 7 µm**)** suspended in isotonic saline.[39] Rats that underwent bronchoalveolar lavage (BAL) examinations received 10 mg/animal, and rats that underwent lung biochemical examinations received 15 mg/animal. Determinations in the BAL and phospholipids in the lung tissue were determined after 15, 60, and 180 d and 90, 180, and 360 d, respectively. Acute/subacute inflammation was observed that gradually became moderate after 60 d. No further details provided.

In another intratracheal study, groups of Hartley-Duncan guinea pigs (sex not specified) received a single instillation of 25 mg flux-calcined Diatomaceous Earth (particles $\leq$3.0 µm in diameter; 72% silica and 28% calcium silicates) in 0.5 ml physiological saline. [40] A control group of 2 animals received 0.5 ml saline only. After 2 or 4 h, 1, 2, 3, 4, 5, 6, or 7 d, and 5, 6, or 15 mo, 2 animals/time period were killed and lungs were dissected. No signs of infection nor significant individual variation in response within time period were observed. Pronounced neutrophil invasion of the bronchioles was observed by

4 h post-exposure, which remained well developed through 1 d post-exposure. The number of macrophages and neutrophils in the alveoli increased through 1 d post-exposure and remained greater than control values through 7 d post-exposure. The number of macrophages, many of which contained Diatomaceous Earth, remained elevated for the duration of the experiment. Phagocytosis of the particles was mainly performed by the macrophages, with some participation by the neutrophils. Many of the reactive macrophages in the groups longer than 2-h post-exposure had various types of pathological alterations. Some particles were found in type I epithelial cells. Edematous changes were observed in some type I epithelial cells, and proliferation of type II epithelial cells was observed in some alveoli, especially near the respiratory bronchiole. Mild, diffuse fibrosis was observed starting at 6 mo post-exposure and persisted at 15 mo post-exposure.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Dermal irritation, sensitization, and phototoxicity studies summarized here are described in Table 6. Diatomaceous Earth (flux-calcined, up to 100% pure) was considered non-corrosive and non-irritating in EpiSkin™ reconstituted human epidermis model tests.[5] In acute skin tolerance patch tests, Diatomaceous Earth (flux-calcined) was not irritating in 10 healthy volunteers at 100% or in 11 volunteers with sensitive skin in a product at 9% - 11%.[41,42] Diatomaceous Earth was not sensitizing in a local lymph node assay (LLNA) at up to 10%.[5] A cosmetic product containing 9% - 11% Diatomaceous Earth (soda ash flux-calcined) was not sensitizing in a human repeated insult patch test (HRIPT) of 100 healthy subjects when tested at a 10% dilution, nor was it phototoxic in a human single application study in 10 healthy female subjects when tested neat. [43,44]

OCULAR IRRITATION STUDIES

In Vitro

The ocular irritation potential of Diatomaceous Earth (flux-calcined, purity not reported) was assessed in a SkinEthic™ reconstituted human corneal epithelium model test.[5] The test material was used as supplied, and 30 mg was applied to the tissue cultures. Triplicate cultures were exposed for 10 min, and then examined after 3 h. Viability of the tissues following exposure to the test material was 99.1% and the qualitative evaluation of the tissue following exposure indicated it was viable. The positive and negative controls yielded expected results. Based on the results of the study, the test material was considered non-irritating.

In another in vitro study, the ocular irritation potential of a formulations containing 9% - 11% Diatomaceous Earth (soda ash flux-calcined) was assessed using the chorio-allantoic membrane of a fertilized hen's egg (HET-CAM test).[45] The material was tested at 2%, 5%, and 10% w/v dilutions in water. Approximately 0.3 ml of the sample was spread over membrane and rinsed with 5 ml of demineralized water after 20 s. The test material was non-irritating at the 2% and 5% dilution, but moderately irritating at the 10% dilution. The 10% dilution had low solubility and rapid sedimentation; however, the results were reproducible between eggs and were considered relevant.

Animal

The ocular irritation potential of Diatomaceous Earth (flux-calcined, purity not reported) was assessed in 2 New Zealand White rabbits (sex not reported) in accordance with OECD TG 405.[5] The undiluted test material was instilled at a volume of 0.1 ml in the right eye of the animals. The left eye was left untreated as a control. After instillation, the rabbits were observed for 72 h. No corneal effects were reported. Iridial inflammation was reported in one animal at 1 and 24 h post-instillation. Moderate conjunctival irritation was noted in both animals at 1 and 24 h post-instillation, and up to 48 h post-instillation in 1 animal. Both animals had recovered by 72 h post-instillation. The test material was considered to be non-irritating to the eye in this study.

CLINICAL STUDIES

Case Report

A 51-yr-old male employed in the Diatomaceous Earth industry for 26 yr (20 in a mill, 6 in an office) was reported to have a history of a recurrent peptic ulcer, pleurisy, and bronchopneumonia, with frequent attacks of bronchitis.[46] The patient was a nonsmoker. An electrocardiogram indicated right ventricular hypertrophy. The patient had a 4-yr history of intermittent palpitation, severe exertional moderate paroxysmal dyspnea, and orthopnea. He also complained of wheezing and hoarseness, with productive cough, until a year and a half before presentation. Cough, but not dyspnea, was relieved by bronchodilator aerosols. At physical examination, no apparent distress or cyanosis were noted; however, slight clubbing of the fingers was observed. Rales were detected over most of the chest except in infraclavicular areas anteriorly. Resonance was diminished over the upper lung fields posteriorly, and on the left anteriorly. Chest films were interpreted as consistent with far-advanced coalescent pneumoconiosis. The patient died 5 yr after the chest films were made, reportedly due to heart failure from cor pulmonale.

OCCUPATIONAL EXPOSURE STUDIES

Occupational exposure studies are described in Table 7. Occupational exposure studies indicate a risk of pneumoconiosis in Diatomaceous Earth mine and mill workers, which can be mitigated with dust control measures and personal protective equipment.[47-52] Studies were of quarry and mill workers in the western US and exposures were to raw, calcined, or flux-calcined Diatomaceous Earth.

OCCUPATIONAL EXPOSURE LIMITS

Occupational exposure to Diatomaceous Earth, and the quartz and amorphous silica dust it contains, can occur during mining, the calcination process, and through handing the calcined product in end-use industries as a filtration agent, mineral charge, refractory, abrasive, carrier, or adsorbent.[3] The National Institute for Occupational Safety and Health (NIOSH) time weighted average (TWA) for recommended exposure limits (REL) for Diatomaceous Earth (also characterized as amorphous silica) is 6 mg/m^3, and the Occupational Safety and Health Administration (OSHA) TWA permissible exposure limit (PEL) is 20 mppcf (80 mg/m^3/% silicon dioxide).[53] The immediately dangerous to life or health (IDLH) value is 3000 mg/m^3.

SUMMARY

Diatomaceous Earth is reported to function as an abrasive, absorbent, anticaking agent, bulking agent, and opacifying agent in cosmetics. The "calcined" form is processed Diatomaceous Earth that is heated to 800 - 1000 ºC to eliminate organic and carbonaceous material. The "flux-calcined" form is Diatomaceous Earth that is heated with the addition of sodium carbonate as a fluxing agent that results in a coarser material). Diatomaceous Earth is considered a natural amorphous form of silica.

The composition of Diatomaceous Earth varies depending on where it is mined and how it is processed. Silica content in Diatomaceous Earth can vary between 83% to 96%. Crystalline silica content of Diatomaceous Earth is dependent on the degree of exposure to high temperatures and pressures; surface chemistry of an individual Diatomaceous Earth sample may vary, depending upon production method and degree of hydration. The crystalline silica content of uncalcined Diatomaceous Earth is 0.1% to 4.0%. Cristobalite content of straight-calcined flux products is between 10% to 20%, and between 40% to 60% in flux-calcined products.

According to 2022 VCRP survey data, Diatomaceous Earth is used in a total of 135 formulations. Of these reported uses, the majority are in leave-on products with over a third of the uses (49) reported to be in nail polish and enamel. Twenty-five uses are reported to be in rinse-off paste masks (mud packs). The results of the concentration of use survey conducted by the Council in 2021 indicate that Diatomaceous Earth is used at 0.001% in hair dyes and colors, up to 0.01% in nail polish and enamel, and at 2% in rinse-off products (paste masks). Diatomaceous Earth is reported to be used in cosmetic powders, and could possibly be inhaled; for examples, it is reported to be used in face powders (concentration not reported).

In a 90-d dietary study, male and female rats were fed a diet containing 5% Diatomaceous Earth. (Estimated intake ranged from about 12 g/kg bw/d at the start of the experiment to about 5 g/kg at the end of the experiment.) Residual silica values in the organs of treated rats were comparable with the controls.

In oral rat studies with flux-calcined Diatomaceous Earth, the LD_{50} was greater than 2000 mg/kg. The LC_{50} was greater than 2.7 mg/l in an inhalation rat study of flux-calcined Diatomaceous Earth.

In 13-wk dietary studies, rats that received up to 5% natural or flux calcined Diatomaceous Earth did not exhibit adverse effects outside of increased body weight gains in one study. An NOAEC could not be determined in a 28-d inhalation rat study of 100% pure flux-calcined Diatomaceous Earth (particle size range 1 to 3 µm) at up to 0.7 mg/l. In a 2-yr rat inhalation study of a flux-calcined Diatomaceous Earth at up to 5 mppcf, no fibrosis was observed. Perivascular and peribronchiolar localization of dust-laden macrophages were observed in the 2 and 5 mppcf dose groups and nodular lesions and reactions of the nodes was greater in the 5 mppcf dose group. A similar study of the same test material in guinea pigs also found no fibrosis after 1.5 yr and a light increase in intra-alveolar macrophages with peribronchiolar localization in the 5 mppcf group. In another guinea pig study of unheated and heated Diatomaceous Earth (particle size range ~0.45 µm to > 10 µm), no fibrosis was noted during observations made at 2-3 mo intervals until study end at 2 yr. No fibrosis was observed in mongrel dogs exposed to up to 5 mppcf flux-calcined Diatomaceous Earth for up to 2.5 yr.

Diatomaceous Earth (100% pure flux-calcined) was not mutagenic in an Ames test (up to 5000 µg/plate) or a mouse lymphoma cell gene mutation test (up to 40 µg/ml); and was not clastogenic in a human lymphocyte chromosome aberration test (up to 40 µg/ml). Abnormal cell proliferation, colony-forming efficiency, and nuclei formation was observed in CHO cells in assays with unprocessed and flux-calcined Diatomaceous Earth (1.3 µm and 2.1 µm, respectively; concentrations tested not reported). In studies with SHE cells, high temperature calcined and flux-calcined Diatomaceous Earth had increased cell division aberrations and cell transformations in a concentration-dependent manner; the induction of transforming potency was correlated with the amount of hydroxyl radicals generated. Cell transformation was decreased or not observed in SHE cells exposed to uncalcined Diatomaceous Earth samples where the likelihood of radical generation was decreased or non-existent.

IARC has determined that there is inadequate evidence in experimental animals for the carcinogenicity of uncalcined Diatomaceous Earth. In an oral feeding study in Sprague-Dawley rats that received 20 mg/d Diatomaceous Earth in cottage cheese, there was no statistically significant difference in cancer incidence between treated and control rats. A subcutaneous study in mice found uncalcined Diatomaceous Earth led to extensive reactive granulomatous and fibroplastic reactions at the injection site, but no malignant tumors were observed. The same research group performed an intraperitoneal study in mice and found lymphosarcomas at the injection site in the abdominal activity.

In an intratracheal rat study of Diatomaceous Earth that was 90% amorphous silica, acute/subacute inflammation was observed that gradually became moderate after 60 d. Guinea pigs that received a single 25 mg intratracheal instillation had mild, diffuse fibrosis observed starting 6 mo after exposure that persisted to 15 mo.

Diatomaceous Earth (flux-calcined, up to 100% pure) was considered non-corrosive and non-irritating in EpiSkin™ reconstituted human epidermis model tests. In acute skin tolerance patch tests, Diatomaceous Earth (flux-calcined) was not irritating in 10 healthy volunteers at 100% or in 11 volunteers with sensitive skin in a product at 9% - 11%. Diatomaceous Earth was not sensitizing in a LLNA at up to 10%. A cosmetic product containing 9% - 11% Diatomaceous Earth (soda ash flux-calcined) was not sensitizing in a HRIPT of 100 healthy subjected when tested at a 10% dilution, nor was it phototoxic in a human single application study in 10 healthy female subjects when tested neat.

In ocular studies, flux-calcined Diatomaceous Earth in a formulation at 9%-11% was non-irritating at 2% and 5% dilutions, but was moderately irritating at a 10% dilution. However, flux-calcined Diatomaceous Earth (tested neat) was not an ocular irritant in an in vitro reconstituted human corneal epithelium model test nor in a rabbit eye test.

A case report of a worker at a Diatomaceous Earth mill observed far-advanced coalescent pneumoconiosis. Occupational studies indicate a risk of pneumoconiosis in Diatomaceous Earth mine and mill workers, which can be mitigated with dust control measures and personal protective equipment. The TWA REL for Diatomaceous Earth set by NIOSH is 6 mg/m^3 and the TWA PEL set by OSHA is 20 mppcf (80 mg/m^3/% silicon dioxide). The IDLH value is 3000 mg/m^3.

No DART studies were discovered in the published literature, and no unpublished data were submitted.

DRAFT DISCUSSION

[Note: This Discussion is in draft form, and changes will be made following the Panel meeting.]

The Panel reviewed the safety of Diatomaceous Earth. The Panel concluded… [to be determined].

The Panel expressed concern about heavy metals that may be present in this naturally-derived ingredient, and stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities. The Panel also expressed concern over the lack of DART studies for Diatomaceous Earth. However, the Panel noted that Diatomaceous Earth did not produce adverse effects in oral rodent studies, and is GRAS for uses in food and beverages. These findings, coupled with noted lack of residual silica absorption in a 13-wk dietary study in rats, helped mitigate concern over the absence of DART data.

Diatomaceous Earth used in cosmetics is a polymorph of silicon dioxide that occurs naturally and may be further processed through heating. The Panel considered the method of manufacture of this ingredient to be of significant importance to safety, as heat processing can create crystalline silica, a known cause of significant lung disease, including cancer. Manufacturers should use Diatomaceous Earth with controlled amounts of crystalline silica, especially in cosmetic products that may be incidentally inhaled.

CONCLUSION

To be determined.

TABLES

Table 1. Chemical properties

Property	Value	Reference
Physical Form	Powder	[5]
Color	White or beige	[5]
	Calcined = pink to light brown or light yellow to light orange	[6]
	Flux-calcined = white to pink or light brown	[6]
Density/Specific Gravity (g/ml @ 20 ºC)	2.36	[5]
Melting Point (ºC)	1710	[4]
Boiling Point (ºC)	2230	[4]
Water Solubility (mg/l @ 20 ºC & pH 3)	3.7	[5]

Table 2. Particle size distributions for flux-calcined Diatomaceous Earth[5]

	Volume % less than		
Diameter of particles (µm)	**Fine Grade**	**Medium Grade**	**Coarse Grade**
1	3.81	1.89	0.68
1.5	6.81	3.09	1.18
2	9.63	3.89	1.56
3	15.7	5.12	2.09
4	22.3	6.28	2.49
6	35.3	8.76	3.18
10	58.7	14.7	4.56
20	90.3	32.2	9.59
28	95.9	43.7	15.1
40	98.4	56.4	24.4
50	99.1	64.1	32.1
75	99.5	76.7	50
90	99.6	81.6	59.5
250	99.996	97	96.2
600	100	99.95	99.98

Table 3. Frequency (2022)[20] and concentration (2021)[21] of use according to duration and exposure

	# of Uses	Max Conc of Use (%)
Totals*	**135**	**0.001-2**
Duration of Use		
Leave-On	92	0.0049-0.01
Rinse-Off	43	0.001-2
Diluted for (Bath) Use	NR	NR
Exposure Type		
Eye Area	2	NR
Incidental Ingestion	17	NR
Incidental Inhalation-Spray	9[a]; 8[b]	NR
Incidental Inhalation-Powder	5; 9[a]	NR
Dermal Contact	67	2
Deodorant (underarm)	3[b]	NR
Hair - Non-Coloring	1	NR
Hair-Coloring	NR	0.001
Nail	50	0.0049-0.01
Mucous Membrane	20	NR
Baby Products	NR	NR

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

[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.

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

NR – not reported

Table 4. Repeated dose toxicity studies of Diatomaceous Earth

Test Material Dose/Concentration	Animals/Group	Study Duration	Vehicle	Protocol	Results	Reference
ORAL						
0%, 1%, 3%, or 5% Diatomaceous Earth of freshwater origin, particle size range was 0.46 µm to 640 µm, with 90% smaller than 100 µm and 55% smaller than 12 µm	Groups of 15 male and 15 female Wistar rats	13-wk study	Dietary pellets	Body weights recorded weekly; at study end animals were killed and necropsied; livers, kidneys, and spleens of rats fed test material at 5% were analyzed for residual silica	Body weights of the 5% dose group were greater than the controls through the course of the study, with the maximum weight differential occurring at week 6; body weight gains in the 3% dose group were similar to those in the 5% group; body weight gains in the 1% dose group were similar to controls; histologic examination of organs of the 5% dose group were comparable to controls; residual silica values in the organs of the 5% dose group were comparable with the controls	[33]
1% and 5% natural Diatomaceous Earth and 5% flux-calcined Diatomaceous Earth as feed; 5% natural mixture contained 4.8% silica, 0.44% quartz, and no cristobalite; 1% natural mixture contained 1.2% silica, 0.24% quartz, and 0.26% cristobalite; 5% flux calcined mixture contained 5.1% silica, 0.43% quartz, and 1.70% cristobalite	Groups of 20 male and 20 female Sprague-Dawley rats	13-wk study	Dietary pellets	Study performed in accordance with OECD TG 408; control animals received plain diet;	No clinical signs of toxicity or mortalities observed; no effects observed in body weight; feed consumption, ophthalmological findings, hematological findings, clinical biochemistry findings, or urinalysis findings; no treatment-related effects were observed at necropsy	[5]
INHALATION						
100% pure flux-calcined; 0, 0.018, 0.58, or 1.57 mg/l; target particle size range was 1 to 3 µm	5 male and 5 female Wistar rats/dose group	5-d range finding study	None described	Nose-only aerosol inhalation study; 6 h/exposure performed	No clinical signs of toxicity or mortalities observed; reduced feed consumption was observed in the high dose group; mean body weight loss was recorded in both male and female animals in the high dose group and a statistically significant reduced body weight gain was observed in male rats in the high dose group only when compared with controls; dose-dependent alveolar histiocytosis was observed in all dose groups; alveolitis was observed in one male in the mid-dose group and in all animals in the high-dose group as well as increased absolute and relative lung weights in the mid- and high-dose groups; microgranulomas were found in one male and female in the mid-dose group and in all animals in the high-dose group; the test material was observed in the alveoli in most of the high-dose group animals; a no-observable-effect-concentration (NOEC) could not be determined	[5]

Table 4. Repeated dose toxicity studies of Diatomaceous Earth

Test Material Dose/Concentration	Animals/Group	Study Duration	Vehicle	Protocol	Results	Reference
100% pure flux-calcined; 0, 0.044, 0.207, or 0.700 mg/l; target particle size range was 1 to 3 µm	20 male and 20 female Wistar rats/dose group	28-d study	Compressed air	Study performed in accordance with OECD TA 412; nose-only aerosol inhalation study; 6 h/exposure performed 5d/wk with a 9-wk recovery period	No clinical signs of toxicity or mortalities observed; a slight and transient effect on body weight gain occurred in the high dose group; dose-dependent increase in lung weights recorded at the end of treatment period that further increased at the end of the recovery period; lymph nodes were also increased in size at the end of the recovery period; increase in spleen, adrenal, and liver weights was observed in the high-dose group at the end of the recovery period; histiocytosis was observed in the alveoli with a dose-dependent increase in incidence and severity that progressed during the recovery period; test material was detected in the alveoli in the mid and high dose group animals at the end of the treatment period that persisted until the end of the recovery period; a NOAEC could not be determined	[5]
Flux-calcined Diatomaceous Earth (61% cristobalite); 0, 2, 5, 50, and 5+50 mppcf; mean particle size 0.7 µm	Male Wistar rats divided as follows in the 0, 2, 5, 50, and 5+50 mppcf dose groups: 47, 79, 82, 46, and 53 animals, respectively	2- yr study	None described	Rats exposed to test material in exposure chambers for 6 h/d, 5 d/wk for up to 2 yr except in the 50 mppcf (1 h, 3 times/wk) and the 5+50 mppcf (daily 5 mppcf exposure plus 50 mppcf 3 times/wk for 1 h each) dose groups; rats killed at 6 mo, 1 yr, 1.5 yr, and 2 yr.	Terminal body weights at 1 yr and 1.5 yr in treated groups were comparable to controls except for in the rats exposed to 5+50 mppcf, which were below the control and 5 mppcf group; tissues studied other than the lungs had no test material-related changes. At 6 mo, rats in 2 and 5 mppcf dose groups had scattered macrophages and occasional giant cell within alveolar spaces; there was no significant septal reaction; pulmonary hilar lymph nodes only slightly enlarged and contained small clusters of macrophages in medullary portions; 5+50 mppcf group had slightly enhanced cellular reaction, when compared to the 5 mppcf group, and macrophages were noted to accumulate around bronchioles. At 1 yr, an increased macrophagic infiltration of perivascular and peribronchiolar areas were observed in the 2 and 5 mppcf groups; reactions were dose dependent; in 5+50 mppcf, macrophagic cells accumulated in a nodular fashion and reticular condensation was evident in lung parenchyma and hilar nodes. At 1.5 yr, no definite parenchymal or lymph node fibrosis was observed. At 2 yr, perivascular and peribronchiolar localization of dust-laden macrophages was observed in the 2 and 5 mppcf dose groups; nodular lesions and reaction of the nodes was greater in the 5 mppcf dose group; no fibrosis evident.	[15]

Table 4. Repeated dose toxicity studies of Diatomaceous Earth

Test Material Dose/Concentration	Animals/Group	Study Duration	Vehicle	Protocol	Results	Reference
Flux-calcined Diatomaceous Earth (61% cristobalite); 0, 2, 5, 50, and 5+50 mppcf; mean particle size 0.7 μm	Male guinea pigs (strain not reported) divided as follows in the 0, 2, 5, 50, and 5+50 mppcf dose groups: 47, 57, 69, 20, and 20 animals, respectively	1.5-yr study	None described	Guinea pigs exposed to test material in exposure chambers for 6 h/d, 5 d/wk for up to 1.5 yr except in the 50 mppcf (1 h, 3 times/wk) and the 5+50 mppcf (50 mppcf for 3 d/wk plus daily 5 mppcf) dose groups; rats killed at 6 mo, 1 yr, and 1.5 yr	Terminal body weights at 1 yr and 1.5 yr were comparable to controls; tissues studied other than the lungs had no test material-related changes. At 6 mo, same as the findings for the rats above. At 1 yr, definite cellular reaction with large clusters of macrophages and multinucleated giant cells in alveolar spaces in the 5 mppcf group; macrophages observed to accumulate around bronchioles and alveolar ducts; hilar lymph nodes were markedly enlarged and medullary portions were packed with dust cells and interwoven reticulum fibers. At 1.5 yr, a slight increase in intra-alveolar macrophages with peribronchiolar localization was observed in the 5 mppcf group; alveolar septa were unaffected and no fibrosis evident	[15]
Diatomaceous Earth at 171 mppcf (natural, unheated), cristobalite at 167 mppcf (from heat-treated Diatomaceous Earth), or sodium silicate; particle size range ~0.45 μm to > 10 μm	Albino guinea pigs (sex and number/group not reported)	21-24 mo study	None described	Guinea pigs were placed in separate cubical dust rooms (512 ft^3) for 24 h/d until killed for examination; dust was generated within the room for 7 to 8 h/d, 5.5 d/wk for 21-24 mo; control animals kept in ambient air; pairs of animals selected at random were killed at 2-3 mo intervals and lung tissues were collected and analyzed for total silica content and total ash	In animals exposed to Diatomaceous Earth, fibrosis was only noted at 24 mo, and not at the same severity as in the cristobalite-exposed animals; in animals exposed to cristobalite, fibrosis first observed after 15 mo and was severe by 21 mo; no fibrosis observed in animals exposed to sodium silicate, but alveoli became heavily packed with phagocytic macrophages. Total silica content per lung increased linearly throughout at least 21 mo in each experiment, and total ash weight increased more rapidly than dust was accumulating. Cristobalite produced a greater increment in ash weight than Diatomaceous Earth and sodium silicate. Total amount of silica accumulated varied inversely with the degree of tissue damage occurring, even though atmospheric dust concentrations were comparable for the 3 silica types. Maximum total content of cristobalite reached only 68 mg/lung, while that of Diatomaceous Earth and sodium silicate was 120 mg/lung and 465/lung, respectively. Author noted that siliceous dust that produces cell damage may be cleared more effectively from the lung than innocuous dust.	[34]

Table 4. Repeated dose toxicity studies of Diatomaceous Earth

Test Material Dose/Concentration	Animals/Group	Study Duration	Vehicle	Protocol	Results	Reference
Flux-calcined Diatomaceous Earth (61% cristobalite); 0, 2, and 5 mppcf; mean particle size 0.7 µm	Male mongrel dogs divided as follows in the 0, 2, and 5 mppcf dose groups: 8, 16, and 17 animals, respectively	2.5-yr study	None described	Dogs exposed to test material in exposure chambers for 6 h/d, 5 d/wk for up to 30 mo; an unreported number of dogs were killed at 6 mo, 1 yr, 1.5 yr, 2 yr, and 2.5 yr. One dog in the control and each dose group was killed 10 mo after cessation of exposure to examine recovery	Terminal weights comparable or slightly greater than controls; no changes in hematology during the course of the study; tissues studied other than the lungs had no test material-related changes. At 6 mo, no reaction observed in the 2 mppcf group and minimal intra-alveolar macrophages observed in the 5 mppcf group; however, hilar nodes had greater macrophagic infiltration than rats and guinea pigs described above. At 1 yr, little to no changes observed. At 1.5 yr, clusters of dust cells in alveolar spaces adjacent to bronchioles observed in 5 mppcf group, with hilar lymph nodes enlarged and medulla replaced with hyalinized tissue. At 2 yr, slight perivascular and peribronchiolar localization of macrophages observed in 2 mppcf group that were definite nodules extending into bronchiolar lumina in the 5 mppcf group; hilar lymph nodes were enlarged and diffusely packed with macrophages; medulla had numerous nodules. At 2.5 yr, observations similar to those in the 2 yr group with no significant progression in reactions; no fibrosis evident. In the recovery animals, parenchymal and nodal changes did not increase compared to 2.5 yr group.	[15]

Table 5. In vitro genotoxicity studies of Diatomaceous Earth

Concentration/Dose	Vehicle	Test System	Procedure	Results	Reference
0, 50, 150, 500, 1500, or 5000 µg/plate flux-calcined (100% pure)	polyethylene glycol 400	*Salmonella typhimurium* strains TA 1535, TA 1537, TA 98, and TA 100; *Escherichia coli* strain WP2 uvr A	Ames test in accordance with OECD TG 471, with and without metabolic activation	Not mutagenic	[5]
0, 2.5, 5, 10, 20, 30 or 40 µg/ml flux-calcined (100% pure)	R0 medium	Mouse lymphoma L5178Y cells	Mammalian cell gene mutation test in accordance with OECD TG 476, with and without S9 metabolic activation	Not mutagenic	[5]
0, 1.25, 2.5, 5, 10, 20, or 40 µg/ml flux-calcined (100% pure)	Minimal essential medium or dimethyl sulfoxide	Human lymphocytes	Mammalian chromosome aberration test in accordance with OECD TG 473, with and without S9 metabolic activation	Not clastogenic	[5]
Natural and flux-calcined Diatomaceous Earth (average diameters 1.3 µm and 2.1 µm, respectively) in addition to titanium dioxide, crocidolite, chrysotile, quartz, and cristobalite; concentration ranges not reported; crystalline silica content of the natural Diatomaceous Earth was 4% quartz and of the flux-calcined Diatomaceous Earth was 40% cristobalite and 2% quartz	Not reported	Cultured Chinese hamster ovary (CHO) cells	Cell proliferation assays; 100,000 cells seeded/dish and incubated for 1 d prior to exposure to test dust for 3 d; cells then harvested and counted	The ranking of toxicity as measured by the inhibition of cell proliferation was chrysotile > crocidolite > natural Diatomaceous Earth > flux-calcined Diatomaceous Earth > quartz > cristobalite > titanium dioxide; effective concentration-50% (EC_{50}) for natural Diatomaceous Earth was 3.6 µg/cm^2 and for flux-calcined Diatomaceous Earth was 10.8 µg/cm^2; responses were concentration-dependent; researchers found that the toxicity of the dusts did not correlate with crystalline silica content, surface area, composition, volume, particles/cm^2, or fibrous geometry; however, toxicity was closely associated with the number of particles/cm^2 culture surface that had one dimension > 7.5 µm; authors indicated that particle size impacted toxicity	[16]
Natural and flux calcined Diatomaceous Earth as described above	Not reported	Cultured CHO cells	Colony-forming efficiency assays; 200 cells seeded/dish and the test dusts added 24 h later; cultures then incubated for 5 d before being fixed and number of colonies containing > 20 cells was determined for each dish.	Similar ranking of toxicity observed as in the cell proliferation assay described above; colony formation was not as inhibited as cell proliferation; results were concentration-dependent	[16]
Natural and flux calcined Diatomaceous Earth as described above	Not reported	Cultured CHO cells	Abnormal nucleus induction assays; cultures prepared in the same manner as the above inhibition of cell proliferation assays, exposed for 2 d and then fixed; percentage of cells containing micronuclei and/or polynuclei was determined for each dish.	Similar qualitative, concentration-dependent results were observed as in the cell proliferation and colony-forming efficiency assays described above	[16]
Three different sourced uncalcined Diatomaceous Earth samples (96%-98% pure; 0.6% -1.4% iron impurities) and 2 calcined Diatomaceous Earth samples (~98% pure; 0.7% - 0.9% iron impurities); concentrations not well defined, but at least 3 concentrations per sample were tested starting at 2 µg/cm^2 and were up to approximately 40 µg/cm^2	Suspended in sterile tridistilled water; culture medium without serum and complete medium	Syrian hamster embryo (SHE) cells	Cell transformation assay; without metabolic activation	Morphological transformation of the uncalcined and calcined Diatomaceous Earth samples occurred in a dose-dependent manner; authors concluded that samples with fractured surfaces and/or iron-active sites were able to generate reactive oxygen species-induced SHE cell transformation	[35]

Table 5. In vitro genotoxicity studies of Diatomaceous Earth

Concentration/Dose	Vehicle	Test System	Procedure	Results	Reference
Uncalcined Diatomaceous Earth (100% amorphous), Diatomaceous Earth heated to 900ºC (98.5% amorphous, 1% quartz, <0.5% cristobalite), Diatomaceous Earth heated to 1200ºC (51% amorphous, 1% quartz, 48% cristobalite), a generically heated flux-calcined Diatomaceous Earth (53% amorphous, 47% cristobalite), and the generically heated flux-calcined Diatomaceous Earth (42% amorphous, 58% cristobalite) depleted of particles greater than 10 µm; concentrations tested for each material were 4.5, 9, and 18 µg/cm^2 (also 36 µg/cm^2 for generically heated Diatomaceous Earth)	Culture medium	SHE cells	Cell division aberration assay; without metabolic activation	A concentration-dependent increase in abnormal mitoses frequency was observed with all dusts tested, except uncalcined Diatomaceous Earth at 4.5 and 9 µg/cm^2; Diatomaceous Earth heated to 900ºC and 1200ºC appeared "less active" than the uncalcined – the authors theorized this may be due to cytotoxic potential, which appeared "blunted" through heating	[36]
Uncalcined Diatomaceous Earth (100% amorphous), Diatomaceous Earth heated to 900ºC (98.5% amorphous, 1% quartz, <0.5% cristobalite), Diatomaceous Earth heated to 1200ºC (51% amorphous, 1% quartz, 48% cristobalite), a generically heated flux-heated Diatomaceous Earth (53% amorphous, 47% cristobalite), and the generically heated flux-calcined Diatomaceous Earth (42% amorphous, 58% cristobalite) depleted of particles greater than 10 µm; concentrations tested for each material were between1.9 and 30.4 µg/cm^2 (up to 60.8 µg/cm^2 for generically heated Diatomaceous Earth)	Culture medium	SHE cells	Cell transformation assay; without metabolic activation	Uncalcined Diatomaceous Earth did not induce morphological transformation while a concentration-dependent increase of the transformation frequency was induced by all other test materials; the heated samples exhibited a certain degree of transformation with the 1200ºC heated sample greater than the 900ºC (which was weakly active only above 15 µg/cm^2); transformation potential appears to be correlated with the ability to generate radicals	[36]
Uncalcined Diatomaceous Earth with 0.03% iron impurities and uncalcined Diatomaceous Earth depleted of iron; concentrations started at 3.5 µg/cm^2 and included up to 60 µg/cm^2	Not reported	SHE cells	Cell transformation assay, with and without antioxidants	Concentration-dependent increase in transformation frequency starting at 3.5 µg/cm^2 was observed in samples with iron, transforming potency was 1.8-fold less in samples depleted of iron; in presence of antioxidants, transformation frequencies were significantly decreased; authors concluded iron may generate reactive oxygen species that increase transforming potency	[37]
Uncalcined Diatomaceous Earth with 0.03% iron impurities and uncalcined Diatomaceous Earth depleted of iron; concentrations between 2.25 and 34 µg/cm^2	Not reported	SHE cells	Cell division aberration assay, with and without antioxidants	A significant concentration-dependent increase in frequency of abnormal mitoses was induced by sample with iron; mitotic spindle disturbances, mono- and multi-polar mitoses, and some chromosome lagging were most frequently observed; iron-depleted samples induced abnormal mitoses in a similar manner to the samples with iron; in presence of antioxidants, frequency of abnormal mitoses were significantly decreased	[37]

Table 6. Dermal irritation and sensitization studies of Diatomaceous Earth

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
IRRITATION					
IN CHEMICO / IN VITRO STUDIES					
100% Diatomaceous Earth; flux-calcined	20 mg; undiluted	Reconstituted human epidermis samples	EpiSkin™ reconstituted human epidermis model test in accordance with OECD TG 431; duplicate tissues treated for 3, 60, and 240 min	Non-corrosive; relative mean viability after exposure to test material for 3, 60, and 240 min was 102.8%, 111.3%, and 114.1%, respectively; qualitative evaluation indicated tissue was viable at each time point following exposure to test material; positive and negative controls yielded expected results	[5]
Diatomaceous Earth; flux-calcined, purity not reported	Not reported	Reconstituted human epidermis samples	EpiSkin™ reconstituted human epidermis model test; tissues treated for 15 min before incubation for 42 h; no further details reported	Not irritating; relative mean viability after exposure to test material was 102.6%; qualitative evaluation indicated tissue was viable following exposure to the test material; positive and negative controls yielded expected results	[5]
HUMAN					
100% Diatomaceous Earth; flux-calcined	0.02 mg; undiluted	10 subjects	Acute skin tolerance test; 48-h single patch test using Finn Chambers; occluded; test material applied to external face of the arm	Not irritating	[41]
Product containing 9% - 11% Diatomaceous Earth (Diatomaceous Earth contained < 0.11% respirable crystalline silica); soda ash flux-calcined	Amount not reported; undiluted	11 subjects with sensitive skin	Acute 24-h skin tolerance patch test; occluded; no further details	Not irritating	[42]
SENSITIZATION					
ANIMAL					
Diatomaceous Earth; flux-calcined, purity not reported	0%, 2.5%, 5%, or 10% in propylene glycol; 25 µl	Groups of 4 female CBA mice	LLNA; animals received test material daily on dorsum of each ear lobe for 3 consecutive days; positive control group received 90% phenylacetaldehyde in a solution of propylene glycol (final concentration 2.5% v/v)	Not sensitizing; all treated animals survived treatment; no clinical signs of toxicity observed in any test groups; stimulation indices (SI) for 2.5%, 5%, and 10% dose groups were 1.13, 0.97, and 0.99, respectively; SI of positive control was 18.43	[5]
HUMAN					
Cosmetic formulation containing 0.9% - 1.1% Diatomaceous Earth (Diatomaceous Earth contained < 0.11% respirable crystalline silica); soda ash flux-calcined	25 µl; applied neat	100 healthy subjects with normal skin	HRIPT according to Marzulli-Maibach method; test material applied on back of subjects with Finn Chambers on Scanpor®; occluded; duplicate patches without test material applied to serve as control only during the induction phase; induction patches occurred 3 times a week for 3 wk and a 2-wk rest period occurred prior to the single challenge patch; patches were in place for 48 h	Not irritating and not sensitizing	[43]
PHOTOTOXICITY					
HUMAN					
Product containing 9% - 11% Diatomaceous Earth (Diatomaceous Earth contained < 0.11% respirable crystalline silica); soda ash flux-calcined	0.2 ml; undiluted	10 healthy female subjects	Phototoxicity study of single application of test material on each forearm; occluded for 24 h; one arm was irradiated with UV-A (4 F4OBL with fluorescent tubes; 320-400 nm), while the other arm served as control	Not phototoxic; no skin reactions observed on irradiated product site and control site without product; very slight transient erythema observed in 1 subject on non-irradiated product site	[44]

Table 7. Occupational exposure studies of Diatomaceous Earth

Diatomaceous Earth Composition	Study Population and Location	Time Frame Examined	Procedure/Parameters Measured/Limitations	Findings	Reference
Quarry dust was essentially amorphous silica with quartz content of crude Diatomaceous Earth being 2%; mill dust had high percentage of cristobalite	869 workers of 5 plants in California, Nevada, and Oregon	1953-1954	X-ray investigation	-9% of the workers had lung changes interpreted as pneumoconiosis and that an equal number had doubtful changes -prevalence of abnormal chest films especially high in employees in mills -exposure in quarries associated with a lower proportion of abnormal films; none of 25 employees who had worked there exclusively for over 5 yr had a positive film, but 40% showed doubtful linear nodular changes	47
Same as above	Follow-up study in 428 workers from one plant from the above study (state not specified); plant included a quarry and a mill	1974; including employees terminated between July 1, 1969 and July 1, 1974	X-ray investigation	-films interpreted as positive for pneumoconiosis (Union for International Cancer Control (UICC)/Cincinnati classification of 1/1) observed in 20 (4.7%) of the workers -another 6 films had a UICC/Cincinnati classification of 1/0 -of these 26, 14 were determined to have findings consistent with Diatomaceous Earth pneumoconiosis, and all but 2 of these 14 had been employed before 1953 -in 129 employees in the industry for 20 yr or more, 13 had positive films considered consistent with Diatomaceous Earth pneumoconiosis, of which 6 had negative films in 1953 -only 4 individuals had complicated or coalescent lesions: these workers had been mill workers employed 27- 46 yr -no massive coalescent lesions or distorting changes noted in the existing work force -researchers pointed out that this evidence agreed with earlier observations indicating that the risk of pneumoconiosis was relatively low in workers whose exposure was confined to crude Diatomaceous Earth, as compared with those exposed to calcined Diatomaceous Earth -researchers noted that strict occupational dust control measures and personal protective equipment led to the near elimination of new cases of Diatomaceous Earth pneumoconiosis	48
Raw material contained ~ 4% crystalline silica; calcined and fluxed-calcined material had 10-20% and 20-25% cristobalite, respectively	2570 white male Diatomaceous Earth mining and processing workers in California; at least 12 mo cumulative service	1942-1987	Mortality patterns analysis; mortality trends assessed in respect of an index of cumulative exposure to crystalline silica and crystalline silica index; workers with known potential occupational asbestos exposure excluded; cigarette smoking was a confounding factor	-all causes combined standardized mortality ratio (SMR) slightly increased when compared with rates among US white males (SMR 1.12: 628 observed) -increased risks from lung cancer (SMR 1.43; 59 observed) and non-malignant respiratory disease (NMRD; excluding infectious diseases and pneumonia; SMR 2.59, 56 observed) were main contributors to the observed excess -excess lung cancer also observed when rates were compared with local county rates instead of the US national rates -increasing gradients of risk detected for lung cancer and NMRD with both crystalline silica exposure indices -researchers stated smoking was not likely to account for all associations between dust exposure and lung cancer -prior to the 1950s, poor dust control measures likely largest contributors to lung cancer and NMRD; the absence of excess lung cancer in workers hired after 1960 and no deaths attributed to pneumoconiosis in workers hired after 1950 indicated exposure reductions were successful in reducing excess risks in workers	49
Same as above	2342 white male Diatomaceous Earth workers; a subset of the above California workers cohort (406 had been excluded due to potential inadequate exposure data or definitive asbestos exposure	1942-1987	Mortality patterns analysis as above; results not likely to be confounded by smoking or asbestos exposure	-mortality excesses detected for NMRD (SMR 2.01) and lung cancer (SMR 1.29) -mortality from NMRD rose sharply with cumulative exposure to respirable crystalline silica (mostly cristobalite), indicating a strong dose-response relationship for crystalline silica and NMRD mortality -while not as strong of a relationship, lung cancer results further support an etiologic role for crystalline silica	50

Table 7. Occupational exposure studies of Diatomaceous Earth

Diatomaceous Earth Composition	Study Population and Location	Time Frame Examined	Procedure/Parameters Measured/Limitations	Findings	Reference
Same as above	1809 white male Diatomaceous Earth workers; a subset of the above California workers cohort; workers had at least 1 yr of exposure to crystalline silica	1942-1987	X-ray investigation	-81 workers (4.5%) had opacities on chest radiographs -age-adjusted relative risk of opacities increased significantly with cumulative exposure to crystalline silica -risk of opacities for cumulative exposure to crystalline silica of 2.0 mg/m^3-yr was 1.1% when average crystalline silica exposure was < 0.50 mg/m^3, but was 3.7% when average crystalline silica exposure was > 0.50 mg/m^3	51
Same as above	759 white male Diatomaceous Earth workers; a subset of the above California workers cohort;	1942-1987	X-ray and spirometry investigation; chest radiographs interpreted by the International Labor Office (ILO) system; individual-based reconstructed exposure indices for total dust (largely Diatomaceous Earth) and cristobalite were used in performing regression analyses	-of 492 chest radiographs, 5% had ILO scores > 1/0 and 25% had score of 0/1 or higher -radiographic patterns were not typical of classic silicosis - regression analyses showed there was a relationship between both total cristobalite exposure and total dust exposure and the ILO score -differences observed in spirometric data according to radiographic ILO category, but the results were inconsistent and did not allow for determining if physiologic changes were associated with radiographic change or through confounding factors, such as smoking -researchers noted that recent exposure level may produce radiographic abnormalities, but a demonstrable physiologic effect may not be observed; this decrease in observed effects was noted to be due to modern dust control measures.	52

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Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: November 22, 2021

SUBJECT: Diatomaceous Earth

Seppic. 2021. Memo concerning type of Diatomaceous Earth used in cosmetic ingredients.

La Garenne Colombes, November 19th, 2021

Object: CIR Review of Diatomaceous Earth

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Paris La Défense
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France

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www.seppic.com

Dear Sirs,

Regarding your request linked to the CIR review of Diatomaceous Earth, we are pleased to share some additional information as requested, based on indication coming from our raw material suppliers and referring to the commercial products we are supplying.

1. Clarification of the type of Diatomaceous Earth used in cosmetics (i.e., natural, calcined, and/or flux-calcined) (Note: The International Diatomite Producers Association has stated that only natural Diatomaceous Earth is used in cosmetics, is this correct?)

Our Diatomaceous Earth is identified by the CAS Number: 68855-54-9 Kieselguhr, soda ash flux-calcined

2. Method of manufacture for the type(s) of Diatomaceous Earth used in cosmetic products

Our ingredients containing Diatomaceous Earth are obtained following this flowchart : Harvesting - Calcination - Milling - Sieving - Quality control - Packaging - Quality control

3. Composition and impurities data (including crystalline silica content) on the type(s) of Diatomaceous Earth that is used in cosmetic products

Our cosmetics ingredients containing Diatomaceous Earth are classically used into finish cosmetic products below 10%.

We have evaluated the RCS: Respirable Crystalline Silica of our ingredients based on Diatomaceous Earth: cristobalite < 1% of RCS based on SWeRF method. (www.crystalline silica.eu)

Best Regards,

Léa Seidenbinder
Head of Beauty Care Actives Ingredients

Hervé Rolland
Head of sectoral Regulatory Affairs

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: November 30, 2021

SUBJECT: Lithothamnion Calcareum Powder and Diatomaceous Earth

Biotech Marine. 2015. Manufacturing process Phycocorail™ (Lithothamnion Calcareum Powder and Diatomaceous Earth).

Biotech Marine. 2017. Statement Phycocorail™ Composition File (Lithothamnion Calcareum Powder and Diatomaceous Earth).

Palmer Research. 2003. Etude de la tolerance cutanee aigue d'un produit cosmetique chez le volontaire adulte: Patch-test 24 heures occlusif. Pycocorail (contains 57-61% Lithothamnion Calcareum Powder and 9-11% Diatomaceous Earth).

Seppic. 2001 Protocol. HET-CAM Test: Pycocorail® (contains 57-61% Lithothamnion Calcareum Powder and 9-11% Diatomaceous Earth).

MANUFACTURING PROCESS
PHYCOCORAIL™

HARVESTING *(Lithothamnion Calcareum)*

↓

DRYING

↓

GRINDING

↓

MICRONISATION

↓

IONIZATION

↓

MIXTURE ← MANNITOL, ZINC SULFATE, DIATOMACEOUS EARTH

↓

PACKAGING

↓

QUALITY CONTROL

Production Manager
Jean-Marc CATROUX

BIOTECHMARINE (06/08/2015)

BiotechMarine - Z.I. - B.P.72 - 22260 Pontrieux (FR)
Tel.: +33 (0)2 96 95 31 32 - Fax: +33 (0)2 96 95 31 30
ww.biotechmarine.com

Statement PHYCOCORAIL™ COMPOSITION FILE

(In accordance with EN 45014 General criteria for supplier's declaration of conformity)

We declare, by the present one, that the following product supplied by BIOTECHMARINE:

PHYCOCORAIL™

INCI NAME (USA): Lithothamnion Calcareum Powder*- Mannitol - Diatomaceous Earth - Zinc Sulfate

**update by PCPC to have the most accurate scientific name for the algae compared with the former INCI name in Lithothamnium Calcarum Powder*

Composition

Components	Components usual Name	Function	% (Concentration range)
Lithothamnion Calcareum Powder* **update by PCPC to have the most accurate scientific name for the algae compared with the former INCI name in Lithothamnium Calcarum Powder**		Active	57,0 - 61,0
Mannitol	D-Mannitol	Active	29,0 - 31,0
Diatomaceous Earth	Kieselguhr, soda ash flux-calcined	Active	9,0 - 11,0
Zinc Sulfate	Zinc Sulfate heptahydrate	Active	0,7 - 1,5

This certificate was established to the best of our knowledge and/or according to our suppliers' statements, at the date of this certificate. It is however your responsibility to abide by any clause of any regulations, which may apply to the product that you manufacture, or to the use you make of our product.

Document approved at Pontrieux, on June 26, 2017

By Laëtitia LE GUILLOU
Regulatory & Documentary Affairs from BIOTECHMARINE

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PALMER
RESEARCH

Etude de la tolérance cutanée aiguë d'un produit cosmétique chez le volontaire adulte: Patch-test 24 heures occlusif

Version n° 01/003 du 06 février 2003

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Etude : TCP24H/PA-03/0063 (1030033PA)

Produit : PHYCOCORAIL 209338

Contains 57-61% Lithothamnion Calcareum Powder

Promoteur : **SECMA BIOTECHNOLOGIES MARINES**
ZI
BP65
22260 PONTRIEUX
FRANCE

St Etienne, le 06 février 2003.

SOMMAIRE

RESUME DU RAPPORT D'ETUDE

Promoteur : SECMA BIOTECHNOLOGIES MARINES **Adresse : ZI** **BP65** **22260 PONTRIEUX** **FRANCE**	**Produit : PHYCOCORAIL 209338** **Code PALMER : PA-03/0063**

ETUDE DE LA TOLERANCE CUTANEE AIGUE D'UN PRODUIT COSMETIQUE CHEZ LE VOLONTAIRE ADULTE : PATCH-TEST 24 HEURES OCCLUSIF

Date de l'étude	L'étude s'est déroulée du 29 au 31 janvier 2003.	
Lieu de l'étude	PALMER Research 13 rue Le Chatelier 42100 ST ETIENNE	
Objectif	Déterminer le potentiel irritant primaire d'un produit cosmétique après application unique sous pansement occlusif pendant 24 heures chez le volontaire.	
Méthodologie	Etude en ouvert.	Nombre de sujets : 11 à peau sensible.
Critères d'inclusion	Peau indemne de toute lésion dermatologique, sujet non allergique.	• Durée de l'application : 24 heures. • Condition d'utilisation : pur
Critères d'évaluation	Détermination du score d'irritation moyen : $I.I.M = \frac{\text{score total des réactions (érythème + œdème)}}{\text{nombre total de volontaires}}$ Les réactions sont cotées de 0 à 3.	
Méthodes d'analyse	Classement du produit en fonction de son I.I.M : Si I.I.M < 0,20 Non Irritant Si 0,20 ≤ I.I.M < 0,50 Légèrement Irritant Si 0,50 ≤ I.I.M < 1 Moyennement Irritant Si I.I.M ≥ 1 Irritant	
Conclusion	L'indice d'irritation moyen du produit **PHYCOCORAIL 209338** est égal à **0** aux lectures 30 minutes et 24 heures. Il est donc **non irritant.**	
Investigateur : **Dr Florence DURAFOUR,** ***Dermatologue***		

Introduction

Certificat d'authenticité des résultats

1 - INTRODUCTION

A la demande de la société **SECMA BIOTECHNOLOGIES MARINES – ZI - BP65 - 22260 PONTRIEUX - FRANCE,** nous avons évalué sur 11 volontaires adultes, la tolérance cutanée aiguë ou potentiel irritant du produit :

PHYCOCORAIL 209338

après application unique sur la peau du dos (zone scapulaire), sous pansement occlusif maintenu pendant 24 Heures (Patch-Test 24 heures).

Cet essai a été réalisé "en ouvert" selon la méthodologie des essais épicutanés sous occlusion.

Pour réaliser cette étude, nous avons reçu le 27 janvier 2003 un échantillon du produit que nous avons référencé sous le code PALMER Research **PA-03/0063**.

L'essai a commencé le 28 janvier 2003 pour s'achever le 31 janvier 2003.

2 - CERTIFICAT D'AUTHENTICITE DES RESULTATS

L'étude faisant l'objet du présent rapport a été conduite sous ma responsabilité, en conformité avec le protocole expérimental et dans le respect des règles des Bonnes Pratiques Cliniques.
Toutes les observations et les données numériques recueillies au cours de cet essai sont rapportées dans le présent document.

Après relecture et en tant qu'Investigateur, je certifie ces données conformes
à la réalité des résultats obtenus.
Docteur Florence DURAFOUR, *Dermatologue.*

Date : 13.02.03 Signature :

Ce rapport a été audité par l'Unité Assurance Qualité.
Il est considéré comme étant le reflet exact des données générées et des procédures en vigueur en rapport avec les Bonnes Pratiques Cliniques.

Date : 14.02.03 Nom : Noncharin Isabelle

Signature :

Protocole expérimental

3 - PROTOCOLE EXPERIMENTAL

L'essai a été réalisé au protocole interne référence TCP24H.

3.1 - Volontaires

3.1.1 - Caractéristiques des sujets inclus

- ✓ 11 sujets à peau sensible ont été inclus dans l'essai,
- ✓ dont 10 de sexe féminin et 1 de sexe masculin,
- ✓ âgés de 18 à 60 ans.

Tous les sujets devaient répondre aux critères d'inclusion et ne présenter aucun critère de non-inclusion, dont en particulier :

3.1.2 - Critères d'inclusion

- ✓ Aucun antécédent d'intolérance ou d'allergie à un produit cosmétique,
- ✓ acceptation de signature du consentement éclairé de participation,
- ✓ phototype I à III.

3.1.3 - Critères de non-inclusion

- ✓ Femme enceinte ou qui allaite ou prévoyant un début de grossesse en cours d'étude,
- ✓ pathologie cutanée sur la zone d'expérience (psoriasis, eczéma, vitiligo, pytiriasis versicolor, acné, etc...),
- ✓ présence d'un traitement médicamenteux per os:
  - antihistaminiques, anti-inflammatoires et/ou antibiotiques < 1 semaine,
  - Néo-codion® et/ou corticoïde < 4 semaines,
  - immunosuppresseur, rétinoïde et/ou anti-cancéreux < 6 mois,
- ✓ début, arrêt ou changement de traitement hormonal (y compris pilule contraceptive) < 1 mois et demi,
- ✓ exposition au soleil ou aux UV < 1 mois au niveau du dos,
- ✓ personne présentant une peau hyper irritable ou personne se sachant déjà sensibilisée au produit (si la formulation du produit est connue du Laboratoire PALMER).
- ✓ personne présentant une pilosité importante, des taches de rousseur, des grains de beauté ou un tatouage au niveau du dos,
- ✓ sujet atteint d'une maladie grave ou évolutive,
- ✓ usage immodéré de l'alcool ou du tabac.

3.2 - Méthodologie

3.2.1 - Matériel, dose, durée

Le produit a été appliqué, pur , une seule fois, sur une surface d'environ 50 mm^2 de peau de la zone scapulaire de chaque volontaire, à la dose d'environ 0,02 ml, imprégnant la surface d'une rondelle de papier filtre déposée dans la cupule du patch.

Note: La raison du choix de la dose est conditionnée par la capacité de la cupule, indiquée par le fabricant des "Finn Chambers®".

Le produit a été maintenu en contact avec la peau pendant 24 heures consécutives.

Cette application a été effectuée parallèlement et dans les mêmes conditions avec un patch-test seul (sans produit) en tant que témoin négatif.

3.2.2 - Lectures

Les examens macroscopiques cutanés ont été réalisés dans les mêmes conditions, en particulier au niveau de l'éclairage (lampe « lumière du jour »), 30 minutes après l'enlèvement des patchs. En l'absence de toute réaction cutanée locale à la lecture de 30 minutes après enlèvement du pansement, l'essai a été arrêté. Cependant, il a été demandé à chaque volontaire de vérifier le lendemain l'absence de réaction. Dans le cas d'une réaction visible, le sujet devait revenir au centre, des lectures pouvant être effectuées jusqu'à réversibilité des réactions cutanées.

Les cotations des éventuelles réactions d'irritation sur chaque site ayant reçu le produit étudié ont été réalisées comparativement au site sans produit, selon les échelles numériques* suivantes :

Erythème « E » :

E = 0 : absence d'érythème
E = 0.5 : érythème très léger (à peine perceptible)
E = 1 : érythème léger (bien visible)
E = 2 : érythème modéré
E = 3 : érythème important

Œdème « O » :

O = 0 : absence d'œdème
O = 0.5 : œdème très léger (palpable, à peine visible)
O = 1 : œdème léger (visible)
O = 2 : œdème modéré (net) avec ou sans présence de papules ou vésicules
O = 3 : œdème important (surface débordant la zone d'application) avec présence de vésicules ou présence d'une bulle

Les modifications de structure cutanée (dessèchement, rugosité, épaississement, réflectivité) pouvant être liées à la nature même du produit étudié ou à l'un des ingrédients, ont fait l'objet d'une description clinique dont l'intensité de chaque modification a été appréciée selon le barème :

?+ = douteux
\+ = net
++ = modéré
+++ = important

*3.2.3 – Interprétation des résultats**

L'analyse et l'interprétation des résultats ont été réalisées en fonction des données obtenues dans les conditions expérimentales, à chaque temps de lecture.

Elles sont descriptives et complétées par le calcul d'un indice d'irritation moyen (IIM) à chaque temps de lecture, selon le rapport :

$$\text{IIM} = \frac{\Sigma \text{ des cotations (érythème + œdème)}}{\text{Nombre de sujets}}$$

Cet indice ainsi obtenu (maximum 12), permet de classer arbitrairement le produit cosmétique étudié selon le barème d'interprétation suivant :

IIM	Classe
< 0.20	**Non irritant (NI)**
0.20 ≤ IIM< 0.50	**Légèrement irritant (LI)**
0.50 ≤ IIM< 1	**Moyennement irritant (MI)**
IIM ≥ 1	**Irritant (I)**

Les valeurs individuelles et la catégorie de produits cosmétiques et d'hygiène à laquelle appartient le produit étudié ont également été prises en compte pour une conclusion adaptée dans les conditions de l'essai (24 heures sous pansement occlusif).

référence bibliographiques :

- *« Les essais cliniques en dermatologie », Thérapie, 1991, Tome 46, pages 183 à 187*
- *« Dermato-allergologie de contact », G. DUCOMBS, Editions MASSON, 1988 pagez 13 à 16 ; 36-37*
- *« Dermatotoxicology Methods : The laboratory worker's VADEMECUM » ; N. MARZULLI – H. MAIBACH. Ed. Taylor & Francis, 1998.*

Résultats

4 - RESULTATS

Les résultats individuels des lectures à chaque temps expérimental sont regroupés dans le tableau ci-dessous.

PHYCOCORAIL 209338
(patch test 24 heures occlusif – pur)

SUJETS				LECTURES									
				Lecture 30 min après enlèvement du patch occlusif					Lecture 24 heures après enlèvement du patch occlusif				
N°	Identification	Age et sexe (1)	Type de peau	Témoin		Produit à l'essai		Modification de structure	Témoin		Produit à l'essai		Modification de structure
				E	O	E	O		E	O	E	O	
14S05	BRI Ma	44 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
15S05	SMA Ch	43 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
16S05	VER Ca	28 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
17S05	BLA Br	41 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
18S05	CON Je	19 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
19S05	LAS Jo	60 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
20S05	WIL Co	30 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
21S05	SEB Ha	20 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
22S05	MON Au	21 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-
23S05	PAT Ni	18 ans / M	Sensible	0	0	0	0	-	0	0	0	0	-
25S05	MIG Co	32 ans / F	Sensible	0	0	0	0	-	0	0	0	0	-

I.I.M	**0**	**0**
Résultats	**non irritant**	**non irritant**

(1) : M = masculin
F = féminin

Conclusion

5 - CONCLUSION

Dans les conditions expérimentales retenues, 30 minutes et 24 heures après l'enlèvement du pansement occlusif, aucun volontaire n'a présenté de réaction d'irritation significative d'une réaction d'intolérance cutanée.

Par ailleurs, aucun effet secondaire n'a été observé.

On peut donc conclure que le produit **PHYCOCORAIL 209338, code PALMER Research PA-03/0063**, appliqué pur et localement sous pansement occlusif pendant 24 heures, sur 11 volontaires adultes ayant la peau sensible, s'est révélé **non irritant.**

Dr Florence DURAFOUR
Dermatologue

STUDY SUMMARY REPORT

Sponsor : SECMA BIOTECHNOLOGIES MARINES **Address :** **ZI-BP65** **22260 PONTRIEUX** **FRANCE**	**Product : PHYCOCORAIL 209338** **PALMER Research code : *PA-03/0063***

DETERMINATION OF THE IRRITATION POTENTIAL OF A COSMETIC PRODUCT ON HUMAN SUBJECT: 24-HOURS SINGLE OCCLUSIVE PATCH-TEST

Study date:	The study took place from January 29th to January 31st, 2003.	
Study place(s):	PALMER Research 13 rue Le Chatelier 42100 ST ETIENNE	
Objective(s):	Determination of the acute skin tolerance of a cosmetic product by application under occlusive patch over a 24-hours period.	
Methodology:	Open Study.	Number of subjects : 11 with sensitive skin.
Included criteria:	Skin without any dermatological lesion, non allergic volunteer.	• Length of application: 24 hours • Condition of use : pure
Evaluation criteria:	Calculation of an acute irritation index : $M.I.I = \frac{\text{total cutaneous reactions score (erythema + oedema)}}{\text{number of volunteers}}$ Skin responses are scored from 0 to 3.	
Analysis:	Classification of the product according to its M.I.I: if M.I.I < 0.20 Non-irritant if $0.20 \leq$ M.I.I < 0.50 Slightly irritant if $0.50 \leq$ M.I.I < 1 Moderately irritant if M.I.I $\geq$ 1 Irritant	
Conclusion:	The irritation index of the product **PHYCOCORAIL 209338** is equal to 0 at the 30-minutes and at the 24-hours readings. It is thus classified as **non-irritant** to human skin.	
Dr Florence DURAFOUR **Dermatologist**		

Phycocorail®

(contains 57-61% Lithothamnion Calcareum Powder)

HET-CAM Test

Tolerance on the chorio allantoïc membrane of a hen's egg

Expert report Tox HETCAM SEPPIC 3493-3495
Phycocorail 2% 10% water a Confidential

1. TEST ITEMS INFORMATION

Test item:	Phycocorail
Batch:	12.04.080
Purity:	Considered as about 100 % dry matter
Tested doses:	2% (TOX13093); 5% (TOX13094) and 10% (TOX13095) w/v dilutions
Vehicle:	Water
pH:	7.4 - 7.7
Physical appearance:	Samples appeared as beige liquids.

2. PROTOCOL

A trial was carried out based on the official method published on 26th December 1996 - Appendix IV - **internal procedure 57CO009 - revised on 26/12/2001.**

• The product was tested on the chorio-allantoïc membrane of fertilised LEGHORN hens' eggs which had been incubated for 10 days at a temperature of 37.8°C (+- 0.5°C) at a humidity of 50 to 60%.

• 0.3 mL of the prepared sample was spread over the chorio-allantoic membrane using a 1 mL pipette. The stop watch was started when the product had been applied. Rinsing with 5 mL of demineralised water was carried out 20 seconds later.

• The objective is to measure the exact moment when the three following phenomena appear (between t0 and 5'):

- °Hyperaemia (Hy): vasodilatation observed from the appearance of new capillaries or the dilation of capillaries which were already visible.
- °Haemorrhage (Ha): Effusion of blood outside of vessels and capillaries
- °Coagulation (Co): Membrane opacity or thrombosis.

• On the basis of the average times (T) obtained on 4 or 6 eggs (depending on the reproducibility of the measurement), a total score (I) is assigned to the tested product, according to the following calculation:

$$I = 5 \times (301 - T_{Hy}) + 7 \times (301 - T_{Ha}) + 9 \times (301 - T_{Co})$$

The classification was carried according to the following chart:

Score	Class
score < 1	*non irritant*
1 ≤ score < 5	*slightly irritant*
5 ≤ score < 9	*moderately irritant*
9 ≤ score < 12	*irritant*
score ≥ 12	*severely irritant*

3. RESULTS AND CONCLUSION

Dose	Reaction time (seconds)			
% (w/v)	HYPERAEMIA	HAEMORRHAGE	COAGULATION	SCORE
2%	301	301	301	0
5%	301	301	301	0
10%	91	91	301	8.4

PHYCOCORAIL (batch 12.04.080) has consequently appeared, under the trial's experimental conditions, to be **NON IRRITANT** in **2%** and **5%** dilutions and **MODERATELY IRRITANT** in **10%** dilution.

Remarks:

- Due to its low solubility and its rapid sedimentation, the 10% dilution was not easy to handle. Nevertheless, the results were reproducible between the eggs and considered as relevant.
- The pure powder form of the product was also tested. Because of its sticky character, it did not allow a good dispersal over the chorio-allantoic membrane. So the results were not considered as relevant.

Catherine PERRIN **Gaelle VINCENT**

Nota

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Tox HETCAM SEPPIC 3493-3495 Phycocorail 2% 10% water :

Tox HETCAM SEPPIC 3493-3495 Phycocorail 2% 10% water a

Concentration of Use by FDA Product Category – Diatomaceous Earth

Product Category	Maximum Concentration of Use
Hair dyes and colors	0.001%
Nail polish and enamels	0.0049-0.01%
Paste masks and mud packs	2%

Information collected in 2021

Table prepared: December 16, 2021

2022 FDA VCRP Raw Data

DIATOMACEOUS EARTH	03C	Eye Shadow	1
DIATOMACEOUS EARTH	03D	Eye Lotion	1
DIATOMACEOUS EARTH	05G	Tonics, Dressings, and Other Hair Grooming Aids	1
DIATOMACEOUS EARTH	07B	Face Powders	5
DIATOMACEOUS EARTH	07E	Lipstick	6
DIATOMACEOUS EARTH	08A	Basecoats and Undercoats	1
DIATOMACEOUS EARTH	08E	Nail Polish and Enamel	49
DIATOMACEOUS EARTH	09A	Dentifrices	11
DIATOMACEOUS EARTH	10A	Bath Soaps and Detergents	1
DIATOMACEOUS EARTH	10B	Deodorants (underarm)	3
DIATOMACEOUS EARTH	10E	Other Personal Cleanliness Products	2
DIATOMACEOUS EARTH	12A	Cleansing	4
DIATOMACEOUS EARTH	12C	Face and Neck (exc shave)	8
DIATOMACEOUS EARTH	12D	Body and Hand (exc shave)	1
DIATOMACEOUS EARTH	12F	Moisturizing	6
DIATOMACEOUS EARTH	12G	Night	1
DIATOMACEOUS EARTH	12H	Paste Masks (mud packs)	25
DIATOMACEOUS EARTH	12J	Other Skin Care Preps	9