Frequency and clinical relevance of contact allergy in dental patients

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Frequency and clinical relevance of contact allergy in dental patients

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Abstract

Background: While many studies have reported on occupational allergic contact dermatitis amongst dental personnel, studies on the relevance of patch testing in dental patients are scarce.

Objectives: To determine the frequency and clinical relevance of contact allergy in patients with intra- and perioral complaints.

Methods: A total of 360 patients with intra- and perioral complaints suspected of having a contact allergy were patch-tested with the dental allergen series, European Baseline Series, and extended Amsterdam Baseline Series at Amsterdam University Medical Centers between January 2015 and November 2021.

Results: A total of 285 patients (79.2%) had a positive patch test reaction for either one (18.6%) or multiple allergens (60.6%). Sodium tetrachloropalladate was the most sensitising allergen with 98 patients (27.2%) testing positive, followed by nickel sulphate (23.3%), methylisothiazolinone (15.6%), and fragrance mix I (14.2%). Clinical relevance was found in 68 of 208 patients (32.7%), with patients having one (15.4%) or multiple (17.3%) patch test reactions clinically relevant to their (peri)oral complaints.

Conclusions: Clinically relevant patch test reactions were frequently seen in dental patients. Although this study provides us with a better understanding on the frequency and clinical relevance of contact allergy in dental patients, further studies are needed to confirm our results.

KEYWORDS

(meth)acrylates, allergic contact dermatitis, clinical relevance, contact allergy, dental patients, dental series, European baseline series, fragrances, metals, oral complaints

1 | INTRODUCTION

Dental patients and professionals are known to be exposed to many chemicals that result in irritant (IR) contact dermatitis or allergic contact dermatitis (ACD).[1] In non-occupational cases, this might result in contact stomatitis, cheilitis, xerostomia, burning mouth syndrome, oral lichen planus, or oral lichenoid lesions.[1] Therefore, it is important to identify the possible dental allergens that might cause ACD.

In a previous study published in 2001, reactions to metals such as nickel, mercury, gold, palladium, and cobalt were most frequently seen in dental patients.[2]

In recent years, the use of mercury in dental amalgam has raised concerns for both health and environmental reasons. In 2017, the European Parliament issued new regulations in order to phase out the use of dental amalgams.[3] Dental amalgam has now been frequently replaced by (meth)acrylates. A Swedish study on the use of (meth)acrylates in dentistry showed contact sensitization in 2.3% of dental patients and 5.8% of dental personnel with the most common allergens being 2-hydroxyethyl methacrylate (2-HEMA), ethyleneglycol dimethacrylate (EGDMA), triethyleneglycol dimethacrylate (TEGDMA), and methyl methacrylate (MMA).[4]

While many studies have reported on occupational contact dermatitis amongst dental personnel, data on dental patients are scarce.[5–7] Most reports on dental patients are limited to case reports, case series, or small observational studies.[8–11] The objectives of this study were (1) to determine the frequency of positive patch test reactions in patients with intra- and perioral complaints tested with an (extended) baseline series and dental series in a tertiary referral centre in The Netherlands and (2) to determine the clinical relevance of positive patch tests of the dental series.

2 | PATIENTS AND METHODS

2.1 | Patients

In this retrospective cohort study, all adult patients with intra- and perioral complaints who underwent patch testing with the dental allergen series at Amsterdam University Medical Centers (AUMC) between January 2015 and November 2021 were analysed. Approval from the Medical Ethics Review Committee of the Academic Medical Centre was obtained (reference number W20_555 #20.618).

2.2 | Patch tests

All patients were tested with a dental series of 31 allergens (Table 1), in addition to the European Baseline Series (EBS) and the extended Amsterdam Baseline Series, both consisting of 29 allergens (Appendix A, Tables A1 and A2). Patch tests were executed using Van der Bend square chambers (Brielle, The Netherlands) on Fixomull stretch tape (Beiersdorf, Hamburg, Germany) at the upper part of the patients' back. Allergens were obtained from Chemotechnique Diagnostics (Vellinge, Sweden) and TrueTest (SmartPractice, Hillerød, Denmark). After 2 days, the patches were removed. Patch test readings were performed on day (D) 2, D3/D4, and if required D6/D7 according to the European Society of Contact Dermatitis.[12] Patch tests were regarded as negative if reactions were IR, negative (−), or questionable (?+) and as positive if reactions were allergic (+, ++, +++) according to the International Contact Dermatitis Research Group guidelines.[13] Positive results of the dental series were categorised as certain, probable, possible, unlikely, or unknown clinical relevance. 'Certain' and 'probable' relevance scores were considered clinically relevant.

2.3 | Data collection

Data collection was performed using the European Surveillance System on Contact Allergies database and from electronic patient files. Data obtained included demographics (sex and age), symptoms, atopic history, and patch test results (allergens applied, concentrations, reactions, and clinical relevance).

2.4 | Statistical analysis

Statistical analyses were performed with SPSS version 28.0 (IBM, SPSS Inc., Chicago IL, USA). Categorical variables were presented as numbers and percentages and continuous variables as medians with interquartile ranges (IQRs). Analyses of demographic variables gender and atopy in relation to the patch test results were performed using Fisher's exact test. Two-sided p-values of <0.05 were considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

A total of 360 patients were included (Table 2). The study population was predominantly female (84.2%) and had a median age of 59 years (IQR: 49–67). Eighty patients (22.2%) reported having an atopic history. Atopy and gender were not related to having a positive patch test ($p < 1.0000$ and $p < 0.328$, respectively).

3.2 | Patch testing

Two hundred and eighty-five patients (79.2%) had a positive patch test reaction for either one (18.6%) or multiple allergens (60.6%). Amongst all 360 patients, there were 1158 positive patch test reactions. Most reactions were caused by allergens in the EBS and extended Amsterdam Baseline Series, which yielded 688 (59.4%) positive reactions (Appendix A, Tables A1 and A2), while the dental series elicited 470 (40.6%) positive reactions (Table 1). Overall, sodium tetrachloropalladate was the most sensitising allergen with 98 patients (27.2%) testing positive, followed by nickel sulphate (23.3%), methylisothiazolinone (15.6%), and fragrance mix I (FMI) (14.2%). N-Ethyl-p-toluenesulfonamide was the only allergen in the dental series without positive reactions. Four IR reactions were found to be caused by three test preparations: silver nitrate (0.6% in water), methylhydroquinone (0.3% in petrolatum), and benzophenone 4 (10% in petrolatum).

TABLE 1 Dental series patch test reactions.

Allergen (in pet. unless otherwise stated)	Positive (%)	−	?+	+	++	+++	IR	Relevance (%)
Ammoniated mercury 1%[b]	8 (2.2)	345 (95.8)	7 (1.9)	8 (2.2)	-	-	-	2 (25.0)
Mercury 0.5%[a]	24 (6.7)	292 (81.1)	44 (12.2)	22 (6.1)	2 (0.6)	-	-	6 (25.0)
Eugenol 2%[a]	1 (0.3)	354 (98.3)	5 (1.4)	-	-	1 (0.3)	-	-
Benzoyl peroxide 1%[b]	40 (11.1)	261 (72.5)	59 (16.4)	40 (11.1)	-	-	-	11 (27.5)
Methylhydroquinone 1%[a]	16 (4.4)	220 (61.1)	123 (34.2)	14 (3.9)	2 (0.6)	-	1 (0.3)	3 (18.8)
Camphoroquinone 1%[a]	1 (0.3)	355 (98.6)	4 (1.1)	1 (0.3)	-	-	-	-
N-ethyl-p-toluenesulfonamide 0.1%[a]	–	357 (99.2)	3 (0.8)	-	-	-	-	-
1,4-butanediol dimethacrylate 2%[b]	6 (1.7)	348 (96.7)	6 (1.7)	3 (0.8)	2 (0.6)	1 (0.3)	-	6 (100.0)
Methyl methacrylate 2%[b]	10 (2.8)	343 (95.3)	7 (1.9)	7 (1.9)	3 (0.8)	-	-	8 (80.0)
Urethane dimethacrylate 2%[b]	7 (1.9)	349 (96.9)	4 (1.1)	5 (1.4)	2 (0.6)	-	-	7 (100.0)
Ethyleneglycol dimethacrylate 2%[b]	11 (3.1)	343 (95.3)	6 (1.7)	4 (1.1)	5 (1.4)	2 (0.6)	-	10 (90.9)
BIS-GMA 2%[b]	4 (1.1)	349 (96.9)	7 (1.9)	4 (1.1)	-	-	-	1 (25.0)
Triethyleneglycol dimethacrylate 2%[b]	9 (2.5)	346 (96.1)	5 (1.4)	5 (1.4)	3 (0.8)	1 (0.3)	-	9 (100.0)
2-hydroxyethyl methacrylate 2%[b]	15 (4.2)	342 (95.0)	3 (0.8)	6 (1.7)	7 (1.9)	2 (0.6)	-	12 (80.0)
Bisphenol A dimethacrylate 2%[b]	2 (0.6)	353 (98.1)	5 (1.4)	-	1 (0.3)	1 (0.3)	-	2 (100.0)
Tetrahydrofurfuryl methacrylate 2%[b]	7 (1.9)	347 (96.4)	6 (1.7)	4 (1.1)	1 (0.3)	2 (0.6)	-	6 (85.7)
1,6-hexanediol diacrylate 0.1%[a]	6 (1.7)	350 (97.2)	4 (1.1)	5 (1.4)	1 (0.3)	-	-	4 (66.7)
N,N-dimethylaminoethyl methacrylate 0.2%[a]	5 (1.4)	351 (97.5)	4 (1.1)	5 (1.4)	-	-	-	4 (80.0)
Bisphenol A 1%[b]	2 (0.6)	357 (99.2)	1 (0.3)	1 (0.3)	1 (0.3)	-	-	1 (50.0)
4-Tolyldiethanolamine 2%[b]	3 (0.8)	353 (98.1)	4 (1.1)	2 (0.6)	1 (0.3)	–	–	1 (33.3)
Ammoniummolybdate 1% (aq.)[b]	5 (1.4)	347 (96.4)	8 (2.2)	5 (1.4)	-	-	-	-
Potassium dicyanoaurate 100 ppm (aq.)[b]	33 (9.2)	310 (86.1)	17 (4.7)	29 (8.1)	4 (1.1)	-	-	5 (15.2)
Potassium sulphate 2.5% (aq.)[b]	18 (5.0)	332 (92.2)	10 (2.8)	17 (4.7)	1 (0.3)	-	-	4 (22.2)
Palladium chloride 1% (aq.)[a]	50 (13.9)	296 (82.2)	14 (3.9)	45 (12.5)	5 (1.4)	-	-	16 (32.0)
Stannous chloride 0.5% (aq.)[a]	47 (13.1)	286 (79.4)	27 (7.5)	46 (12.8)	1 (0.3)	-	-	11 (23.4)
Silver nitrate 1% (aq.)[b]	16 (4.4)	331 (91.9)	11 (3.1)	13 (3.6)	3 (0.8)	-	2 (0.6)	3 (18.8)
Sodium tetrachloropalladate 3%[a]	98 (27.2)	236 (65.6)	26 (7.2)	67 (18.6)	28 (7.8)	3 (0.8)	-	29 (29.6)
Peppermint oil 2%[b]	6 (1.7)	344 (95.6)	10 (2.8)	6 (1.7)	-	-	-	3 (50.0)
Menthol 1%[b]	6 (1.7)	349 (96.9)	5 (1.4)	6 (1.7)	-	-	-	4 (66.7)
Beryllium sulphate tetrahydrate 1%[a]	12 (3.3)	321 (89.2)	27 (7.5)	9 (2.5)	3 (0.8)	-	-	2 (16.7)
Gallium(III)oxide 1%[a]	2 (0.6)	354 (98.3)	4 (1.1)	2 (0.6)	-	-	-	-
Total	470 (4.2)	10 221 (91.6)	466 (4.2)	381 (3.4)	76 (0.7)	13 (0.1)	3 (0.0)	170 (36.2)

Abbreviations: aq, aqueous; pet, petrolatum; −, negative reaction; ? +, doubtful reaction; IR, irritant reaction.
[a]Chemotechnique Diagnostics, Vellinge, Sweden.
[b]TrueTest (SmartPractice, Hillerød, Denmark).

3.3 | Allergen groups

One hundred ninety-six (54.4%) of the 285 patients tested positive to one or more metal allergens. The metals that most frequently tested positive were sodium tetrachloropalladate (27.2%), nickel sulphate (23.3%), palladium chloride (13.9%), stannous chloride (13.1%), cobalt chloride (10.0%) and potassium dicyanoaurate (9.2%). Furthermore, 95 patients (26.4%) had positive patch test reactions to fragrances. The most common reactions were caused by FMI (14.2%), balsam of Peru (8.3%), and fragrance mix II (FMII) (7.5%). Sensitization to (meth)acrylates was found in 26 patients (7.2%) and was most commonly caused by 2-HEMA (4.2%), EGDMA (3.1%), MMA (2.8%) and TEGDMA (2.5%).

TABLE 2 Summary of patch test results ($N = 360$).

Summary of patch test results	*n* (%)
Positive patch tests	1158 (100)
Patients with positive reactions	285 (79.2)
Patients with one positive reaction	67 (18.6)
Patients with multiple positive reactions	218 (60.6)
Patients with positive reactions in dental series	208 (57.8)
Patients with relevant positive reactions in dental series	68 (32.7)
Patients with one relevant positive reaction in dental series	32 (15.4)
Patients with multiple relevant positive reactions in dental series	36 (17.3)
Total number allergens in dental series	31
Total number of allergens with positive reactions in dental series	30 (96.8)
Total number relevant allergens in dental series	26 (86.7)

Five patients (1.8%) had a positive patch test reaction to Caine mix III, and 14 patients (4.9%) to cocamidopropyl betaine.

3.4 | Dental series and clinical relevance

Sensitization to allergens in the dental series was present in 208 patients (57.8%). In total, 26 of 30 allergens (86.7%) with positive patch test reactions in the dental series proved clinically relevant (Table 1). This resulted in 68 patients (32.7%) having one (15.4%) or multiple (17.3%) patch test reactions clinically relevant to their (peri) oral complaints. 1,4-butanediol dimethacrylate urethane dimethacrylate, TEGDMA, and Bisphenol A dimethacrylate were clinically relevant for all positive patch tests, whereas eugenol, camphoroquinone, ammoniummolybdate, and gallium(III)oxide only had clinically irrelevant positive patch test reactions.

4 | DISCUSSION

This retrospective cohort study evaluated the frequency of positive patch test reactions to the (extended) EBS and dental series and the clinical relevance of positive patch test reactions to the dental series in dental patients. To our knowledge, it is one of few studies that has investigated the clinical relevance of performing patch testing with a dental series in non-occupational cases. This study showed positive patch tests in 79.2% of patients and clinical relevance in 32.7%, indicating the importance of (further) research in dental patients.

4.1 | Metals

In a recent Japanese study, 60 patients with (peri)oral complaints were analysed for oral metal allergies. Nickel sulphate (20%), cobalt chloride (10%), zinc chloride (8%) were most often positive.[9] These results are similar to the present study, with the exception of zinc which was not patch tested. Studies from Finland and Israel showed a lower percentage of nickel sensitivity (13.2%–14.6%).[2,14] This difference might be caused by patient selection. In these studies, not only patients with oral complaints but also patients suspected of having occupational ACD were included.[2,14] All three of the studies mentioned above did not include sodium tetrachloropalladate, which was the most common metal sensitizer in this study. The use of sodium tetrachloropalladate has only recently proved to be a more reliable test material for diagnosing a palladium allergy.[15] Palladium, is commonly used as a component of dental casting alloy and dental plates with other metals such as dental gold, silver, zinc, and copper.[16] However, due to the low dissolution rate of palladium ions in these dental castings, it is often tolerated by patients.[17] A study of 906 patients suspected of having contact allergy with or without eczema showed that 10.7% reacted positively to palladium chloride and 24.3% reacted to sodium tetrachloropalladate. These findings are in line with our study as positive reactions to palladium chloride and sodium tetrachloropalladate were seen in 13.9% and 27.2% respectively.[18]

In addition, a cross-reaction between palladium and nickel has been proposed, which makes it difficult to detect the clinical relevance of a positive patch test to palladium.[19] Nickel is found in casting alloys used for dental prosthetics and orthodontic alloys. Since it is technically difficult to separate nickel and cobalt, nickel and cobalt are frequently found in combination.[1] However, research has shown that little to no adverse reactions are seen in nickel-allergic patients with nickel-containing orthodontic appliances.[20,21]

Metals are also commonly used in dental amalgam, which comprises mercury, tin, silver, zinc, and copper, used for the permanent filling of cavities.[22] Even though adverse reactions to metals are rare and measures have been taken to reduce the use of common metal sensitizers in dental material, ideally, the production of new low-metal exposure dental material for patients highly susceptible to metal allergies could provide an outcome.[3]

4.2 | Fragrances

In previous studies, dental patients were most often only tested with a dental series.[2,14] Therefore, common allergens such as fragrances are often missing. In the present study, fragrances yielded many positive reactions: FMI (14.2%), balsam of Peru (8.3%), and FMII (7.5%). Previous research has reported lower rates of allergies to FMI (9.8% and 6.7%) and balsam of Peru (7.2%).[23,24] This difference might be caused by selection and referral bias. Fragrance mixes I and II are composed of eight and six different fragrances, respectively, including eugenol and lyral. Both eugenol and Lyral® were tested separately which resulted in an allergy in 0.3% and 2.2% of patients, respectively. Previous literature has shown that fragrances are one of the most frequent causes of contact allergy.[25,26] Therefore, it seems advisable to also patch test fragrances in patients suspected of having oral complaints possibly caused by contact allergy to dental materials.

4.3 | (Meth)acrylates

A previous Swedish study showed sensitization of (meth)acrylates in 2.3% of dental patients and 5.8% of dental personnel.[4] This is lower compared to this study where 7.2% of dental patients had (meth)acrylate sensitization. The study also showed the most common allergens in patients to be 2-HEMA (2.2%), EGDMA (1.1%), TEGDMA (0.5%), and MMA (0.3%),[4] which is also lower compared to our findings (2-HEMA (4.2%), EGDMA (3.1%), TEGDMA (2.5%) and MMA (2.8%)). Authors of the previously mentioned Israeli study found 5.8% of 121 patients to have positive patch test reactions to 2-HEMA.[14] Other (meth)acrylates were not mentioned.

4.4 | Clinical relevance of positive patch tests to dental materials

In this study, 68 of 208 patients (32.7%) were found to have positive patch tests to dental materials clinically relevant to their (peri)oral complaints. This is lower compared to previous studies.[27,28] The discrepancies in clinical relevance could be a result of the specific patient population. Authors of a German study found clinical relevance in 50% of patients with visible inflammatory changes at the lining of the oral mucosa.[27] A Thai study showed a clinical relevance of 76.9% in patients with clinically or histologically proven oral lichen planus or oral lichenoid lesions.[28] In the current study, patients with subjective (peri)oral complaints were also included. Furthermore, both studies analysed clinical relevance in only dental metals or a dental series focused on components of dental amalgam.[27,28] Neither study reported the most frequently seen clinically relevant reactions.

4.5 | Limitations

The main limitation of this study is that it is a monocentric study, in a tertiary referral centre for contact dermatitis, possibly resulting in referral bias. Additionally, selection bias may have occurred as patients suspected of having dental material allergies were included in the study. The study's retrospective design forms another limitation. Furthermore, clinical relevance was only assessed for sensitizers in the dental series and cross-reactivity was not analysed. Another shortcoming lies in the absence of a comparison between our patch test reactions and the general dermatitis population.

5 | CONCLUSION

To conclude, it is important to test dental patients presenting with intra- and peri-oral complaints for contact allergy with a dental series in addition to the EBS. Metals were found to be the largest group of sensitizers, followed by fragrances and (meth)acrylates. Overall, sodium tetrachloropalladate was the most sensitising allergen, followed by nickel sulphate, methylisothiazolinone, and FMI. One third of patients were found to have positive patch tests to dental materials clinically relevant to their (peri)oral complaints.

Although this study provides us with some information on contact allergy in dental patients, further studies are needed. These studies should investigate patch test reactions and clinical relevance in both dental series and (extended) EBS, including allergens such as dental amalgam and sodium tetrachloropalladate, and should also include an analysis on cross-reactivity with comparison to other populations.

AUTHOR CONTRIBUTIONS

Malak Al-Gawahiri: Conceptualization; methodology; formal analysis; investigation; visualization; writing – review and editing; writing – original draft. **Thomas Rustemeyer:** Conceptualization; methodology; data curation; supervision; visualization; writing – review and editing. **Sylvie M. Franken:** Conceptualization; data curation; writing – review and editing. **Esther J. van Zuuren:** Conceptualization; project administration; writing – review and editing. **Norbertus A. Ipenburg:** Conceptualization; data curation; writing – review and editing; methodology; resources; supervision; investigation.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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APPENDIX A

TABLE A1 European baseline series patch test reactions.

Allergen (in pet. unless otherwise stated)	Positive (%)	− (%)	? + (%)	+ (%)	++ (%)	+++ (%)	IR (%)
Potassium dichromate 0.5%[a]	13 (3.6)	334 (92.8)	13 (3.6)	10 (2.8)	3 (0.8)	-	-
Neomycin sulphate 20%[b]	-	358 (99.4)	2 (0.6)	-	-	-	-
Thiuram mix 1%[b]	5 (1.4)	352 (97.8)	3 (0.8)	4 (1.1)	1 (0.3)	-	-
p-phenylenediamine 1%[b]	16 (4.4)	341 (94.7)	3 (0.8)	9 (2.5)	6 (1.7)	1 (0.3)	-
Fragrance mix II 14%[b]	27 (7.5)	319 (88.6)	14 (3.9)	22 (6.1)	3 (0.8)	2 (0.6)	-
Propolis 10%[b]	4 (1.1)	350 (97.2)	6 (1.7)	4 (1.1)	-	-	-
Mercapto mix 1%[b]	3 (0.8)	354 (98.3)	3 (0.8)	2 (0.6)	-	1 (0.3)	-
Formaldehyde 1% (aq.)[b]	4 (1.1)	352 (97.8)	4 (1.1)	4 (1.1)	-	-	-
Caine mix III 10%[a]	5 (1.4)	349 (96.9)	6 (1.7)	5 (1.4)	-	-	-
Colophony 20%[b]	12 (3.3)	343 (95.3)	5 (1.4)	12 (3.3)	-	-	-
N-isopropyl-N-phenyl-p-phenylenediamine 0.1%[b]	1 (0.3)	357 (99.2)	2 (0.6)	-	-	1 (0.3)	-
Lanolin 30%[b]	9 (2.5)	344 (95.6)	7 (1.9)	9 (2.5)	-	-	-
Myroxylon pereirae resin (balsam of Peru) 25%[b]	30 (8.3)	308 (85.6)	22 (6.1)	29 (8.1)	1 (0.3)	-	-
Epoxy resin 1%[b]	6 (1.7)	347 (96.4)	7 (1.9)	4 (1.1)	2 (0.6)	-	-
Parabens 16%[b]	-	357 (99.2)	3 (0.8)	-	-	-	-
p-tert-butylphenol formaldehyde resin 1%[b]	6 (1.7)	346 (96.1)	8 (2.2)	5 (1.4)	1 (0.3)	-	-
Fragrance mix I 8%[b]	51 (14.2)	294 (81.7)	15 (4.2)	42 (11.7)	7 (1.9)	2 (0.6)	-
Budesonide 0.01%[b]	3 (0.8)	344 (95.6)	13 (3.6)	3 (0.8)	-	-	-
Nickel sulphate 5%[b]	84 (23.3)	267 (74.2)	9 (2.5)	62 (17.2)	20 (5.6)	2 (0.6)	-
Quaternium-15 1%[b]	2 (0.6)	358 (99.4)	-	2 (0.6)	-	-	-
Hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyral) 5%[b]	8 (2.2)	346 (96.1)	6 (1.7)	6 (1.7)	1 (0.3)	1 (0.3)	-
Methyl(chloro)isothiazolinone 0.02% (aq.)[a]	40 (11.1)	290 (80.6)	30 (8.3)	36 (10.0)	4 (1.1)	-	-
2-Mercaptobenzothiazole (MBT) 2%[b]	3 (0.8)	353 (98.1)	4 (1.1)	2 (0.6)	-	1 (0.3)	-
Tixocortol pivalate 0.1%[b]	3 (0.8)	351 (97.5)	6 (1.7)	2 (0.6)	1 (0.3)	-	-
Sesquiterpene lactone mix 0.1%[b]	2 (0.6)	353 (98.1)	5 (1.4)	2 (0.6)	-	-	-
Methyldibromo glutaronitrile 0.3%[b]	31 (8.6)	300 (83.3)	29 (8.1)	28 (7.8)	2 (0.6)	1 (0.3)	-
Cobalt chloride 1%[b]	36 (10.0)	311 (86.4)	13 (3.6)	29 (8.1)	6 (1.7)	1 (0.3)	-
Methylisothiazolinone 0.2% (aq.)[b]	56 (15.6)	267 (74.2)	37 (10.3)	54 (15.0)	1 (0.3)	1 (0.3)	-
Textile dye mix 6.6%[b]	6 (1.7)	344 (95.6)	10 (2.8)	5 (1.4)	1 (0.3)	-	-
Total	466 (4.5)	9689 (92.8)	285 (2.7)	392 (3.8)	60 (0.6)	14 (0.1)	0 (0.0)

Abbreviations: aq, aqueous; pet, petrolatum; −, negative reaction; ? +, doubtful reaction; IR, irritant reaction.
[a]Chemotechnique Diagnostics, Vellinge, Sweden.
[b]TrueTest (SmartPractice, Hillerød, Denmark).

TABLE A2 Extended Amsterdam baseline series patch test reactions.

Allergen (in pet. unless otherwise stated)	Positive %	–	?+	+	++	+++	IR
Disperse blue 106 1%[a]	3 (0.8)	353 (98.1)	4 (1.1)	3 (0.8)	-	-	-
Diazolidinyl urea 2%[b]	1 (0.3)	359 (99.7)	–	1 (0.3)	-	-	-
Benzisothiazolinone 0.1%[a]	12 (3.3)	340 (94.4)	8 (2.2)	11 (3.1)	1 (0.3)	-	-
Imidazolidinyl urea 2%[b]	1 (0.3)	357 (99.2)	2 (0.6)	1 (0.3)	-	-	-
Oil of turpentine 10%[b]	6 (1.7)	347 (96.4)	7 (1.9)	6 (1.7)	-	-	-
2-Bromo-2-nitropropane-1,3-diol 0.25%[a]	1 (0.3)	358 (99.4)	1 (0.3)	1 (0.3)	-	-	-
Carba mix 3%[b]	14 (3.9)	335 (93.1)	11 (3.1)	12 (3.3)	2 (0.6)	-	-
Ethylenediamine dihydrochloride 1%[b]	7 (1.9)	349 (96.9)	4 (1.1)	7 (1.9)	-	-	-
Thiomersal 0.1%[b]	7 (1.9)	348 (96.7)	5 (1.4)	6 (1.7)	1 (0.3)	-	-
Amerchol 101 50%[b]	20 (5.6)	326 (90.6)	14 (3.9)	20 (5.6)	-	0 (0.0)	-
Toluenesulfonamide formaldehyde resin 10%[b]	1 (0.3)	358 (99.4)	1 (0.3)	1 (0.3)	-	-	-
Cocamidopropyl betaine 1% (aq.)[b]	14 (3.9)	325 (90.3)	21 (5.8)	14 (3.9)	–	–	–
Hydrocortisone-17-butyrate 0.1%[b]	1 (0.3)	354 (98.3)	5 (1.4)	1 (0.3)	-	-	-
Octylisothiazolinone 0.1%[a]	7 (1.9)	346 (96.1)	7 (1.9)	7 (1.9)	-	-	-
Iodopropynyl butylcarbamate 0.2%[b]	10 (2.8)	326 (90.6)	24 (6.7)	10 (2.8)	-	-	-
Sorbitan sesquioleate 20%[b]	4 (1.1)	328 (91.1)	28 (7.8)	3 (0.8)	1 (0.3)	-	-
Phenoxyethanol 1%[b]	–	354 (98.3)	6 (1.7)	-	-	-	-
Compositae mix II 2.5%[a]	–	360 (100.0)	-	-	-	-	-
Tixocortol-21-pivalate 1%[b]	3 (0.8)	356 (98.9)	1 (0.3)	3 (0.8)	-	-	-
Benzophenone-4 10%[b]	8 (2.2)	339 (94.2)	12 (3.3)	7 (1.9)	1 (0.3)	-	1 (0.3)
Sodium metabisulfite 1%[a]	39 (10.8)	311 (86.4)	10 (2.8)	38 (10.6)	1 (0.3)	-	-
Propyl gallate 0.5%[b]	1 (0.3)	359 (99.7)	-	1 (0.3)	-	-	-
3-(dimethylamino)-propylamine 1% (aq.)[b]	10 (2.8)	334 (92.8)	16 (4.4)	8 (2.2)	2 (0.6)	-	-
Linalool hydroperoxide 1%[a]	19 (5.3)	316 (87.8)	25 (6.9)	19 (5.3)	-	-	-
Linalool hydroperoxide 0.5%[a]	9 (2.5)	339 (94.2)	12 (3.3)	9 (2.5)	-	-	-
Limonene hydroperoxide 0.3%[a]	8 (2.2)	343 (95.3)	9 (2.5)	8 (2.2)	-	-	-
Limonene hydroperoxide 0.2%[a]	12 (3.3)	338 (93.9)	10 (2.8)	12 (3.3)	-	-	-
Decyl glucoside 5%[b]	2 (0.6)	353 (98.1)	5 (1.4)	-	-	-	-
Lauryl glucoside 3%[b]	2 (0.6)	355 (98.6)	3 (0.8)	2 (0.6)	-	-	-
Total	222 (2.1)	9966 (95.5)	251 (2.4)	213 (2.0)	9 (0.1)	-	1 (0.0)

Abbreviations: aq, aqueous; pet, petrolatum; –, negative reaction; ? +, doubtful reaction; IR, irritant reaction.

[a]Chemotechnique Diagnostics, Vellinge, Sweden.

[b]TrueTest (SmartPractice, Hillerød, Denmark).