

# Safety Assessment of Boron Nitride as Used in Cosmetics

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## Abstract

The Cosmetic Ingredient Review Expert Panel (Panel) assessed the safety of boron nitride which functions in cosmetics as a slip modifier (ie, it has a lubricating effect). Boron nitride is an inorganic compound with a crystalline form that can be hexagonal, spherical, or cubic; the hexagonal form is presumed to be used in cosmetics. The highest reported concentration of use of boron nitride is 25% in eye shadow formulations. Although boron nitride nanotubes are produced, boron nitride is not listed as a nanomaterial used in cosmetic formulations. The Panel reviewed available chemistry, animal data, and clinical data and concluded that this ingredient is safe in the present practices of use and concentration in cosmetic formulations.

## Keywords

boron nitride, safety, cosmetics

## Introduction

This report reviews the safety of boron nitride as used in cosmetics. Boron nitride is an inorganic compound reported to function in cosmetics as a slip modifier. Although the *International Cosmetic Ingredient Dictionary and Handbook* does not specify which crystal form(s) is(are) used in cosmetics,<sup>1</sup> it is presumed that the hexagonal form of boron nitride is used because that form (similar to graphite) matches the functionality in cosmetics.

In the 2011 Associations Survey of Nanomaterials Used in Cosmetic Products, a report prepared for the International Cooperation on Cosmetic Regulation by a working group of the Personal Care Products Council (Council), Canadian Cosmetic Toiletry, and Fragrance Association, COLIPA (now known as Cosmetics Europe), and the Japanese Cosmetic Industry Association, boron nitride is not listed as a nanomaterial used in cosmetic formulations.<sup>2</sup> This safety assessment prepared by the Cosmetic Ingredient Review (CIR) includes (limited) toxicity data on boron nitride nanotubes because although boron nitride is not thought to be a nanomaterial used in cosmetic formulations, these data demonstrate the lack of toxicity of boron nitride.

## Chemistry

### Definition and Structure

Boron nitride (CAS No. 10043-11-5) is an inorganic compound, with the chemical formula BN.<sup>1</sup> The compound can assume 3

crystal polymorphs. One is a flat, hexagonal crystalline structure, similar to graphite, except that the carbon atoms are replaced by boron and nitrogen atoms.<sup>3,4</sup> The alternate boron and nitrogen atoms form interlocking hexagonal rings, each with 3 boron atoms and 3 nitrogen atoms, and the layers are held together by van der Waals forces (Figure 1).<sup>5</sup> There is no boron–nitrogen bonding between the layers.<sup>6</sup> A spherical form, with a hexagonal crystal structure, can also occur.<sup>7</sup> Additionally, boron nitride can be in cubic form in which alternately linked boron and nitrogen atoms form a tetrahedral bond network (Figure 2).<sup>5</sup>

### Physical and Chemical Properties

The physical and chemical properties of boron nitride are provided in Table 1. The 3-ring, layered structure gives hexagonal boron nitride a lubricating effect, high thermal stability, and oxidation resistance.<sup>8</sup> The mean particle size of cosmetic-grade hexagonal boron nitride powder varies by trade names and grade, with sizes of 1 to 47  $\mu\text{m}$  reported.<sup>4,6,9-14</sup> Cubic boron

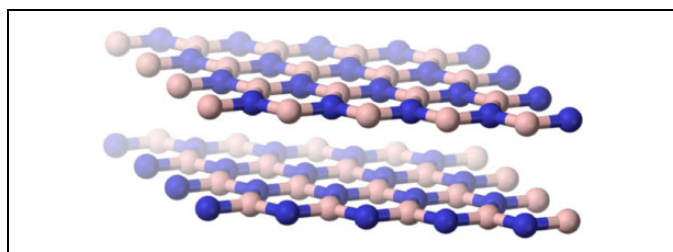
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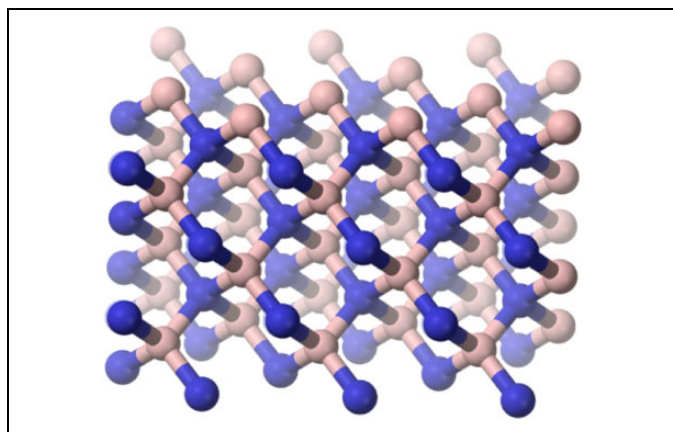
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**Figure 1.** Hexagonal boron nitride. Adapted from Barron.<sup>15</sup>



**Figure 2.** Cubic boron nitride. Adapted from Barron.<sup>15</sup>

nitride is the second hardest material known, with diamond being the hardest.<sup>5</sup>

### Method of Manufacture

Cosmetic-grade hexagonal boron nitride is synthesized using borax and a nitrogen source at a high temperature, resulting in a lamellar structure.<sup>6</sup> Industrial synthesis of hexagonal boron nitride powder is based on a 2-stage process.<sup>8</sup> First, at approximately 900°C, a boron source such as boron oxide or boric acid is converted in a reaction with a nitrogen source, mostly melamine, urea, or possibly, ammoniac, to amorphous boron nitride. In the second step, crystallization occurs at temperatures usually >1,600°C in a nitrogen atmosphere, and a transition into hexagonal boron nitride occurs. At high temperatures (600-2,000°C) and pressures (50-200 kbar), hexagonal boron nitride can be converted to the cubic phase.<sup>15</sup>

### Composition/Impurities

The typical chemical analysis of hexagonal cosmetic-grade boron nitride is ≥98 to 99.8% BN, 0.2% to 1.6% O<sub>2</sub>, 0.02% to 0.1% B<sub>2</sub>O<sub>3</sub>, and <1 ppm metals (such as Hg, As, and Pb).<sup>4,6,9-12</sup>

### Use

#### Cosmetic

Boron nitride is reported to function in cosmetics as a slip modifier, which means it purportedly helps other substances

**Table 1.** Chemical and Physical Properties.

Property	Description	Reference
Appearance	White powder; hexagonal or cubic crystals	39
	White, photostable, odorless powder (hexagonal, cosmetic grade)	40
	Colorless (cubic)	15
Bond length	Hexagonal: 1.466 Å (with interlayer spacing of 3.331 Å)	41
	Cubic: 1.56 Å	15
		15
Melting point	2,973°C; sublimes (hexagonal)	15
Mean particle size	1-47 μm (varies by trade name and grade)	4,6,9-14
	30 μm (spherical morphology)	7
		39
Density	2.18 g/cm <sup>3</sup>	6
	2.26 g/cm <sup>3</sup> (hexagonal, cosmetic grade)	4,6,9-12
Surface area	0.82-30 m <sup>2</sup> /g (hexagonal; varies by grade)	7
	4 m <sup>2</sup> /g (spherical morphology)	6
Refractive index	1.74 (hexagonal)	39
Solubility	Insoluble in water and in acid solutions	6
Stability	Chemically inert and stable (hexagonal)	8
Hardness	1-2 on the Mohs scale (hexagonal)	6
Coefficient of friction	<0.3	

to flow more easily and more smoothly, without reacting chemically, much like graphite.<sup>1,16</sup> This ingredient is a type of ceramic, having the smoothness and the chemical and thermal inertness associated with most ceramics.<sup>9</sup> According to the information supplied to the US Food and Drug Administration (FDA) by industry, as part of the Voluntary Cosmetic Registration Program (VCRP), the data reported (2013) that boron nitride is used in 643 cosmetic formulations (Table 2).<sup>17</sup> Data received in response to a survey of the maximum reported use concentration by category conducted by the Personal Care Products Council (Council) reported that boron nitride is used at concentrations up to 25%; the highest concentration of use is in eye shadow formulations.<sup>18</sup>

Although use in baby products was reported to the VCRP, concentration of use data were not reported by industry. Products containing boron nitride may be applied to the eye area (≤25% in eye product formulations), could possibly be ingested (2% in lipstick formulations), or may possibly be inhaled (≤16% in powders and at up to 0.9% in fragrance preparations). In practice, 95% to 99% of the particles released from cosmetic sprays have aerodynamic equivalent diameters in the 10 to 110 μm range.<sup>19,20</sup> Therefore, most particles incidentally inhaled from these sprays are deposited in the nasopharyngeal region and are not respirable to any appreciable amount.<sup>21,22</sup> Boron nitride is listed in the European Union inventory of cosmetic ingredients, and no restrictions are specified.<sup>23</sup>

#### Noncosmetic Use

The properties of hexagonal boron nitride allow for its use in a number of technological processes. Different forms of

**Table 2.** Frequency and Concentration of Use According to Duration and Type of Exposure.

	No. of uses <sup>17</sup>	Maximum concentrations of use, % <sup>18</sup>
Totals <sup>a</sup>	643	0.01-25
Duration of use		
Leave-on	641	0.01-25
Rinse-off	2	0.05
Diluted for (bath) use	NR	NR
Exposure Type		
Eye area	320	0.08-25
Incidental ingestion	3	2
Incidental inhalation—spray	12 <sup>b</sup>	0.8-0.9
Incidental inhalation—powder	103	1-16
Dermal contact	636	0.01-25
Deodorant (underarm)	NR	NR
Hair—noncoloring	4	0.05
Hair—coloring	NR	NR
Nail	2	2
Mucous membrane	3	2
Baby products	1	NR

Abbreviation: NR, none reported.

<sup>a</sup>Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

<sup>b</sup>Includes fragrance and suntan products.

hexagonal boron nitride are used for different applications: boron nitride, compacted by hot pressing or hot isostatic pressing, can be used in making shaped components for various industries; boron nitride-coating systems using suspensions and sprays are used to selectively change the properties of substrate surfaces; and powdered boron nitride-coating systems using powders and granules can be used in thermal management.<sup>8</sup> Hexagonal boron nitride can be used as an electrical insulator; as thermocouple protection sheaths, in crucibles and linings for reaction vessels; and as a coating for refractory molds used in glass forming and in superplastic forming of titanium.<sup>24</sup> It can also be incorporated in ceramics, alloys, resins, plastics, and rubber to give them self-lubricating properties.<sup>5</sup> Hexagonal boron nitride is used in the formulation of coatings and paints for high-temperature applications, and it is also used as a substrate for semiconductors, lens coatings, and transparent windows.<sup>25</sup>

Hexagonal boron nitride can be made in single layers to form nanotubes, and bundles of boron nanotubes are used for wire sleeving.<sup>5</sup> Boron nitride nanotubes are being produced commercially.<sup>26</sup>

Cubic boron nitride is used as an abrasive and wear-resistant coating; it is used for cutting tools and as abrasive components for shaping/polishing with low carbon ferrous metals.<sup>5</sup>

## Toxicokinetics

In a pharmacokinetics study, 4 New Zealand white rabbits were given an intravenous (IV) injection of 10 mg/kg body weight (bw) sterilized glycol chitosan (G-chitosan)-coated boron

nitride nanotubes in physiological solution.<sup>27</sup> Blood samples were taken at various intervals for up to 10 hours. Boron concentration was measured as an indicator of the presence of boron nitride nanotube. The terminal half-life was  $98 \pm 37$  minutes. The researcher stated that an absence of multiexponential kinetic components indicated no significant temporary accumulation of boron nitride nanotubes in tissues. The researchers also stated that the data suggested a “relatively high” clearance of boron nitride nanotubes from the blood and a quick distribution and/or excretion but also noted that the functionalization of the nanoparticles has a role in their behavior at a systemic level.

## Toxicological Studies

### Single-Dose (Acute) Toxicity

**Parenteral.** A single IV injection of 1, 5, or 10 mg/kg bw coated boron nitride nanotubes did not produce toxicity in rabbits.<sup>27,28</sup> In a pilot study, 3 New Zealand White rabbits received a single 1 mg/kg IV dose of G-chitosan boron nitride nanotubes in physiological saline at a concentration of 1 mg/mL.<sup>28</sup> Two control rabbits were given an IV dose of G-chitosan only. Blood samples were collected at 0, 2, 24, and 72 hours. No signs of toxicity were observed, and with the exception of an increased platelet count at 72 hours (that was still in the reference range), no differences in hematological parameters were observed between treated and control animals.

In a follow-up study, groups of 3 male New Zealand white rabbits were given a single IV dose of 5 or 10 mg/kg sterilized G-chitosan boron nitride nanotubes in physiological solution (average hydrodynamic size 500 nm).<sup>27</sup> Blood samples were collected 0, 1, 3, and 7 days after dosing. No signs of toxicity were observed, and the results of the hematological analysis were within normal limits.

### Repeated Dose Toxicity

**Parenteral.** G-chitosan boron nitride nanotubes also did not produce toxicity in a repeated dose study.<sup>27</sup> Three male New Zealand white rabbits were dosed by IV injection with 5 mg/kg bw/day sterilized G-chitosan boron nitride nanotubes in physiological solution for 3 consecutive days, and blood samples were taken as mentioned previously. As in the single-dose studies, no signs of toxicity were observed and results of the hematological analysis were within normal limits.

### Cytotoxicity

Contradictory results have been reported on the cytotoxicity of boron nitride nanotubes; this may be due to that fact the nanotubes were coated in one study but not in the other. In one study, boron nitride nanotubes (not coated) were found to be cytotoxic when evaluated using lung epithelial cells (A549), alveolar macrophages (RAW 264.7), and fibroblast cells (3T3-L1), as well as in human embryonic kidney cells (HEK 293).<sup>26</sup>

Tween 80 was used as the dispersing agent and yielded a suspension of individual nanotubes with long-term stability; the typical diameters were less than 80 nm (average of  $\sim 50$  nm), and the average length was  $\sim 10$   $\mu$ m. Cells were exposed to 0.02, 0.2, 2, and 20  $\mu$ g/mL of the nanomaterial. In a 3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay of cell proliferation, 2  $\mu$ g/mL boron nitride nanotubes produced a decrease in the MTT signal when compared to the untreated cells. At 48 hours, this result was time-, dose-, and cell type-dependent, with the greatest effect observed in cells with high endocytic (phagocytic) activity, that is, macrophages, and the lowest toxicity observed in cells with the lowest endocytic activity, that is, HEK 293 cells. A fluorometric DNA assay and fluorometric microculture assay were performed with lung A549 epithelial cells and RAW 264.7 macrophage cells to confirm these results, and exposures of 0.2, 2, and 20  $\mu$ g/mL nanomaterial were used. Similar results were obtained; a decrease of 60% to 80% in viable cell number was observed with 2  $\mu$ g/mL in macrophage cells, and a 30% loss was observed with 20  $\mu$ g/mL in A549 epithelial cells.

The results presented previously contradict earlier studies on boron nitride nanotubes that did not report cytotoxicity. In one study using human neuroblastoma SH-SY5Y cells, up to 100  $\mu$ g/mL G-chitosan-coated boron nanotubes were tested in 2 cell proliferation assays, an MTT-assay and a 2-(4-iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfophenyl)-2H-tetrazolium monosodium salt (WST-1) assay, a DNA content assessment, a viability/cytotoxicity assay, an early apoptosis detect assay, and a reactive oxygen species (ROS) assay.<sup>29</sup> A statistically significant reduction in MTT was observed at a concentration of 20  $\mu$ g/mL boron nitride nanotubes, but this reduction was not observed with G-chitosan alone or in WST-1. The researchers stated that, most likely, the boron nitride nanotubes interact with some tetrazolium salts, such as MTT, but not with others, such as WST-1, suggesting that the interference is due to the water insoluble nature of MTT formazan. The boron nitride nanotubes did not affect the DNA concentration, cell viability, apoptosis, or ROS formation.

In another study, HEK 293 cells were cultured with 100 mg/mL boron nitride tubules, which formed aggregates in culture media.<sup>30</sup> Cells cultured with boron nitride nanotubes were not different from cells cultured in media. Similar results were found with Chinese hamster ovary (CHO) cells.

The Expert Panel noted that all of these studies should be viewed with caution because the very low solubility of the test compounds requires solution vehicles that could bias the results. The exposures to cells *in vitro* are very different from the ways in which boron nitride might be presented to skin or epithelia in humans.

## Reproductive and Developmental Toxicity

Published reproductive and developmental toxicity studies were not found, and unpublished data were not provided.

## Genotoxicity

Published genotoxicity studies were not found, and unpublished data were not provided.

## Carcinogenicity

Published carcinogenicity studies were not found, and unpublished data were not provided.

## Irritation and Sensitization

### Dermal

**Human.** Boron nitride was a weak skin irritant in a 24-hour human patch test.<sup>31</sup> Occlusive patches of boron nitride, 50% in olive oil, were applied to 20 participants. Two participants exhibited a  $\pm$  response (Additional details were not provided).

Eye shadow formulations containing 13% boron nitride, tested at a concentration of 70% in squalane oil,<sup>32</sup> and 18.7% boron nitride, tested neat,<sup>33</sup> and face powder formulations containing 16% boron nitride<sup>34,35</sup> were not dermal irritants or sensitizers in human repeated insult patch tests (HRIPTs). The details of these studies are presented in Table 3.

### Ocular

**Nonhuman.** A short-term exposure (STE) test was performed to evaluate the irritation potential of boron nitride. An STE is an *in vitro* assay for ocular irritation that assesses cytotoxicity in a rabbit corneal cell line (SIRC cells) following a 5-minute treatment.<sup>36</sup> Boron nitride, tested at 0.05 and 5% in mineral oil, was ranked a minimal irritant in an STE test.<sup>31</sup>

Results of chorioallantoic membrane (CAM) assays also predicted that boron nitride is not an ocular irritant.<sup>31</sup> Boron nitride was assayed at 50% in Vaseline using the hen's-egg test-CAM (HET-CAM; which determines hemorrhage, lysis, and coagulation in the CAM of the egg after exposure to test chemicals<sup>37</sup>) and the CAM-trypan blue staining method (CAM-TB; which measures the amount of trypan blue adsorbed onto the CAM as the end point of the assay<sup>37</sup>).

**Human.** An eye shadow containing 13% boron nitride did not cause any adverse effects in a 2-week use study.<sup>38</sup> Thirty female participants completed the study, 17 of whom wore contact lenses. The eye shadow was applied at least 1 time daily.

## Summary

Boron nitride is an inorganic compound that can be hexagonal, spherical, or cubic in form. Hexagonal boron nitride is similar to graphite, whereas cubic boron nitride is similar to diamond. The mean particle size of cosmetic-grade hexagonal boron nitride powder varies by trade name and grade, with mean particle sizes of 1 to 47  $\mu$ m reported. Boron nitride nanotubes are produced commercially; however, boron nitride is not listed as a nanomaterial used in cosmetic formulations.

**Table 3.** Human Repeated Insult Patch Tests.

Test article	Concentration tested	No. of participants	Induction	Challenge <sup>a</sup>	Results	Reference
Eye shadow containing 13% boron nitride	70% in squalane oil	55	Occlusive 24-hour patches applied to the back 3×/wk for 3 weeks 0.1-0.15 g of the test material (dose of 25-39 mg/cm <sup>2</sup> ) per patch Test sites were examined 24-48 hours after patch removal	The patch was applied to a previously unpatched site  The site was scored immediately and 48 hours after patch removal	Not an irritant or sensitizer  No reactions were observed at any time	32
Pressed powder containing 16% boron nitride	Applied neat	107	20 mg of the test article was distributed evenly over the surface of an 8-mm filter paper Finn chambers were used  48-72 hours of patches were applied to the back 3×/wk for 3 weeks Test sites were examined 15-20 minutes after patch removal	Concurrent 48-hour challenge applications were made to the induction site and to a previously unpatched site  The sites were examined daily for 3 days upon patch removal	Not an irritant or sensitizer  No adverse effects were observed during induction or challenge	34
Face powder containing 16% boron nitride	Applied neat	104	As described previously	As described previously, with the exception that the sites were examined 30 minutes and 48 hours after patch removal	Not an irritant or a sensitizer  No adverse effects were observed during induction or challenge	35
Eye shadow containing 18.7% boron nitride	Applied neat	55	Occlusive 24-hour patches applied to the back 3×/wk for 3 weeks Amount applied was not stated  Test sites were examined 24-48 hours after patch removal	The challenge patch was applied to a previously unpatched site  the test sites were evaluated immediately and 24 hours and 48 hours after patch removal	Not an irritant or sensitizer  No reactions were elicited during induction of challenge	33

<sup>a</sup>The challenge followed a 2-week nontreatment period in each study.

Boron nitride is reported to function as a slip modifier in cosmetics, and it is presumed that this means the hexagonal form is used. The VCRP data report 643 uses of boron nitride, and concentrations of use of up to 25% were reported by the cosmetics industry, with the highest use concentration reported in eye shadow formulations.

In a pharmacokinetic study in which 4 New Zealand white rabbits were given an IV injection of 10 mg/kg bw sterilized glycol chitosan-coated (G-chitosan) boron nitride nanotubes in physiological solution, no significant temporary accumulation of boron nitride nanotubes in tissues was found. The researchers concluded there was a relatively high clearance of boron

nitride nanotubes from the blood and a quick distribution and/or excretion.

A single IV injection of 1, 5, or 10 mg/kg G-chitosan boron nitride nanotubes did not produce toxicity in rabbits. Toxicity also was not observed following repeated dosing with 5 mg/kg bw/day sterilized G-chitosan boron nitride nanotubes in physiological solution for 3 consecutive days.

Contradictory results have been reported on the cytotoxicity of boron nitride nanotubes. One study found that boron nitride nanotubes were cytotoxic when evaluated using lung epithelial A549 cells, alveolar macrophages RAW 264.7 cells, fibroblast 3T3-L1 cells, and human embryonic kidney HEK 293 cells, whereas another study reported that boron nitride was not cytotoxic to HEK 293 or CHO cells. In human neuroblastoma SH-SY5Y cells, up to 100 µg/mL G-chitosan-coated boron nanotubes caused a statistically significant reduction in MTT at a concentration of 20 µg/mL boron nitride nanotubes, but this reduction was not observed with G-chitosan alone or in WST-1 and was attributed to the water insoluble nature of MTT formazan. Boron nitride nanotubes did not affect DNA concentration, cell viability, apoptosis, or ROS formation in these cells.

Boron nitride, 50% in olive oil, was a weak skin irritant in a 24-hour human patch test. Eye shadow formulations containing 13% boron nitride, tested at a concentration of 70% in squalane oil, and 18.7% boron nitride, tested neat, and face powder formulations containing 16% boron nitride were not dermal irritants or sensitizers in HRIPTs.

In nonhuman testing, boron nitride, tested at 0.05% and 5% in mineral oil, was ranked a minimal irritant in an STE test. Additionally, boron nitride, assayed at a concentration of 50% in Vaseline, was negative in a HET-CAM assay and a CAM-TB assay. In human testing, an eye shadow containing 13% boron nitride did not produce any adverse effects in a 2-week use study.

## Discussion

Human repeat insult patch test data were available on formulations that contained boron nitride at concentrations up to 18.7%. Although sensitization data were not provided at the maximum reported leave-on use concentration of 25%, the Expert Panel concluded that the existing data were adequate. At a 50% concentration, boron nitride caused minimal irritation. At 18.7%, it was not a sensitizer nor would it be expected to sensitize given its inability to penetrate the stratum corneum. Additionally, boron nitride is not expected to be an ocular irritant at the maximum reported concentration of use; in a 2-week use study, an eye shadow containing 13% boron nitride did not cause any adverse effects.

The Expert Panel stated that although there are data gaps, this ingredient is stable, chemically inert, and completely insoluble, and the extended hexagonal crystal lattice structure makes boron nitride a very large molecule that is not expected to penetrate the stratum corneum. Even if it were to penetrate, it would not be expected to have chemical activity in biological

systems. Although boron nitride is not reported to be used in nanomaterial form in cosmetic formulations, the lack of toxicity observed in single- and repeated-dose IV studies with coated boron nitride nanotubes further supported the safety of boron nitride in other forms. Also, the fact that boron nitride is not expected to penetrate the skin precluded the need for repeated dose toxicity, reproductive and developmental toxicity, and carcinogenicity studies to complete this safety assessment.

The Panel discussed the issue of incidental inhalation exposure to boron nitride from powders and from products that may be aerosolized. Boron nitride is reportedly used at up to 16% in products that may become airborne (ie, in face powders) but only at very low concentrations in cosmetic products that may be aerosolized (ie, up to 0.9% in fragrance preparations). Because boron nitride is not expected to have chemical activity in biological systems, particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products that may be aerosolized is available at <http://www.cir-safe.org/cir-findings>.

## Conclusion

The CIR Expert Panel concluded that boron nitride is safe in cosmetics in the present practices of use and concentration described in this safety assessment.

## Author Contributions

M. Fiume contributed to conception and design, contributed to acquisition, analysis, and interpretation, and drafted the manuscript. L. Gil, F. A. Andersen, W. Bergfeld, D. Belsito, R. Hill, C. Klaassen, D. Liebler, R. Shank, T. Slaga, and P. Snyder contributed to conception and design, contributed to analysis and interpretation, and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

## Authors' Note

Unpublished sources cited in this report are available from the Lillian Gill, Director, Cosmetic Ingredient Review, Washington, DC.

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## References

1. Gottschalck TE, Breslawec H. *International Cosmetic Ingredient Dictionary and Handbook*. Washington, DC: Personal Care Products Council; 2012.
2. Ansell JM, Ito K. Report for International Cooperation of Cosmetic Regulation. Associations Survey of Nanomaterials Used in Cosmetic Products. 2011. Web site. [http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/iccr5\\_nano\\_en.pdf](http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/iccr5_nano_en.pdf). Accessed January 17, 2013. Updated 2011.
3. Pease RS. Crystal structure of boron nitride. *Nature*. 1950; 165(4201):722-723.
4. MomentivePerformance Materials Holdings, Inc. Softouch CC6058. Technical data sheet. Web site. <http://www.momentive.com/products/technicaldatasheet.aspx?id=14457>. Accessed October 17, 2012. Updated 2012.
5. Brown P. Cubic and hexagonal boron nitride. Web site. <http://www.docbrown.info/page03/nanochem06.htm>. Accessed November 4, 2012. Updated 2012.
6. Saint-Gobain Ceramic Materials. TRÈS BN<sup>®</sup> Cosmetic Powders. Boron nitride powders for color cosmetic and skin care. Web site. [http://www.bn.saint-gobain.com/uploadedFiles/SGbn/Documents/TRES\\_BN/TresBN-CosmeticPowders-ds.pdf](http://www.bn.saint-gobain.com/uploadedFiles/SGbn/Documents/TRES_BN/TresBN-CosmeticPowders-ds.pdf). Accessed October 17, 2012. Updated 2012.
7. Saint-Gobain Ceramic Materials. TRÈS BN<sup>®</sup> Spherique<sup>™</sup>. Web site. [http://www.bn.saint-gobain.com/uploadedFiles/SGbn/Documents/TRES\\_BN/TRESBN-Spherique-PUHP50S.pdf](http://www.bn.saint-gobain.com/uploadedFiles/SGbn/Documents/TRES_BN/TRESBN-Spherique-PUHP50S.pdf). Accessed October 17, 2012. Updated 2010.
8. Engler M, Lesniak C, Damasch R, Rulsinger B, Elchler J. Hexagonal boron nitride (hBN)—applications from metallurgy to cosmetics. *Ceramic Forum International*. 2007;12:E49-E53. v 84 no 12.
9. MomentivePerformance Materials Holdings, Inc. Softouch CCS402 Technical Data Sheet. Web site. <http://momentive.com/products/technicaldatasheet.aspx?id=14463>. Accessed October 17, 2012. Updated 2012.
10. MomentivePerformance Materials Holdings, Inc. Softouch CC6004 Technical Data Sheet. Web site. <http://momentive.com/products/technicaldatasheet.aspx?id=14456>. Accessed October 17, 2012. Updated 2012.
11. MomentivePerformance Materials Holdings, Inc. Softouch CC6059. Technical Data Sheet. Web site. <http://momentive.com/products/technicaldatasheet.aspx?id=14458>. Accessed October 17, 2012. Updated 2012.
12. MomentivePerformance Materials Holdings, Inc. Softouch CC6097. Technical Data Sheet. Web site. <http://momentive.com/products/technicaldatasheet.aspx?id=14461>. Accessed October 17, 2012. Updated 2012.
13. MomentivePerformance Materials Holdings, Inc. Softouch CCS102. Technical Data Sheet. Web site. <http://momentive.com/products/technicaldatasheet.aspx?id=14462>. Accessed October 17, 2012. Updated 2012.
14. UK Abrasives. Hexagonal Boron Nitride Powder. Web site. <http://www.ukabrasives.com/boron-nitride/boron-nitride-hexagonal-powder-hbn.html>. Accessed October 17, 2012. Updated 2002.
15. Barron AR. Boron Compounds with Nitrogen Donors. OpenStax CNX. Web site. <http://cnx.org/contents/d2630ac5-39d3-48b1-8b5c-df8e7c1095e5@2>. Accessed March 21, 2013. Updated January 25, 2010.
16. Personal Care Products Council. CosmeticsInfo Glossary. Web site. <http://www.cosmeticsinfo.org/glossary.php?glossary=S>. Date Accessed January 31, 2013. Updated 2013.
17. Food and Drug Administration. Frequency of use of cosmetic ingredients. *FDA Database*. 2013.
18. Personal Care Products Council. Concentration of Use by FDA Product Category: Boron Nitride. 2012. Unpublished data submitted by Personal Care Products Council. 2 pages.
19. Rothe H. Special Aspects of Cosmetic Spray Evaluation. Unpublished data presented at the CIR Expert Panel Meeting; Washington, DC; 2011.
20. Johnsen MA. The influence of particle size. *Spray Technol Mark*. 2004;14(11):24-27.
21. Rothe H, Fautz R, Gerber E, et al. Special aspects of cosmetic spray safety evaluations: principles on inhalation risk assessment. *Toxicol Lett*. 2011;205(2):97-104.
22. Bremmer HJ, Prud'homme de Lodder LCH, Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. 2006. Report No. RIVM 320104001/2006: 1-77.
23. European Commission. Cosmetics Directive (v.1). Boron nitride. Web site. <http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details&id=32211>. Accessed August 28, 2012. Updated 2012.
24. Ceram Research. Boron nitride (BN)—properties and information on boron nitride. Web site. [http://www.azom.com/article.aspx?ArticleID=78#\\_Cubic\\_Boron\\_Nitride](http://www.azom.com/article.aspx?ArticleID=78#_Cubic_Boron_Nitride). Accessed November 4, 2012. Updated November 2, 2011.
25. Huntington Specialty Materials. Hexagonal Boron Nitride. Web site. <http://huntspecmat.com/products/boron-nitride.html>. Accessed November 4, 2012. Updated 2011.
26. Horváth L, Magrez A, Golberg D, et al. In vitro investigation of the cellular toxicity of boron nitride nanotubes. *ACS Nano*. 2011; 5(5):3800-3810.
27. Ciofani G, Danti S, Nitti S, Mazzolai B, Mattoli V, Giorgi M. Biocompatibility of boron nitride nanotubes: an up-date of *in vivo* toxicological investigation. *Int J Pharm*. 2013;444(1-2):85-88.
28. Ciofani G, Danti S, Genchi GG, et al. Pilot in vivo toxicological investigation of boron nitride nanotubes. *Int J Nanomed*. 2012;7: 19-24.
29. Ciofani G, Danti S, D'Alessandro D, Moscato S, Menciasci A. Assessing cytotoxicity of boron nitride nanotubes: interference with MTT assay. *Biochem Biophys Res Comm*. 2010;394(2):405-411.
30. Chen X, Wu P, Rouseas M, et al. Boron nitride nanotubes are noncytotoxic and can be functionalized for interaction with proteins and cells. *J Am Chem Soc*. 2009;131(3):890-891.
31. Anonymous. Summary of boron nitride studies (skin irritation and eye irritation). Unpublished data submitted by Personal Care Products Council. 2013.
32. Essex Testing Clinic Inc. Clinical safety evaluation repeated insult patch test of an eye shadow containing 13% boron nitride. Unpublished data submitted by Personal Care Products Council. 2009.

33. Clinical Research Laboratories Inc. Repeated insult patch test of an eye shadow containing 18.7% boron nitride. Unpublished data submitted by Personal Care Products Council. 10 pages. 2011.
34. Product Investigations Inc. Human repeated insult patch test of poudre compacte (pressed powder containing 16% boron nitride). Unpublished data submitted by Personal Care Products Council. 2008.
35. TKL Research Inc. Human repeat insult patch test with challenge (face powder containing 16% boron nitride). TKL Study No. DS101909; TKL Study Report No. DS101909-5. Unpublished data submitted by Personal Care Products Council. 2009.
36. Takahashi Y, Hayashi K, Abo T, Koike M, Sakaguchi H, Nishiyama N. The short-time exposure (STE) test for predicting eye irritation potential: Intra-laboratory reproducibility and correspondence to globally harmonized system (GHS) and EU eye irritation classification for 109 chemicals. *Toxicol In Vitro*. 2011; 25(7):1425-1434.
37. Eskes C, Bessou S, Bruner L, et al. Report for establishing the timetable for phasing out animal testing for the purpose of the Cosmetics Directive. Subgroup 3. Eye Irritation. Web site. [http://ec.europa.eu/consumers/sectors/cosmetics/files/doc/antest/\(5\)\\_chapter\\_3/3\\_eye\\_irritation\\_en.pdf](http://ec.europa.eu/consumers/sectors/cosmetics/files/doc/antest/(5)_chapter_3/3_eye_irritation_en.pdf). Accessed January 23, 2013. Updated 2004.
38. Essex Testing Clinic Inc. Clinical evaluation of the ophthalmologic safety-in-use of an eye shadow containing 13% boron nitride. Unpublished data submitted by Personal Care Products Council. 2009.
39. Lide DR. *CRC Handbook of Chemistry and Physics*. 90th ed. Boca Raton, FL: CRC Press; 2009.
40. Saint-Gobain Ceramic Materials. Boron nitride products. Web site. <http://www.bn.saint-gobain.com/tres-bn-cosmetic-powder.s.aspx>. Accessed October 17, 2012. Updated 2012.
41. Pauling L. The structure and properties of graphite and boron nitride. *Proc Natl Acad Sci U S A*. 1966;56(6):1646-1652.