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# Accepted Manuscript

Opinion of the Scientific Committee on Consumer safety (SCCS) - Opinion on the use of 2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) (nano) – S79 - in cosmetic products

Dr. S.H. Doak



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### **Author's information**

- **Corresponding author:** Scientific Committee of Consumer Safety - SCCS
- **Order of authors:** SCCS, Dr. S. H. Doak<sup>b 1</sup>
- **Corresponding author institution and address:**

SCCS Secretariat at the European Commission, Directorate General for Health and Food Safety, 11, rue E. Ruppert, L-2920 Luxembourg, Luxembourg, e-mail: SANTE-C2-SCCS@ec.europa.eu

- **Author affiliation:**

<sup>b</sup> Swansea University Medical School, Singleton Park, Swansea SA2 8PP, Wales, UK

### **<sup>1</sup>Rapporteur of the Opinion**

**Keywords:** SCCS, scientific opinion, UV-filter, S79, 2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) nano, Regulation 1223/2009, CAS 103597-45-1, EC 403-800-1

### **Conclusion of the opinion**

The calculation for margin of safety in this Opinion is based on a 39-week dermal toxicity study in the mini-pig, as no repeated dose toxicity study with the nano-sized material is available in rats. Also, dermal penetration data are not available for mini-pig skin. The SCCS has based this Opinion on the overall weight of evidence that suggests a very low absorption of MBBT in human skin, and the lack of adverse effects in mini-pigs up to the highest dose tested (1000mg a.i./kg bw/day) over 39 weeks. These together indicate that dermal application of nano-sized MBBT with regard to systemic effects is not a safety concern. The SCCS has therefore concluded that the use of MBBT [2,2'-methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol)] in nano-structured form with the following characteristics as a UV-filter at a concentration up to 10% in dermally applied cosmetic products is considered to not pose a risk of adverse effects in humans after application on healthy, intact skin:

The material has a purity of  $\geq 98.5\%$  with the isomer fraction not exceeding 1.5%, and the impurity profile not significantly different from that indicated in section 3.1.5.

The material has a median particle size ( $d_{0.5}$ ) of 120 nm or larger in terms of mass distribution, and/or 60 nm or larger in terms of number size distribution (by laser diffraction).

The material complies with other physicochemical specifications of the evaluated material as listed under section 3.1 of this opinion in terms of chemical identity, physical form, chemical composition, solubility, zeta potential, etc.

In view of the limited available information on inhalation toxicity, which indicates severe inflammatory effects of microfine MBBT in the respiratory tract, caution is warranted against the use of the material in applications that could lead to exposure of the consumer's lungs by inhalation. This Opinion therefore does not apply to such

particle forms. If any new evidence emerges in the future to show that the nano-form of MBBT used in cosmetic products can penetrate skin (healthy, compromised, sunburnt or damaged skin) in any significant amounts to reach viable cells, the SCCS may consider revising this assessment.

The in vitro genotoxicity assessment of MBBT was negative in two different test systems. These tests were appropriately applied and demonstrate that there was no evidence for chromosomal damage or mutagenicity when mammalian cells were exposed to both non-micronised and nano-forms of MBBT. Although these test data are accepted by the SCCS, no experimental data on uptake/internalisation of the particle by cells has been provided.

In addition, the SCCS has the following concerns:

- In the study in rats, clinical effects (pain and vocalisation) after dermal application were noted at concentrations of 20% (500mg a.i. /kg bw/d and higher). In the carcinogenicity study, scabs were seen at a dose level of 100 mg a.i./kg/bw/day and higher. It is worthwhile to monitor possible irritation effects via the cosmetovigilance programs.
- Given the physicochemical properties (high lipophilicity) of the substance, potential bioaccumulation in selected tissues is of concern, especially over long-term use.

This opinion does not address the effects of MBBT on the environment.

**Opinion to be cited as:** SCCS (Scientific Committee on Consumer Safety), Opinion on 2,2'-methylene-bis-(6(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) nano, SCCS/1546/15, 25 March 2015, revision of 25 June 2015

**Authors of the Opinion**

**SCCS members:** Dr. U. Bernauer, Dr. Q. Chaudhry (chairperson), Prof. M. Dusinska, Dr. W. Lilienblum, Dr. E. Nielsen, Prof. T. Platzek, Dr. J. van Benthem

**Former SCCS member:** Dr. S. Ch. Rastogi

**SCENIHR members:** Prof. P. H. M. Hoet, Dr. K. Rydzynski

**External experts:** Dr. O. Bussolati, Dr. N. von Goetz, Dr. S. H. Doak (rapporteur), Dr. T. Jung

**SCCS Number:** SCCS/1546/15

**Doi:** /

**Adopted on:** 25 June 2015

**Link to the SCCS Opinion:**

**[http://ec.europa.eu/health/scientific\\_committees/consumer\\_safety/docs/sccs\\_o\\_168.pdf](http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_168.pdf)**

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5 **Opinion of the Scientific Committee on Consumer safety (SCCS) - Opinion on the use of 2,2'-**  
6 **methylene-bis-(6-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) (nano) – S79 - in**  
7 **cosmetic products**

8

9

10 The substance 2,2'-methylene-bis-(6(2H-benotriazol-2-yl)-4-(l, 1,3,3-  
11 tetramethylbutyl)phenol) (MBBT) (CAS No 103597-45-1), Methylene bis-benzotriazolyl  
12 tetramethylbutylphenol (INCI) (COLIPA S79) is currently regulated in Entry 23 Annex VI  
13 of the Cosmetics Regulation (EC) 1223/2009 with the maximum concentration of 10% in  
14 cosmetic products such as sunscreens, day care products and skin lightening products.  
15 The safety of mentioned use conditions was confirmed by the Scientific Committee on  
16 Cosmetic Products and Non-Food (SCCNFP) in 1998 following submission I by COLIPA<sup>1</sup>  
17 (SCCNFP/0080/98)<sup>2</sup>.

18 Submission II on MBBT was submitted to the Scientific Committee on Consumer Safety  
19 (SCCS) in January 2013 to assess the safety of its nano form. The SCCS opinion  
20 concluded that:

21 "Since no appropriate data on genotoxicity of nano form of MBBT were provided, no  
22 conclusion on the safety of this substance can be drawn. However regarding systemic

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<sup>1</sup> COLIPA - now Cosmetics Europe,- European Cosmetics Toiletry and Perfumery Association

<sup>2</sup> [http://ec.europa.eu/health/scientific\\_committees/consumer\\_safety/opinions/sccnfp\\_opinions\\_97\\_04/sccp\\_out73\\_en.htm](http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/sccnfp_opinions_97_04/sccp_out73_en.htm)

3 In August 2014 the applicant has transmitted a new safety dossier that summarizes  
4 analytical and toxicological results obtained for genotoxicity studies performed with nano  
5 and non-nano forms of MBBT.

6 The calculation for margin of safety in this Opinion is based on a 39-week dermal toxicity  
7 study in the mini-pig, as no repeated dose toxicity study with the nano-sized material is  
8 available in rats. Also, dermal penetration data are not available for mini-pig skin. The  
9 SCCS has based this Opinion on the overall weight of evidence that suggests a very low  
10 absorption of MBBT in human skin, and the lack of adverse effects in mini-pigs up to the  
11 highest dose tested (1000mg a.i./kg bw/day) over 39 weeks. These together indicate  
12 that dermal application of nano-sized MBBT with regard to systemic effects is not a safety  
13 concern. The SCCS has therefore concluded that the use of MBBT [2,2'-methylene-bis-  
14 (6(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol)] in nano-structured form  
15 with the following characteristics as a UV-filter at a concentration up to 10% in dermally  
16 applied cosmetic products is considered to not pose a risk of adverse effects in humans  
17 after application on healthy, intact skin:

18 The material has a purity of  $\geq 98.5\%$  with the isomer fraction not exceeding 1.5%, and  
19 the impurity profile not significantly different from that indicated in section 3.1.5.

20 The material has a median particle size ( $d_{0.5}$ ) of 120 nm or larger in terms of mass  
21 distribution, and/or 60 nm or larger in terms of number size distribution (by laser  
22 diffraction).

23 The material complies with other physicochemical specifications of the evaluated material  
24 as listed under section 3.1 of this opinion in terms of chemical identity, physical form,  
25 chemical composition, solubility, zeta potential, etc.

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<sup>3</sup> [http://ec.europa.eu/health/scientific\\_committees/consumer\\_safety/docs/sccso\\_129.pdf](http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccso_129.pdf)

4 consumer's lungs by inhalation. This Opinion therefore does not apply to such  
5 applications that might lead to exposure of the consumer's lungs to MBBT nanoparticles  
6 by inhalation.

7 It should also be noted that this Opinion is based on the currently available scientific  
8 evidence, which shows an overall very low dermal absorption of MBBT in nano- or larger  
9 particle forms. If any new evidence emerges in the future to show that the nano-form of  
10 MBBT used in cosmetic products can penetrate skin (healthy, compromised, sunburnt or  
11 damaged skin) in any significant amounts to reach viable cells, the SCCS may consider  
12 revising this assessment.

13 The in vitro genotoxicity assessment of MBBT was negative in two different test systems.  
14 These tests were appropriately applied and demonstrate that there was no evidence for  
15 chromosomal damage or mutagenicity when mammalian cells were exposed to both non-  
16 micronised and nano-forms of MBBT. Although these test data are accepted by the SCCS,  
17 no experimental data on uptake/internalisation of the particle by cells has been provided.

18 In addition, the SCCS has the following concerns:

19 - In the study in rats, clinical effects (pain and vocalisation) after dermal application were  
20 noted at concentrations of 20% (500mg a.i. /kg bw/d and higher). In the carcinogenicity  
21 study, scabs were seen at a dose level of 100 mg a.i./kg/bw/day and higher. It is  
22 worthwhile to monitor possible irritation effects via the cosmetovigilance programs.

23 - Given the physicochemical properties (high lipophilicity) of the substance, potential  
24 bioaccumulation in selected tissues is of concern, especially over long-term use.

25 This opinion does not address the effects of MBBT on the environment.

4 benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol) nano, Regulation 1223/2009, CAS

5 103597-45-1, EC 403-800-1

6

7 **Reference:**

8 **[http://ec.europa.eu/health/scientific\\_committees/consumer\\_safety/docs/sccs\\_o\\_168.pdf](http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_168.pdf)**

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- SCCS has concerns on possible irritation effects and potential bioaccumulation in selected tissues is of concern
- This opinion does not address the effects of MBBT (nano) on the environment.

**Max. 125 characters incl. spaces per highlight**

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