




REVIEW OPEN ACCESS

Benzoyl Peroxide's Sensitisation Potential and Potency in Experimental Methods and Review of Contact Allergy and Allergic Contact Dermatitis

Kerstin Egele¹  | Hans Drexler² | Manigé Fartasch³ | Vera van Kampen⁴ | Hans F. Merk⁵ | Dennis Nowak⁶ | Axel Schnuch⁷  | Wolfgang Uter⁸ | Patricia Kreis⁹ | Brunhilde Blömeke¹ 

¹Department of Environmental Toxicology, Trier University, Trier, Germany | ²Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany | ³Dermatological & Allergological Private Practice, Siegburg, Germany | ⁴Institute for Prevention and Occupational Medicine of the German Social Accident Insurance, Institute of the Ruhr University Bochum (IPA), Bochum, Germany | ⁵Department of Dermatology and Allergology, Medical Faculty, RWTH Aachen University, Aachen, Germany | ⁶Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine, Member of German Center for Lung Research (DZL), Comprehensive Pneumology Center (CPC München), Clinical Center of the Ludwig Maximilian University Munich (LMU), Munich, Germany | ⁷University Medical Center Göttingen, Göttingen, Germany | ⁸Department of Medical Informatics, Biometry and Epidemiology (IMBE), Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany | ⁹Department of Food Chemistry and Toxicology, Institute for Applied Biosciences, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany

Correspondence: Brunhilde Blömeke (bloemeke@uni-trier.de)

Received: 25 September 2024 | **Revised:** 6 January 2025 | **Accepted:** 12 January 2025

Funding: This study was supported by the Deutsche Forschungsgemeinschaft: 516142524.

Keywords: allergic contact dermatitis | benzoyl peroxide [CAS-no. 94-36-0] | non-animal methods | occupational allergen

ABSTRACT

Positive patch test responses to benzoyl peroxide (BPO) have been reported from patients without and with known exposure. Up to 6.5% were found in the United States and 7.8% in a study including patients from Germany, Austria and Switzerland. We provide an overview of the skin sensitisation potential and potency of BPO based on animal experiments and non-animal methods. BPO tested positive in Guinea Pig Tests and the Local Lymph Node Assay. Application of the current OECD guideline to identify a skin sensitizer by combining non-animal method results gave differing outcomes. Moreover, patch test responses of patients to BPO were considered to determine the importance of BPO as a relevant occupational contact allergen. Another well-known BPO exposure is the topical application to treat acne. Despite widespread use, extensive and long-term skin exposure, we found for this group only studies reporting few positive patch test reactions. Further, occupational handling of BPO and contact allergy is reported by dental technicians. In-depth evaluation of the prevalence of contact allergy in different professions with suspected BPO exposure did not reveal an association with occupational handling of BPO. Consequently, a generally increased risk for those professions is not supported.

1 | Introduction

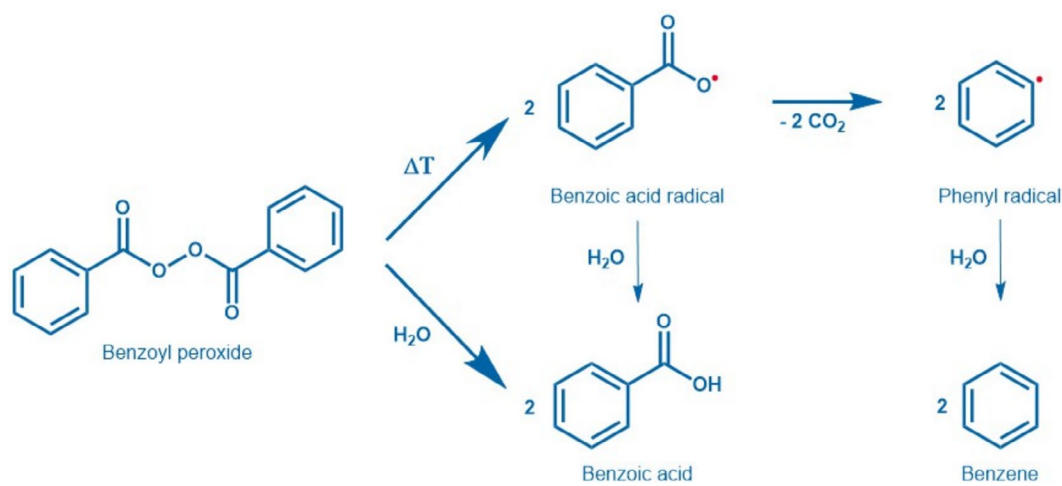
Benzoyl peroxide (BPO, CAS-no. 94-36-0) is used to manufacture a broad range of products. The chemical structure of BPO and the formation of benzoic acid, phenyl radical and benzene are shown Figure 1A. Under aqueous conditions BPO hydrolyses

to benzoic acid/benzoate, while the formation of a stable phenyl radical by homolytic cleavage of the peroxide group is promoted by increased temperature. The BPO-mediated methacrylate polymerisation reaction is shown in Figure 1B. BPO (~1 wt%) is a prominent initiator for radical polymerisations in the manufacturing of synthetic resins, plastics, adhesives, dental materials

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2025 The Author(s). *Contact Dermatitis* published by John Wiley & Sons Ltd.

A



B

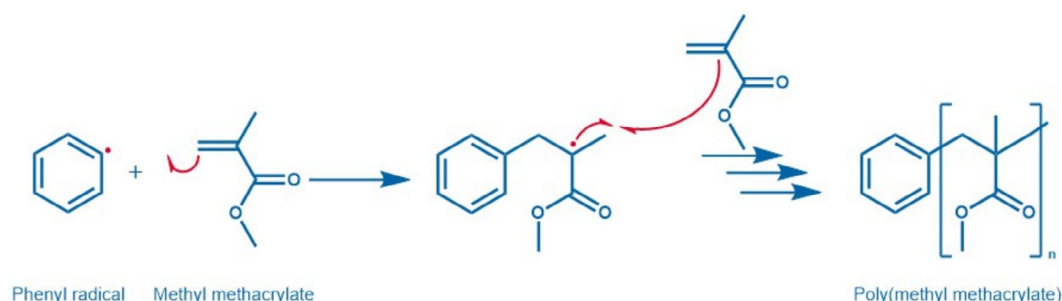


FIGURE 1 | Chemical structure of BPO and mechanism of radical formation (A) and its use in free radical polymerisation of methyl methacrylate to poly methyl methacrylate (B).

and bone cement [1–4]. Furthermore, BPO (1%) was used to bleach candles and remains used in some countries to bleach flour and dairy products (lower ppm range) because of its oxidative properties [5–7].

The potential of BPO to induce skin sensitisation has been studied in experimental animal studies and non-animal methods. BPO was tested in guinea pig tests such as the Guinea Pig Maximisation Test, Bühler Test and the murine Local Lymph Node Assay (LLNA) [8–10]. There is a common agreement that as of today, one single non-animal test method is not sufficient to fully recapitulate the complexity of skin sensitisation. Thus, non-animal methods are being developed along four defined key events (KE 1–4) of a defined Adverse Outcome Pathway for Skin Sensitisation (AOP) [11]. The first key event (KE 1) is the binding of electrophilic chemicals to nucleophilic centres of skin proteins, and OECD-validated test methods (OECD 422 C) evaluate the relative reactivity of substances with synthetic model peptides containing cysteine and/or lysine (Direct Peptide Reactivity Assay, DPRA; kinetic DPRA, kDPRA). Other methods are using single amino acid derivatives instead of model peptides (Amino Acid Derivative Reactivity Assay, ADRA) [12]. Methods addressing the activation of keratinocytes (KE 2, OECD 442 D) are measuring the chemical-induced changes in the expression of a marker gene in genetically modified HaCaT keratinocytes (KeratiNoSens, LuSens) or gene expression of

markers in human reconstructed epidermis (EpiSensA) [13]. Maturation of dendritic cells (KE 3, OECD 442 E) is evaluated by measuring cell surface expression of specific markers on monocytic THP-1 or U937 cell lines (Human Cell Line Activation Test, h-CLAT; U937 cell line activation Test, U-SENS), cytokines (Interleukin-8 Reporter Gene Assay, IL-8 Luc assay) or expression of a set of marker genes (GARDskin) [14]. Validated methods to study the potential of a chemical to activate naive T cells (KE 4) are still under development. For the other methods validated test protocols are already provided by the Organisation for Economic Co-operation and Development (OECD, guideline 442 C, D, E) [12–14]. Furthermore strategies (so-called Defined Approaches) to combine individual results of testing KE 1–3, as well as in silico data of a given chemical into a final outcome was developed (OECD 497) [15]. BPO has been tested in several of the developed methods.

Humans may have skin contact under certain occupational settings, that is, during the synthesis of the molecule and manufacturing of products, while non-occupational contact may be because of minimal residues of non-reacted BPO during handling of BPO-containing products [4, 16]. Consequently, under circumstances of intensive handling activities or non-compliance with safety instructions of BPO-containing products, skin sensitisation to BPO may occur. Independently, BPO itself is used in significant amounts in some drugs. In the past,

BPO (<20%) was used to treat leg ulcers in chronic venous insufficiency [17]. Up to 10% BPO has been used since the early 20th century and is considered a staple in treating acne, where high daily doses for several months are applied [18]. In the context of medical use and occupational handling cases of ACD have been reported [5, 17, 19].

The present article aims at reviewing available results of experimental animal studies, non-animal methods and human patch test data to conclude on the human sensitisation potency of BPO and to identify occupational groups at risk for skin sensitisation.

2 | Methodology of Literature Search and Data Analysis

Published data were collected (PubMed, Web of Science libraries). We included publications written in English and German Language. A systematic analysis of the literature of experimental animal studies and non-animal methods were performed using the following keywords ((BPO) OR 94-36-0) AND ((guinea pig maximisation test) OR (Bühler test) OR Buehler OR LLNA OR GPMT OR LLNA) or ((Peptide reactivity) OR (keratinocyte activation) OR (dendritic cell activation) OR DPRA OR ADRA OR kDPRA OR (ARE-Nrf2 luciferase KeratinoSens) OR (ARE-Nrf2 luciferase LuSens) OR h-CLAT OR U-Sens OR (IL-8 Luc assay) OR GARD OR EpiSensA OR (RHE-IL18) OR SensCeeTox) was performed. We included all studies using OECD-validated or scientifically accepted methods. The literature search to review the clinical results (contact allergy and allergic contact dermatitis) was performed using the following keywords: ((BPO) OR CAS 94-36-0) AND (allerg* OR dermat* OR sensitiz* OR sensitiz* OR skin OR contact OR hypersensitiv* OR hypersensitiz* OR hypersensitis*). Here, we restricted the analysis to January 1999–December 2022, as data from earlier patch test studies were already summarised [20]. In total, the initial search in Pubmed retrieved 918 articles and 1082 articles were found in Web of Science. Study eligibility was first assessed based on the title and abstract. The second assessment of eligibility was based on the full text of the articles and was done by two independent investigators.

With respect to clinical data, we restricted the analysis to studies using a maximum 1% BPO in pet. for patch testing based on reported irritancy at higher concentrations [21, 22]. Application of these defined criteria resulted in 68 publications. In addition, we reviewed relevant publications that were already reviewed [20]. References in the articles obtained were also screened to identify other potential sources of information.

Individual test results of the different non-animal methods were analysed by applying the Defined Approaches ‘2 out of 3’ and Integrated Testing Strategy version 1 (ITSv1) and 2 (ITSv2) for skin sensitisation hazard as described in OECD guideline no. 497 [15]. In detail, in the ‘2 out of 3’ approach results from DPRA, KeratinoSens and h-CLAT are considered, and any two of the three methods determine the final outcome, that is, if two methods result positive, the overall results yield the prediction of a test chemical to be a sensitizer, while any two negative test results would yield the prediction of a test chemical to be a non-sensitizer. In ITSv1 and ITSv2, scores are assigned for relative

test results of DPRA (0–3 scores), h-CLAT (0–3 scores) and for in silico results from the Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus (ITSv1, 0–1 scores) or the OECD QSAR Toolbox (ITSv2, 0–1 scores) to yield an overall result that predicts the skin sensitisation potency of a chemical: United Nations Globally Harmonised System (UN GHS) of Classification and Labelling of Chemicals category 1A (6–7 scores, strong sensitizer), category 1B (2–5 scores, other sensitizer), not classified (0–1 scores, non-sensitizer) or inconclusive.

3 | Results of the Literature Search and Data Analysis

3.1 | Skin Sensitisation Potential and Potency of BPO

BPO was tested positive in different experimental animal studies such as the Guinea Pig Maximisation Test, Bühler Test and LLNA [8–10]. The LLNA allows also the determination of a chemicals’ relative sensitisation potency based on estimation of the concentration inducing positivity (effective concentration, EC3 value), and comprehensive comparison with human data [23]. With respect to potency, BPO gave different EC3 values ranging between 0.0044% and 0.3% [10, 24–26]. This finding led to the classification of BPO as an extreme or strong sensitizer following the criteria defined by the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) [27].

BPO was frequently tested in non-animal methods under development to identify the skin sensitisation potential of chemicals and possibly derive continuous potency values. Methods cover the molecular initiation event (protein reactivity, Key Event (KE) 1), activation of keratinocytes (KE 2) and dendritic cells (KE 3) and in silico calculations. BPO was tested positive in different methods addressing KE 1 (4 of 4), KE 2 (4 of 7), KE 3 (3 of 4) and in silico methods (2 of 2) (Figure 2). We evaluated the individual results by applying the Defined Approaches ‘2 out of 3’ and Integrated Testing Strategy version 1 (ITSv1) and 2 (ITSv2) (see Methods). In the ‘2 out of 3’ approach, BPO yields the prediction to be a non-sensitizer.

In the ITSv1 and ITSv2, BPO achieved 4 of a total of 7 score points, predicting category 1B skin sensitizer according to the criteria of the Globally Harmonised System of Classification and Labelling of Chemicals.

3.2 | Prevalence of BPO Contact Allergy in Patients With and Without Occupational Contact Dermatitis

Next, we reviewed published studies on the prevalence of contact allergy under different exposure scenarios, although (exact) exposure measurements are not available. In general, no routine patch testing of BPO in consecutive patients is performed in Europe or North America. As skin contact and sensitisation may occur because of occupational and non-occupational exposure, the German Contact Dermatitis Research Group (DKG) for instance recommends BPO patch testing as part of several test series, namely ‘Bone Cement’, ‘Synthetic Resins and Adhesives’

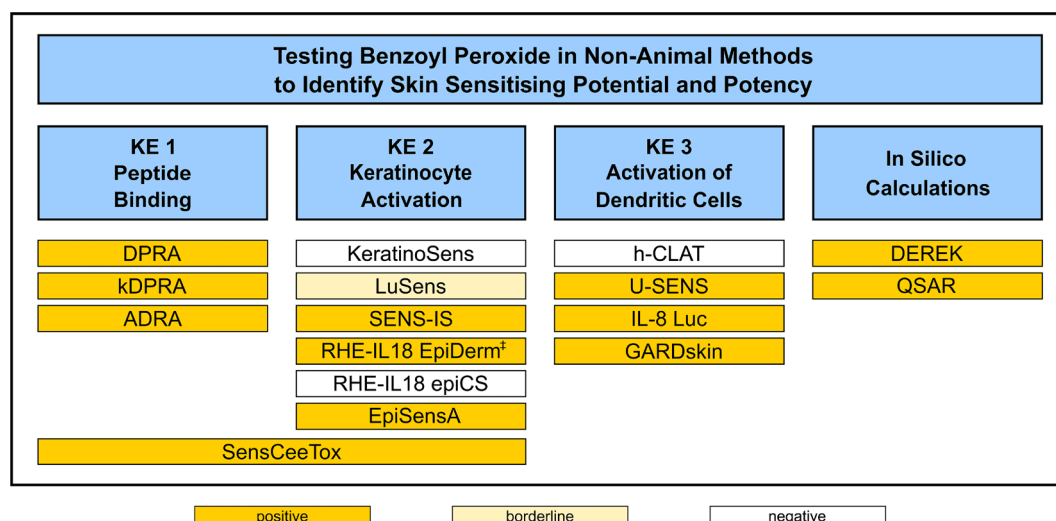


FIGURE 2 | Graphical summary of testing (positive, negative, borderline (close to cut off)) BPO in non-animal methods for skin sensitisation in KE 1 (4 methods), KE 2 (7 methods), KE 3 (4 methods) and in silico calculations (2 methods). In single methods testing KE 1, KE 2 and KE 3 as well as in silico calculations, positivity was achieved. ADRA, Amino acid Derivative Reactivity Assay [28]; DEREK, Deductive Estimation of Risk from Existing Knowledge [29]; DPRA, Direct Peptide Reactivity Assay [29]; EpiSensA, Epidermal Sensitization Assay [30]; GARDskin, Genomic Allergen Rapid Detection for assessment of skin sensitizers [31]; h-CLAT, Human Cell Line Activation Test [29]; IL-8 Luc, Interleukin-8 Luciferase Assay [32]; kDPRA, Kinetic Direct Peptide Reactivity Assay [33]; KeratinoSens, Keratinocyte Sensitization Assay [29]; LuSens, Luciferase Sensitization Assay [34]; OECD QSAR, Quantitative Structure–Activity Relationship Toolbox v.3.2 [29]; RHE-IL18 epiCs, Reconstructed Human Epidermis (EpiCS) Interleukin-18 [35]; RHE-IL18 EpiDerm, Reconstructed Human Epidermis (EpiDERM) Interleukin-18 [35]; SensCeeTox, Sensitization CeeTox Inc. [35]; SENS-IS, Testing of keratinocyte activation via analysis of the gene expression profile using a skin model [35, 36]; U-Sens, U937 Sensitization Assay [37–39]. [†] only positive with an adapted protocol.

and the ‘Dental Technician’. For some years, the chemical was also part of the ‘Topical Drug’, ‘Rubber’, ‘Metal Working’ and ‘Plastic and Glues’ series. Because of low clinical relevance, BPO was taken out [40, 41].

In the past, BPO (<20%) was used to treat leg ulcers in chronic venous insufficiency and cases of Allergic Contact Dermatitis (ACD) have been reported. A considerable number of positive patch test reactions was reported in two smaller studies, namely 31 of 41 [42] and 12 of 120 (10%) [43]. In contrast, evaluation of a larger patient group found markedly lower numbers of positive patch test reactions, namely in 30 of 739 patients (3.8%) [17]. For acne patients, larger studies performed earlier than 1999 found between 0% and 1% positive reactions [17, 44]. These results contrast with only one newer small patch test study testing BPO in relation to acne therapeutics, finding 17 of 20 patients showing a positive reaction [45]. In addition, there are 14 recently published case reports with positive patch test results [46–52]. Taking into consideration the high daily BPO exposure over months of acne treatment, sensitisation to BPO seems to be a rare adverse event in acne treatment. This finding may be because of relatively low penetration, namely 3% of all BPO in a 10% formulation applied on ex vivo skin were absorbed within 8 h and the hydrolysis to benzoic acid/benzoate already in the stratum corneum may also be involved [53, 54]. Higher prevalences of up to 13% in studies involving between 193 and 311 patients with skin or mucous membrane symptoms following bone and dental implants were reported [3, 55–61]. On the other hand, prevalences around 9%–10% were reported in studies including between 126 and 539 patients with suspected allergic contact dermatitis in the context of occupational and non-occupational handling of plastics and adhesives [62–66].

TABLE 1 | Patch test results to BPO (1% pet.) in groups without and with OCD.

Patch test with BPO (1% pet., reading \geq D3)	N (IR, ? +, pos, neg)	Sum (pos, neg)	Positive reactions (% of N)	References
Patients without and with OCD	29 758	26 869	2316 (7.8%)	[22] ^a
Patients without OCD	15 771	—	879 (5.6%)	[68] ^a
Patients with OCD	241	—	26 (10.8%)	[62] ^a

Note: Total N, the sum of positive and negative reactions and the number of positive reactions are shown.
Abbreviations: — no data available; ?+, doubtful reaction; IR, irritant reaction; neg, negative reaction; OCD, Occupational Contact Dermatitis; pos, positive reaction.

^aOverlap of patient samples possible.

Variable prevalences were also seen in studies focusing on patients with occupational contact dermatitis (OCD). Table 1 provides an overview of patch test results of patients with OCD and without OCD. Twenty-six out of 241 patients with OCD showed

a positive response to BPO (10.8%), while a prevalence of 5.6% was recorded in patients without OCD. Subsequent studies investigating an association of a positive reaction to BPO among patients with OCD and professions without and with BPO handling found heterogeneous results. Table 2 shows results for mechanics and metal workers with OCD that have no occupational contact with BPO. In these groups, prevalences between 3.8% and 10.7% were found in three studies, although a certain degree of overlap has to be taken into account. Today's occupations that might be at risk of developing contact allergy to BPO are shown in Table 3. This table provides a compilation of patch test results of patients with OCD and with possible occupational exposure to BPO including larger studies and case reports. Similar

to mechanics and metalworkers, prevalences between 8.7% and 10.1% were found among dental technicians that are known to have occupational contact with BPO. Surprisingly low levels of positive reactions to BPO were found for dental technicians and related professions because of possible exposure to BPO during the production of dentures, specifically for initiation of the acrylate and methacrylate polymerisation reaction [4]. However, individual cases of allergic contact dermatitis of the fingertips have been reported for dental technicians, dentists and dental assistants. Further professions that require the use of BPO when manufacturing materials may have repeated skin contact with BPO, especially during work steps where gloves cannot be worn [20, 67]. Accordingly, some positive reactions were described

TABLE 2 | Patch test results to BPO (1% pet.) in mechanics and metal workers with OCD.

Patch test with BPO (1% pet., reading \geq D3)	N (IR, ? +, pos, neg)	sum (pos, neg)	Positive reactions (% of N, N > 100)	References
Mechanics	704	—	27 (3.8%)	[69] ^a
Cutting metal workers	118	—	7 (5.9%)	
Other metal workers	103	—	11 (10.7%)	
Mechanics and metal workers	—	598	26 (n.d.)	[68] ^a
	57 ^b	—	2 (n.d.)	[70]

Note: Total N, the sum of positive and negative reactions and the number of positive reactions are shown.

Abbreviations: — no data available; ?+, doubtful reaction; IR, irritant reaction; n.d., not defined; neg, negative reaction; pos, positive reaction.

^aOverlap of patient samples possible.

^bReading day not indicated.

TABLE 3 | Patch test results to BPO (1% pet.) in patients with OCD in different professions with contact to BPO.

Patch test with BPO (1% pet., reading \geq D3)	N (IR, ? +, pos, neg)	Sum (pos, neg)	Positive reactions (% of N, N > 100)	References
Dental technicians	576	512	58 (10.1%)	[22] ^a
	199	184	19 (9.5%)	[21] ^a
	126	—	11 (8.7%)	[64]
	—	123	11 (n.d.)	[68] ^a
Dental assistants (incl. dentists)	—	180	25 (n.d.)	[68]
Dentists	79	—	2 (n.d.)	[63]
Orthopaedic technician ^b	1	1	1 (n.d.)	[71]
Electrical-, electronic equipment mechanics and fitters	—	117	9 (n.d.)	[68]
Electrical technician	1	1	1 (n.d.)	[72]
Carpenter, cabinet maker, model maker	—	135	11 (n.d.)	[68]
Bakers	—	80	3 (n.d.)	[68]
	1	1	1 (n.d.)	[73]
Marble grinder	1	1	1 (n.d.)	[74]
Health care professionals	—	95	10 (n.d.)	[68]

Note: Total N, the sum of positive and negative reactions and the number of positive reactions are shown.

Abbreviations: — no data available; ?+, doubtful reaction; IR, irritant reaction; n.d., not defined; neg, negative reaction; pos, positive reaction.

^aOverlap of patient samples possible.

^bReading day not indicated.

TABLE 4 | Scoring of patch test responses to BPO (1% pet.) in patients with and without OCD.

Patch test with BPO (1% pet., reading ≥ D3)	Irritant reaction	Scoring according to reference				References
		?+	+	++	+++	
Patients with and without OCD (%)						
29 758	619 (2.1%)	2270 (7.6%)	1931 (6.5%)	326 (1.1%)	59 (0.2%)	[22] ^a
3758 ^b	86 (2.3%)	318 (8.5%)	235 (6.3%)	45 (1.2%)	14 (0.4%)	[79]
721	4 (0.6%)	57 (7.9%)	33 (4.6%)	2 (0.3%)	2 (0.3%)	[67]
Patients with OCD (%)						
Dental technicians 199	4 (2%)	11 (5.5%)	14 (7.0%)	3 (1.5%)	2 (1%)	[21] ^a
Dental technicians 41 ^c	0	10	2	2	0	[67]
Metal workers 1128	8 (0.7%)	99 (8.8%)	49 (4.3%)	6 (0.5%)	2 (0.2%)	[41]
Patients without OCD						
Acne 20 ^c	3 (?+/IR)	—	14	3	0	[45]
Acne 7 ^c	0	0	2	4	1	[46]
Ulcus cruris 20 ^{c,d} (partly testing with 0.5%)	—	—	4	2	3	[86]

Note: The number of irritant, doubtful, +, ++ and +++ reactions are indicated.

Abbreviations: — no data available; ?+ doubtful reaction; IR, irritant reaction; OCD, occupational contact dermatitis.

^aOverlap of patient samples possible.

^bReading day not indicated.

^cNo % calculated for $N < 100$.

^dPartly testing with 0.5% BPO.

from carpenters, cabinet makers, model makers and technicians; electrical and electronic equipment mechanics and fitters; as well as health care professionals. Again, no clear differences between different occupational groups were apparent.

4 | Discussion

The present article reviews available data on the sensitisation potential and potency of BPO in humans. The capacity of BPO to induce skin sensitisation has been demonstrated in experimental animal studies by evaluation of induction or elicitation. Thus, the prediction of a test chemical to be a sensitizer is derived from a single test method. In contrast, using non-animal methods this prediction is derived from so-called Defined Approaches that define how individual test results of a chemical have to be combined to come to the final outcome. As each method has limitations, different methods have been developed for defined KEs during the acquisition of skin sensitisation.

For BPO, negative results have been achieved with several non-animal methods, namely KeratinoSens, h-CLAT and RHE-IL18 EpiCS (Figure 2). In principle, several of those methods including KeratinoSens and h-CLAT are based on aqueous systems that may lead to false negative results and underprediction of

the sensitising potential of fast hydrolysing substances. The latter is of high importance for BPO that can hydrolyse under aqueous milieu to benzoic acid/benzoate which is a very weak sensitizer. In line, benzoic acid tested negative in various non-animal methods, including DPRA, KeratinoSens and h-CLAT [29]. On the other hand, BPO has also been tested positive in methods assessing peptide reactivity (KE 1), even under aqueous conditions. This apparent contradiction could be based on the fact that these methods are carried out with comparably higher concentrations compared with KeratinoSens and h-CLAT and thus assure that sufficient non-hydrolysed BPO is available for reaction. Testing BPO with non-aqueous methods based on skin models, positive results were obtained with two out of three methods. Furthermore, not all methods are able to detect all classes of chemical reactivity of known sensitizers. For instance, acylating agents are tested negative with KeratinoSens [13]. As BPO acts as an acylating agent, the negative test result in this assay seems plausible. Thus, applying the Defined Approaches according to OECD [15] leads to heterogeneous final outcomes. Because of the negative result with the KeratinoSens, for BPO, the prediction is to be a non-sensitizer in the '2 out of 3' approach. However, it should be clearly acknowledged that the '2 out of 3' approach was shown to have a high accuracy (89%) in predicting human skin sensitisation hazard and its accuracy is comparable to the predicted accuracy of the LLNA (82%) [15]. Furthermore,

the Defined Approaches are contiguously improved [75, 76]. For instance, considering the positive result of BPO in U-SENS instead of the negative h-CLAT, the final outcome is positive.

Furthermore, the second type of integration strategies, namely Integrated Testing Strategies version 1 (ITSv1) and 2 (ITSv2) do not consider the results of the KeratinoSens. Both strategies allow one to decide whether a substance is a significant skin sensitizer and, if so, whether it is a stronger (category 1A) or weaker (category 1B) skin sensitizer according to the criteria of the United Nations Globally Harmonised System (UN GHS) of Classification and Labelling of Chemicals. It should be noted that a lower category 'not classified' exists containing both true non-sensitizers and the very weakest skin sensitizers. These GHS categories based on animal testing can be mapped to human potency categories [77]. For instance, a substance categorised into 1B has a low to moderate frequency of contact allergy and/or a low to moderate potency based on its evaluation in the murine LLNA, in which potency is quantified by the EC3 value. In the latter assay, BPO has been classified as an extreme to strong sensitizer. In contrast, ITSv1 and ITSv2 predicted BPO correctly but categorised BPO as a weaker skin sensitizer (category 1B). There is a clear disparity between its relative skin-sensitising potency in the well-established predictive LLNA test versus ITSv1 and ITSv2. The discrepancy is also apparent when the frequency with which BPO induces contact allergy is taken into account. Indeed, it remains unresolved why only very few positive patch test reactions were reported among patients with extensive BPO exposure during acne treatment. We found only a few cases in the more recent literature, while a prevalence of 1% was reported earlier [44]. Thus, the potency prediction of BPO using non-animal methods (ITSv1 and ITSv2) reflects the human situation better than the prediction based on the LLNA. It can be speculated that the higher potency of BPO observed in mice could be explained by the thinner stratum corneum of mice, which reduces BPO hydrolysis to the very weak and unclassified skin sensitizer benzoic acid/benzoate, which has already been detected in this part of the epidermis [78]. The different potency of BPO and benzoic acid/benzoate is further supported by patch test studies indicating that only 2.7% of the cases that reacted positive to BPO (1% pet.) react to sodium benzoate (5% pet.) [79].

Overall, positive reactions to BPO and high prevalences (up to 10%) were observed among groups with and without occupational exposure. In general, a positive patch test may be because of the molecule itself or because of sensitisation to another, structurally related chemical [80]. Indeed, cross-elicitation by similar molecules most likely because of T-cell receptor cross-reactivity caused by allergen-specific T lymphocytes has been observed for certain chemicals [81]. Specifically BPO can be degraded to benzoic acid/benzoate within the stratum corneum. Consequently, dermal application of BPO may elicit positive reactions in persons with sensitisation to benzoic acid/sodium benzoate, which is a widely used substance and cosmetic ingredient but a very weak allergen. Regardless, a + positive patch test response to BPO must be interpreted cautiously, as this concentration can trigger false-positive patch test reactions (0.6%–2.3%) [1, 82]. Therefore, we and others did not consider studies using higher patch test concentrations [22, 83]. Distinction between irritant and allergic patch test responses to BPO—as with any

allergen—is crucial [21, 83]. Consequently, several readings are needed to discriminate a one plus positive (+) decrescendo reaction from allergic reactions, and it is debatable whether a single + patch test reaction to BPO at D2 is truly an indicator of weak sensitisation. Furthermore, there are several studies that draw attention to a lack of clinical relevance of + reactions compared with ++ and +++ reactions [20, 22]. Nevertheless, only a few studies provide results on several reading days and the strength of the reactions. Table 4 shows a compilation of studies providing patch test scores to BPO (?+; +; ++; +++). Overall, few ++ and +++ reactions were observed, varying between 0.6% and 2.5% of tested patients. Again, no significant increase in ++ and +++ patch test responses was observed among acne patients. The same was observed testing dental technicians with hand eczema and likely BPO exposure. The integration of BPO in a baseline series is indeed not justified, taking into account the above-mentioned difficulties and the low probability of finding relevant responses in unselected patients. When BPO patch testing is indicated, readings should be performed on multiple days. In cases with occupational exposure, testing with several dilutions might be considered. Regardless of the context, the clinical relevance of any positive result must be thoroughly assessed to ensure its significance in the individual's exposure history. In certain cases, the Safety Data Sheet (SDS) of BPO-containing products may provide information on the amounts of BPO. If the reaction is caused by residues, it will be more difficult to identify them, as they are usually not declared in the SDS. However, several simple analytical methods such as colorimetry, fluorescence [84] or high-performance liquid chromatography [85] have been developed to detect BPO.

5 | Conclusion

Experimental animal studies and non-animal methods demonstrate the skin sensitising potential of BPO. Contact allergy and ACD to BPO have been documented in patients without and with OCD, indicating both non-occupational and occupationally acquired sensitisation. As there are no clear differences in prevalences between occupational groups with and without exposure, no reliable evidence of an increased risk of sensitisation because of occupational exposure in the dental sector or of electromechanical and adhesive processing workers was found.

Author Contributions

Kerstin Egele: writing – original draft, investigation, methodology, writing – review and editing, visualization, data curation. **Hans Drexler:** writing – review and editing, methodology. **Manigé Fartasch:** writing – review and editing, methodology. **Vera van Kampen:** writing – review and editing, methodology. **Hans F. Merk:** writing – review and editing, methodology. **Dennis Nowak:** writing – review and editing, methodology. **Axel Schnuch:** writing – review and editing, methodology. **Wolfgang Uter:** writing – review and editing, methodology. **Patricia Kreis:** writing – review and editing. **Brunhilde Blömeke:** funding acquisition, writing – original draft, methodology, writing – review and editing, project administration, supervision.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Acknowledgements

Open Access funding enabled and organized by Projekt DEAL.

References

1. A. Bircher, N. F. Friederich, W. Seelig, and K. Scherer, "Allergic Complications From Orthopaedic Joint Implants: The Role of Delayed Hypersensitivity to Benzoyl Peroxide in Bone Cement," *Contact Dermatitis* 66, no. 1 (2012): 20–26, <https://doi.org/10.1111/j.1600-0536.2011.01996.x>.
2. B. Björkner, M. Frick-Engfeldt, A. Pontén, and E. Zimerson, "Plastic Materials," in *Contact Dermatitis*, eds. J. D. Johansen, P. J. Frosch, and J. P. Lepoittevin, Weinheim, Germany: 5th ed. (Berlin/Heidelberg: Springer, 2011), 695–728, https://doi.org/10.1007/978-3-642-03827-3_37.
3. R. Eben, K. A. Dietrich, C. Nerz, et al., "Kontaktallergieraten Gegen Metalle Und Knochenzementbestandteile Bei Patienten Mit Endoprothesenunverträglichkeit," *Deutsche Medizinische Wochenschrift* 135 (2010): 1418–1422, <https://doi.org/10.1055/s-0030-1262426>.
4. N. Torbica and S. Krstev, "World at Work: Dental Laboratory Technicians," *Occupational and Environmental Medicine* 63, no. 2 (2006): 145–148, <https://doi.org/10.1136/oem.2004.019059>.
5. B. Bonnekoh and H. F. Merk, "Airborne Allergic Contact Dermatitis From Benzoyl Peroxide as a Bleaching Agent of Candle Wax," *Contact Dermatitis* 24, no. 5 (1991): 367–368, <https://doi.org/10.1111/j.1600-0536.1991.tb01753.x>.
6. E. J. Kang, R. E. Campbell, E. Bastian, and M. A. Drake, "Invited Review: Annatto Usage and Bleaching in Dairy Foods," *Journal of Dairy Science* 93, no. 9 (2010): 3891–3901, <https://doi.org/10.3168/jds.2010-3190>.
7. A. I. Saiz, G. D. Manrique, and R. Fritz, "Determination of Benzoyl Peroxide and Benzoic Acid Levels by HPLC During Wheat Flour Bleaching Process," *Journal of Agricultural and Food Chemistry* 49, no. 1 (2001): 98–102, <https://doi.org/10.1021/jf9912304>.
8. A. M. Kligman and D. A. Basketter, "A Critical Commentary and Updating of the Guinea Pig Maximization Test," *Contact Dermatitis* 32, no. 3 (1995): 129–134, <https://doi.org/10.1111/j.1600-0536.1995.tb00801.x>.
9. D. A. Basketter and G. F. Gerberick, "An Interlaboratory Evaluation of the Buehler Test for the Identification and Classification of Skin Sensitizers," *Contact Dermatitis* 35, no. 3 (1996): 146–151, <https://doi.org/10.1111/j.1600-0536.1996.tb02332.x>.
10. I. Kimber, J. Hilton, R. Dearman, et al., "Assessment of the Skin Sensitization Potential of Topical Medicaments Using the Local Lymph Node Assay: An Interlaboratory Evaluation," *Journal of Toxicology and Environmental Health Part A* 53, no. 7 (1998): 563–579.
11. OECD, "Series on Testing and Assessment No.168: The Adverse Outcome Pathway for Skin Sensitisation Initiated by Covalent Binding to Proteins," (2012), <https://www.oecd-ilibrary.org/docserver/9789264221444-en.pdf?expires=1657519514&id=id&accname=oid210234&checksum=08C45BC1425C8A92FA12DC7A16E18720>.
12. OECD, "Test no. 442C: In Chemico Skin Sensitisation: Assays Addressing the Adverse Outcome Pathway Key Event on Covalent Binding to Proteins," (2024), Organisation for Economic Co-Operation and Development, https://www.oecd-ilibrary.org/environment/test-no-442c-in-chemico-skin-sensitisation_9789264229709-en.
13. OECD, "Test No. 442D: In Vitro Skin Sensitisation: Assays Addressing the Adverse Outcome Pathway Key Event on Keratinocyte Activation," (2024), Organisation for Economic Co-Operation and Development, https://www.oecd-ilibrary.org/environment/test-no-442d-in-vitro-skin-sensitisation_9789264229822-en.
14. OECD, "Test No. 442E: In Vitro Skin Sensitisation: In Vitro Skin Sensitisation Assays Addressing the Key Event on Activation of Dendritic Cells on the Adverse Outcome Pathway for Skin Sensitisation," (2024), Organisation for Economic Co-Operation and Development, https://www.oecd-ilibrary.org/environment/test-no-442e-in-vitro-skin-sensitisation_9789264264359-en.
15. OECD, "Guideline No. 497: Defined Approaches on Skin Sensitisation," (2023), Organisation for Economic co-Operation and Development, https://www.oecd-ilibrary.org/environment/guideline-no-497-defined-approaches-on-skin-sensitisation_b92879a4-en.
16. G. Kim, H. Lee, I. Baek, B. K. Cho, and M. S. Kim, "Quantitative Detection of Benzoyl Peroxide in Wheat Flour Using Line-Scan Short-Wave Infrared Hyperspectral Imaging," *Sensors and Actuators B: Chemical* 352 (2022): 130997, <https://doi.org/10.1016/j.snb.2021.130997>.
17. M. Agathos and H. J. Bandmann, "Benzoyl Peroxide Contact Allergy in Leg Ulcer Patients," *Contact Dermatitis* 11, no. 5 (1984): 316–317, <https://doi.org/10.1111/j.1600-0536.1984.tb01018.x>.
18. M. Segransky, B. A. Yentzer, and S. R. Feldman, "Benzoyl Peroxide: A Review of Its Current Use in the Treatment of Acne Vulgaris," *Expert Opinion on Pharmacotherapy* 10, no. 15 (2009): 2555–2562, <https://doi.org/10.1517/14656560903277228>.
19. R. L. Rietschel and S. H. Duncan, "Benzoyl Peroxide Reactions in an Acne Study Group," *Contact Dermatitis* 8, no. 5 (1982): 323–326, <https://doi.org/10.1111/j.1600-0536.1982.tb04238.x>.
20. H. Greim, ed., "Dibenzoylperoxid," in *Gesundheitsschädliche Arbeitsstoffe, Toxikologisch-arbeitsmedizinische Begründung von MAK-Werten* (Weinheim, Germany: Wiley-VCH, 1999).
21. A. Heratizadeh, T. Werfel, S. Schubert, J. Geier, and for the IVDK, "Contact Sensitization in Dental Technicians With Occupational Contact Dermatitis. Data of the Information Network of Departments of Dermatology (IVDK) 2001-2015: Contact Sensitization in Dental Technicians With OCD," *Contact Dermatitis* 78, no. 4 (2018): 266–273, <https://doi.org/10.1111/cod.12943>.
22. H. M. Ockenfels, W. Uter, H. Lessmann, A. Schnuch, and J. Geier, "Patch Testing With Benzoyl Peroxide: Reaction Profile and Interpretation of Positive Patch Test Reactions," *Contact Dermatitis* 61 (2009): 209–216, <https://doi.org/10.1111/j.1600-0536.2009.01603.x>.
23. D. A. Basketter and P. Cadby, "Reproducible Prediction of Contact Allergenic Potency Using the Local Lymph Node Assay," *Contact Dermatitis* 50, no. 1 (2004): 15–17, <https://doi.org/10.1111/j.0105-1873.2004.00278.x>.
24. S. Hoffmann, N. Kleinstreuer, N. Alépée, et al., "Non-Animal Methods to Predict Skin Sensitization (I): The Cosmetics Europe Database," *Critical Reviews in Toxicology* 48, no. 5 (2018): 344–358, <https://doi.org/10.1080/10408444.2018.1429385>.
25. D. Basketter and I. Kimber, "Predictive Test for Irritants and Allergens and Their Use in Quantitative Risk Assessment," in *Contact Dermatitis*, 5th ed., eds. P. Frosch, T. Menn, and J.-P. Lepoittevin (Berlin, Heidelberg: Springer Verlag, 2006), 229–239.
26. K. Schneider and Z. Akkan, "Quantitative Relationship Between the Local Lymph Node Assay and Human Skin Sensitization Assays," *Regulatory Toxicology and Pharmacology* 39, no. 3 (2004): 245–255, <https://doi.org/10.1016/j.yrtph.2004.02.002>.
27. S. E. Loveless, A. M. Api, R. W. R. Crevel, et al., "Potency Values From the Local Lymph Node Assay: Application to Classification, Labelling and Risk Assessment," *Regulatory Toxicology and Pharmacology* 56, no. 1 (2010): 54–66, <https://doi.org/10.1016/j.yrtph.2009.08.016>.
28. M. Fujita, Y. Yamamoto, and S. Watanabe, "Cause of and Countermeasures for Oxidation of the Cysteine-Derived Reagent Used in the Amino Acid Derivative Reactivity Assay," *Journal of Applied Toxicology* 39 (2019): 191–208, <https://doi.org/10.1002/jat.3707>.
29. OECD, "Series on Testing and Assessment No. 336: Supporting Document to the Guideline (GL) on Defined Approaches (DAs) for Skin Sensitisation - Annex 2: Reference Data Matrix and Comparison," (2021), *ENV/CBC/MONO(2021)11, OECD*.

30. K. Saito, O. Takenouchi, Y. Nukada, M. Miyazawa, and H. Sakaguchi, "An In Vitro Skin Sensitization Assay Termed EpiSensA for Broad Sets of Chemicals Including Lipophilic Chemicals and Pre/Pro-Haptens," *Toxicology In Vitro* 40 (2017): 11–25, <https://doi.org/10.1016/j.tiv.2016.12.005>.
31. J. Li, H. Johansson, and A. Forreryd, "Applicability of GardSkin for Accurate Assessment of Challenging Substances in the Context of Skin Sensitization Testing," 2020.
32. Y. Kimura, C. Fujimura, Y. Ito, et al., "Optimization of the IL-8 Luc Assay as an In Vitro Test for Skin Sensitization," *Toxicology In Vitro* 29, no. 7 (2015): 1816–1830, <https://doi.org/10.1016/j.tiv.2015.07.006>.
33. B. Wareing and S. Kolle, "Kinetic Direct Peptide Reactivity Assay (KDPRA): Validation Study Report," (2020), BASF SE.
34. S. N. Kolle, M. Mathea, A. Natsch, and R. Landsiedel, "Assessing Experimental Uncertainty in Defined Approaches: Borderline Ranges for *in Chemico* and *in Vitro* Skin Sensitization Methods Determined From Ring Trial Data," *Applied In Vitro Toxicology* 7, no. 3 (2021): 102–111, <https://doi.org/10.1089/aivt.2021.0003>.
35. A. Mehling, E. Adriaens, S. Casati, et al., "In Vitro RHE Skin Sensitisation Assays: Applicability to Challenging Substances," *Regulatory Toxicology and Pharmacology* 108 (2019): 104473, <https://doi.org/10.1016/j.yrtph.2019.104473>.
36. F. Cottrez, E. Boitel, J. C. Ourlin, et al., "SENS-IS, a 3D Reconstituted Epidermis Based Model for Quantifying Chemical Sensitization Potency: Reproducibility and Predictivity Results From an Inter-Laboratory Study," *Toxicology In Vitro* 32 (2016): 248–260, <https://doi.org/10.1016/j.tiv.2016.01.007>.
37. EURL ECVAM, "U-SENS Test Submission Template Validation Report," (2013), Institute for Health and Consumer Protection, The European Union Reference Laboratory for Alternatives to Animal Testing, https://www.oecd.org/env/ehs/testing/Validation-report_USENS.pdf.
38. A. Natsch, C. A. Ryan, L. Foertsch, et al., "A Dataset on 145 Chemicals Tested in Alternative Assays for Skin Sensitization Undergoing Prevalidation: 145 Chemicals Tested in Alternative Assays for Skin Sensitization," *Journal of Applied Toxicology* 33 (2013): 1337–1352, <https://doi.org/10.1002/jat.2868>.
39. C. Piroird, J. M. Ovigne, F. Rousset, et al., "The Myeloid U937 Skin Sensitization Test (U-SENS) Addresses the Activation of Dendritic Cell Event in the Adverse Outcome Pathway for Skin Sensitization," *Toxicology In Vitro* 29, no. 5 (2015): 901–916, <https://doi.org/10.1016/j.tiv.2015.03.009>.
40. W. Uter, S. Schaller, F. Bahmer, et al., "Contact Allergy in Metal Workers: A One-Year Analysis Based on Data Collected by the Information Network of Dermatological Clinics (IVDK) in Germany," *Dermatosen in Beruf und Umwelt* 41 (1993): 220–227, <https://www.semanticscholar.org/paper/Contact-allergy-in-metal-workers%3A-a-one-year-based-Uter-Schaller/0d8df4b251289b621d6951862ad00acbb903c73b>.
41. W. Uter, J. Geier, and H. Ippen, Aktuelle Sensibilisierungshäufigkeiten bei der DKG-Testreihe Metallverarbeitung (1996), <https://www.semanticscholar.org/paper/Aktuelle-Sensibilisierungsh%C3%A4ufigkeiten-bei-der-Schnuch-Geier/a8b068905481df5e887ab72ab465a68fa9ccd4a3>.
42. H. J. Bandmann and M. Agathos, "Post-Therapeutic Benzoyl Peroxide Contact Allergy in Ulcus Cruris Patients," *Hautarzt* 36, no. 12 (1985): 670–674.
43. G. A. Vena, G. Angelini, and C. L. Meneghini, "Contact Dermatitis to Benzoyl Peroxide," *Contact Dermatitis* 8, no. 5 (1982): 338, <https://doi.org/10.1111/j.1600-0536.1982.tb04243.x>.
44. U. F. Haustein, L. Tegetmeyer, and V. Ziegler, "Allergic and Irritant Potential of Benzoyl Peroxide," *Contact Dermatitis* 13, no. 4 (1985): 252–257, <https://doi.org/10.1111/j.1600-0536.1985.tb02559.x>.
45. S. Iijima and T. Tsunoda, "Twenty Cases of Allergic Contact Dermatitis due to Benzoyl Peroxide in Acne Patients in Japan," *J Cutan Immunol Allergy* 2, no. 4 (2019): 108–112, <https://doi.org/10.1002/cia.2.12069>.
46. A. Bulinckx, C. Dachelet, A. Leroy, A. Goossens, D. Tennstedt, and M. Baeck, "Contact Dermatitis to the Combination Gel of Adapalene 0.1% and Benzoyl Peroxide (BPO) 2.5%," *European Journal of Dermatology* 22, no. 1 (2011): 139–140, <https://doi.org/10.1684/ejd.2011.1578>.
47. C. Holden, "Case Reports: Reactions: Benzoyl Peroxide/Clindamycin," *Contact Dermatitis* 70, no. s1 (2014): 41–51, <https://doi.org/10.1111/cod.12261>.
48. S. J. Felton, D. Orton, and J. D. Williams, "Benzoyl Peroxide in Topical Acne Preparations: An Underreported Contact Allergen?," *Dermatitis: Contact, Atopic, Occupational, Drug* 24, no. 3 (2013): 146–147, <https://doi.org/10.1097/DER.0b013e31828d02e2>.
49. P. L. Minciullo, M. Patafi, L. Giannetto, et al., "Allergic Contact Angioedema to Benzoyl Peroxide," *Journal of Clinical Pharmacy and Therapeutics* 31, no. 4 (2006): 385–387, <https://doi.org/10.1111/j.1365-2710.2006.00738.x>.
50. A. Hernández-Núñez, J. Sánchez-Pérez, M. Pascual-López, M. Aragüés, and A. García-Díez, "Allergic Contact Dermatitis From Benzoyl Peroxide Transferred by a Loving Son: Contact Point," *Contact Dermatitis* 46, no. 5 (2002): 302, <https://doi.org/10.1034/j.1600-0536.2002.460512.x>.
51. C. Kim, B. G. Craiglow, K. L. Watsky, and R. J. Antaya, "Allergic Contact Dermatitis to Benzoyl Peroxide Resembling Impetigo," *Pediatric Dermatology* 32, no. 4 (2015): e161–e162, <https://doi.org/10.1111/pde.12585>.
52. M. Sandre and S. Skotnicki-Grant, "A Case of a Paediatric Patient With Allergic Contact Dermatitis to Benzoyl Peroxide," *Journal of Cutaneous Medicine and Surgery* 22, no. 2 (2018): 226–228, <https://doi.org/10.1177/1203475417733462>.
53. S. Nacht, D. Yeung, J. N. Beasley, M. D. Anjo, and H. I. Maibach, "Benzoyl Peroxide: Percutaneous Penetration and Metabolic Disposition," *Journal of the American Academy of Dermatology* 4, no. 1 (1981): 31–37, [https://doi.org/10.1016/s0190-9622\(81\)70004-5](https://doi.org/10.1016/s0190-9622(81)70004-5).
54. D. Yeung, S. Nacht, D. Bucks, and H. I. Maibach, "Benzoyl Peroxide: Percutaneous Penetration and Metabolic Disposition. II. Effect of Concentration," *Journal of the American Academy of Dermatology* 9, no. 6 (1983): 920–924, [https://doi.org/10.1016/s0190-9622\(83\)70209-4](https://doi.org/10.1016/s0190-9622(83)70209-4).
55. B. Thomas, D. Kulichova, R. Wolf, B. Summer, V. Mahler, and P. Thomas, "High Frequency of Contact Allergy to Implant and Bone Cement Components, in Particular Gentamicin, in Cemented Arthroplasty With Complications: Usefulness of Late Patch Test Reading: Gentamicin Allergy in Complicated Arthroplasty?," *Contact Dermatitis* 73, no. 6 (2015): 343–349, <https://doi.org/10.1111/cod.12465>.
56. G. Rojas-Alcayaga, A. Carrasco-Labra, P. Danus, et al., "Determination of Susceptibility to Sensitization to Dental Materials in Atopic and Non-Atopic Patients," *Medicina Oral* 17 (2012): e320–e324, <https://doi.org/10.4317/medoral.17424>.
57. F. C. Yoshimura, V. d. E. S. Cunha, R. L. Hahnstadt, and M. C. Pires, "Evaluation of Dental Material Series From Patients With Dental Prostheses and Suspicion of Delayed Hypersensitivity," *Anais Brasileiros de Dermatologia* 91, no. 2 (2016): 141–148, <https://doi.org/10.1590/abd1806-4841.20164116>.
58. R. Treudler and J. C. Simon, "Benzoyl Peroxide: Is It a Relevant Bone Cement Allergen in Patients With Orthopaedic Implants?," *Contact Dermatitis* 57, no. 3 (2007): 177–180, <https://doi.org/10.1111/j.1600-0536.2007.01195.x>.
59. R. R. Torgerson, M. D. P. Davis, A. J. Bruce, S. A. Farmer, and R. S. Rogers, "Contact Allergy in Oral Disease," *Journal of the American Academy of Dermatology* 57, no. 2 (2007): 315–321, <https://doi.org/10.1016/j.jaad.2007.04.017>.
60. S. Furrer, K. Scherer Hofmeier, L. Grize, and A. J. Bircher, "Metal Hypersensitivity in Patients With Orthopaedic Implant Complications-A

- Retrospective Clinical Study," *Contact Dermatitis* 79, no. 2 (2018): 91–98, <https://doi.org/10.1111/cod.13032>.
61. P. Thomas, K. Stauner, A. Schraml, et al., "Charakteristika Von 200 Patienten Mit Verdacht Auf Implantatallergie Im Vergleich Zu 100 Beschwerdefreien Endoprothesenträgern," *Orthopäde* 42, no. 8 (2013): 607–613, <https://doi.org/10.1007/s00132-012-2038-0>.
62. U. Hillen, H. Lessmann, S. Grabbe, and J. Geier, "Kontaktsensibilisierungen Gegen Bestandteile Von Klebstoffen Unter Berücksichtigung Beruflicher Kontaktsensibilisierungen," *Dermatologie in Beruf Und Umwelt* 55, no. 1 (2007): 10–19, <https://doi.org/10.5414/DBP55010>.
63. M. Kiec-Swierczyńska and B. Krecisz, "Allergic Contact Dermatitis in Dentists and Dental Nurses," *Exogenous Dermatology* 1, no. 1 (2002): 27–31, <https://doi.org/10.1159/000047988>.
64. D. Peiler, B. Pflug, P. J. Frosch, and Deutsche Kontaktallergie-Gruppe, "Empfehlungen für die Epikutantestung von Zahntechnikern," *Dermatologie in Beruf Und Umwelt* 48 (2000): 19–20.
65. E. Shmidt, S. A. Farmer, and M. D. P. Davis, "Patch-Testing With Plastics and Glues Series Allergens," *Dermatitis* 21, no. 5 (2010): 269–274, <https://doi.org/10.2310/6620.2010.10024>.
66. T. J. Widman, H. Oostman, and F. J. Storrs, "Allergic Contact Dermatitis From Medical Adhesive Bandages in Patients Who Report Having a Reaction to Medical Bandages," *Dermatitis* 19, no. 1 (2008): 32–37, <https://doi.org/10.2310/6620.2008.07053>.
67. M. Gebhart and J. Geier, "Evaluation of Patch Test Results With Denture Material Series," *Contact Dermatitis* 34, no. 3 (1996): 191–195, <https://doi.org/10.1111/j.1600-0536.1996.tb02172.x>.
68. J. Geier and S. Schubert, "Frequency of Skin Sensitization to Specific Substances and in Specific Occupational Groups," (2021), Baua, <https://doi.org/10.21934/baua:bericht20210122>.
69. S. Schubert, R. Brans, A. Reich, et al., "Contact Sensitization in Metalworkers: Data From the Information Network of Departments of Dermatology (IVDK), 2010–2018," *Contact Dermatitis* 83, no. 6 (2020): 487–496, <https://doi.org/10.1111/cod.13686>.
70. J. C. H. Donovan, I. Kudla, and L. D. Holness, "Hand Dermatitis in Auto Mechanics and Machinists," *Dermatitis* 18, no. 3 (2007): 143–149, <https://doi.org/10.2310/6620.2007.06039>.
71. K. Forschner, T. Zuberbier, and M. Worm, "Benzoyl Peroxide as a Cause of Airborne Contact Dermatitis in an Orthopaedic Technician: Contact Points," *Contact Dermatitis* 47, no. 4 (2002): 241, <https://doi.org/10.1034/j.1600-0536.2002.470415.x>.
72. V. Elangasinghe and G. Johnston, "Occupational Hand Dermatitis Caused by Benzoyl Peroxide in Transformer Coil Binding Tape," *Contact Dermatitis* 66, no. 5 (2012): 293, <https://doi.org/10.1111/j.1600-0536.2012.02007.x>.
73. A. Adelman, T. Mohammed, and H. Kerr, "Allergic Contact Dermatitis due to Benzyl Peroxide From an Unlikely Source," *Journal of the American Academy of Dermatology* 81, no. 4 (2019): AB18, <https://doi.org/10.1016/j.jaad.2019.06.105>.
74. E. Tsovilis, M. N. Crepy, A. M. Jonathan, and J. Ameille, "Occupational Contact Dermatitis due to a Marbler's Exposure to Benzoyl Peroxide," *Contact Dermatitis* 52, no. 2 (2005): 117–118, <https://doi.org/10.1111/j.0105-1873.2005.004981.x>.
75. S. N. Kolle, A. Natsch, G. F. Gerberick, and R. Landsiedel, "A Review of Substances Found Positive in 1 of 3 In Vitro Tests for Skin Sensitization," *Regulatory Toxicology and Pharmacology* 106 (2019): 352–368, <https://doi.org/10.1016/j.yrtph.2019.05.016>.
76. B. Wareing, A. Aktalay Hippchen, S. N. Kolle, B. Birk, D. Funk-Weyer, and R. Landsiedel, "Limitations and Modifications of Skin Sensitization NAMs for Testing Inorganic Nanomaterials," *Toxics* 12, no. 8 (2024): 616, <https://doi.org/10.3390/toxics12080616>.
77. D. W. Roberts and A. M. Api, "Chemical Applicability Domain of the Local Lymph Node Assay (LLNA) for Skin Sensitisation Potency. Part 4. Quantitative Correlation of LLNA Potency With Human Potency," *Regulatory Toxicology and Pharmacology* 96 (2018): 76–84, <https://doi.org/10.1016/j.yrtph.2018.04.022>.
78. S. Seubert, A. Seubert, and H. Ippen, "Penetration of Benzoyl Peroxide in the Skin," *Hautarzt* 35, no. 9 (1984): 455–458.
79. W. Uter, "Zur Kreuzreaktivität Zwischen Benzoylperoxid Und Benzoesäure," *Dermatosen* 43, no. 4 (1995): 184–185.
80. J. D. Johansen, C. M. Bonefeld, J. F. B. Schwensen, J. P. Thyssen, and W. Uter, "Novel Insights Into Contact Dermatitis," *Journal of Allergy and Clinical Immunology* 149, no. 4 (2022): 1162–1171, <https://doi.org/10.1016/j.jaci.2022.02.002>.
81. B. Blömeke, L. M. Pot, P.-J. Coenraads, J. Hennen, M. Kock, and C. Goebel, "Cross-Elicitation Responses to 2-Methoxymethyl-p-Phenylenediamine Under Hair Dye Use Conditions in p-Phenylenediamine-Allergic Individuals," *British Journal of Dermatology* 172, no. 4 (2015): 976–980, <https://doi.org/10.1111/bjd.13412>.
82. C. Shwerek and E. J. Lowenstein, "Delayed Type Hypersensitivity to Benzoyl Peroxide," *Journal of Drugs in Dermatology* 3, no. 2 (2004): 197–199.
83. J. Geier, H. Lessmann, P. J. Frosch, et al., "Patch Testing With Components of Water-Based Metalworking Fluids," *Contact Dermatitis* 49, no. 2 (2003): 85–90, <https://doi.org/10.1111/j.0105-1873.2003.00187.x>.
84. Q. Hu, W. Li, C. Qin, L. Zeng, and J. T. Hou, "Rapid and Visual Detection of Benzoyl Peroxide in Food by a Colorimetric and Ratiometric Fluorescent Probe," *Journal of Agricultural and Food Chemistry* 66, no. 41 (2018): 10913–10920, <https://doi.org/10.1021/acs.jafc.8b04733>.
85. Y. Abe-Onishi, C. Yomota, N. Sugimoto, H. Kubota, and K. Tanamoto, "Determination of Benzoyl Peroxide and Benzoic Acid in Wheat Flour by High-Performance Liquid Chromatography and Its Identification by High-Performance Liquid Chromatography–Mass Spectrometry," *Journal of Chromatography A* 1040, no. 2 (2004): 209–214, <https://doi.org/10.1016/j.chroma.2004.03.059>.
86. F. A. Bahmer, A. Schulze-Dirks, and H. Zaun, "Sensitizing Effect of a 20% Benzoyl Peroxide Preparation Used for the Treatment of Leg Ulcer," *Dermatosen in Beruf und Umwelt* 32, no. 1 (1984): 21–24.