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## Introduction

Experimental animal studies and data from new approach methods (NAMs) indicate that benzoyl peroxide [CAS-No. 94-36-0] is a skin sensitizer [1]. In humans, sensitization is detected in some patients exposed to daily high doses of benzoyl peroxide for several months during acne therapy (see a recent publication [2]), and treatment of leg ulcers in the past [3]. Occupational exposure may occur during manufacturing of resins, adhesives and dental materials, as benzoyl peroxide is an initiator in polymerization reactions. In addition, bakers might also be exposed to benzoyl peroxide residues in wheat. We evaluated benzoyl peroxide regarding its relevance as a Type IV contact allergen.

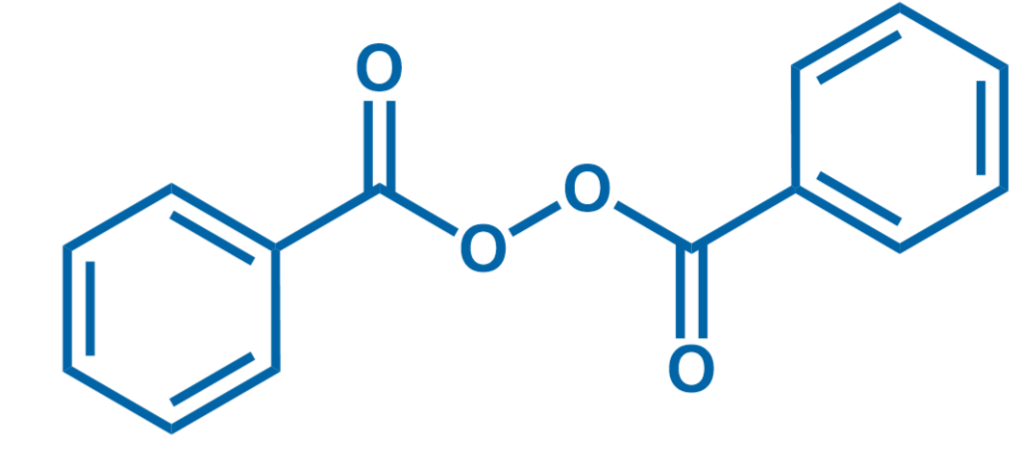


Figure 1: Chemical Structure of Benzoyl Peroxide.

## Method & Results

We reviewed data between 1998 and 2021. Benzoyl peroxide (1% pet) is tested in different series of the German Contact Dermatitis Research Group (“Bone Cement”, “Synthetic Resins and Adhesives”, and “Dental Technician”). Table 1 shows published positive and negative reactions following the International Contact Dermatitis Research Group and the European Society of Contact Dermatitis criteria [4]. Overlap of patients is possible. Positive patch test reactions were found in patients without and with occupational contact dermatitis. In general, a high response rate to benzoyl peroxide was observed although results of patch test preparations  $\leq 1\%$  were only considered, most likely based on the high irritancy of benzoyl peroxide [5]. Reaction rates were higher in patients with occupational contact dermatitis (10.8%) compared to patients without (5.6%). Positive reactions were found among dentists as well as dental technicians and assistants, showing that individuals working with benzoyl peroxide may be sensitized. However, a clear association with one or more specific occupational groups was not evident.

**Table 1: Patch Test Reactions to Benzoyl Peroxide (1% pet) in Patients with and without Occupational Contact Dermatitis (OCD).** Positive and negative reactions are shown for different occupational groups with and without contact to benzoyl peroxide. Questionable and irritative reactions are not listed, but typically make up between 2 – 11% [5, 6].

| Tested patients (1% pet)  | N      | N <sub>(pos+neg)</sub> | Positive reaction(s)<br>(% of tested) | Negative reaction(s)<br>(% of tested) | Ref. |
|---|--------|------------------------|---------------------------------------|---------------------------------------|------|
| Patients without and with OCD   | 29 758 | 26 869                 | 2316 (7.8%)                           | 24 553 (82.5%)                        | [5]  |
| Patients without OCD  | 15 771 | -                      | 879 (5.6%)                            | -                                     | [7]  |
| Patients with OCD   | 241    | -                      | 26 (10.8%)                            | -                                     | [8]  |
| <b>Patients with OCD in different occupational groups with exposure</b> |        |                        |                                       |                                       |      |
| Dental technicians  | 576    | 512                    | 58 (10.1%)                            | 454 (78.8%)                           | [5]  |
|   | 199    | 184                    | 19 (9.5%)                             | 165 (82.9%)                           | [6]  |
|   | 126    | -                      | 11 (8.7%)                             | -                                     | [9]  |
|   | -      | 123                    | 11                                    | 112                                   | [7]  |
| Dental assistants (incl. dentists)                                      | -      | 180                    | 25                                    | 155                                   | [7]  |
| Dentists  | 79     | -                      | 2                                     | -                                     | [10] |
| Technicians (orthopaedic)   | 1      | 1                      | 1                                     | 0                                     | [11] |
| Electrical and electronic equipment mechanics and fitters               | -      | 117                    | 9                                     | 108                                   | [7]  |
| Technician (manufacturing electrical transformers)                      | 1      | 1                      | 1                                     | 0                                     | [12] |
| Carpenter, cabinet maker, model maker                                   | -      | 135                    | 11                                    | 124                                   | [7]  |
| Marble grinder  | 1      | 1                      | 1                                     | 0                                     | [13] |
| Bakers  | -      | 80                     | 3                                     | 77                                    | [7]  |
|   | 1      | 1                      | 1                                     | 0                                     | [14] |
| Health care professionals   | -      | 95                     | 10                                    | 85                                    | [7]  |
| <b>Patients with OCD in occupational groups without exposure</b>        |        |                        |                                       |                                       |      |
| Mechanics (no specification)  | 704    | -                      | 27 (3.9%)                             | -                                     | [15] |
| Mechanics, metal, machinery and related trades workers                  | -      | 598                    | 26                                    | 572                                   | [7]  |
|   | 57     | -                      | 2                                     | -                                     | [16] |
| Cutting metal workers   | 118    | -                      | 7 (6.0%)                              | -                                     | [15] |
| Other metal workers   | 103    | -                      | 11 (10.9%)                            | -                                     | [15] |

- indicates no data

## Conclusion

The data of an extensive literature review did not indicate a significantly increased skin sensitization risk for occupational groups with possible exposure to benzoyl peroxide such as dental technicians and related professions. Therefore, we conclude that benzoyl peroxide is not a relevant occupational contact allergen.

References: [1] OECD, 2021, ENV/CBC/MONO(2021)11, Annex 2; [2] Iijima & Tsunoda, 2019, DOI: 10.1002/cia2.12069; [3] Agathos & Bandmann, 1984, DOI: 10.1111/j.1600-0536.1984.tb01018.x [4] Johansen et al., 2015, DOI: 10.1111/cod.12432 [5] Ockenfels et al., 2009, DOI: 10.1111/j.1600-0536.2009.01603.x; [6] Heratizadeh et al., 2018, DOI:10.1111/cod.12943; [7] Geier & Schubert, 2021, DOI: 10.21934/baua:bericht20210122; [8] Hillen et al., 2007, DOI: 10.5414/DBP55010; [9] Peiler et al., 2000, Dermatol. Beruf Umwelt 48(1); [10] Kiec-Swierczyńska & Krecisz, 2002, DOI: 10.1159/000047988; [11] Forschner et al., 2002, DOI:10.1034/j.1600-0536.2002.470415.x; [12] Elangasinghe & Johnston, 2012, DOI: 10.1111/j.1600-0536.2012.02007.x; [13] Tsovilis et al., 2005, DOI: 10.1111/j.0105-1873.2005.004981.x; [14] Adelman et al., 2019, DOI: 10.1097/DER.0000000000000470; [15] Schubert et al., 2020, DOI: 10.1111/cod.13686; [16] Donovan et al., 2007, DOI: 10.2310/6620.2007.06039.