

DR. SUSANN FORKEL (Orcid ID : 0000-0002-1106-2464)

PROF. TIMO BUHL (Orcid ID : 0000-0002-3139-129X)

Article type : Original article

The Benefit of Late Readings in Patch Testing Depends both on Allergen and Patient Characteristics

Manuscript Acceptance Date: 09-Oct-2021

Susann Forkel^{1#}, Steffen Schubert^{2#}, Heinrich Dickel³, Michal Gina⁴, Claudia Schröder-Kraft⁵, Dieter Vieluf⁶, Richard Brans^{7,8,9}, Burkhard Kreft¹⁰, Gerda Wurpts¹¹, Johannes Geier^{2,9}, Timo Buhl^{1,9}

¹ Department of Dermatology, Venereology and Allergology, University Medical Center Göttingen, Göttingen, Germany

² Information Network of Departments of Dermatology, Institute at the University Medical Center Göttingen, Göttingen, Germany

³ Department of Dermatology, Venereology and Allergology, St. Josef Hospital, University Medical Center of the Ruhr University Bochum (UK RUB), Bochum, Germany

⁴ Department of Occupational Dermatology, BG Hospital Falkenstein, Falkenstein, Germany

⁵ Institute for Interdisciplinary Dermatological Prevention and Rehabilitation (iDerm), BG Hospital Hamburg, Hamburg, Germany.

⁶ Department of Allergology, Photodermatology and Occupational dermatology, Dermatologikum Hamburg, Hamburg, Germany

⁷ Institute for Interdisciplinary Dermatological Prevention and Rehabilitation (iDerm) at the University of Osnabrück, Osnabrück, Germany

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/ALL.15149](https://doi.org/10.1111/ALL.15149)

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⁸ Department of Dermatology, Environmental Medicine and Health Theory, University of Osnabrück, Osnabrück, Germany

⁹ Lower Saxony Institute of Occupational Dermatology, Universities of Osnabrück and Göttingen, Osnabrück and Göttingen, Germany

¹⁰ Department of Dermatology, Venereology and Allergology, University Medical Center Halle, Martin Luther University Halle-Wittenberg, Halle (Saale), Germany

¹¹ Department of Dermatology, Venereology and Allergology, University Medical Center Aachen, Aachen, Germany

#Shared First Co-authors

Key words: Patch Test, Day 7 reading, late patch test reaction, metal, sodium thiosulfate aurate, epoxy resin, preservatives, phenol formaldehyde resin, allergic contact dermatitis, reaction pattern

Running title: Benefit of Day 7 reading

Words: 3395 words, 4 tables + supplement

Correspondence:

Susann Forkel, MD

University Medical Center Göttingen

Department of Dermatology, Venereology and Allergology

Robert-Koch-Str. 40

37075 Göttingen, Germany

Email: susann.forkel@med.uni-goettingen.de

Declarations

Consent for publication

All authors reviewed the final manuscript version and consented to its submission.

Competing interests

None of the authors has a conflict of interest in relation to this work. The authors have no ethical conflicts to disclose.

Funding

Funding sources: none.

Contribution of each author

SF, SS, JG, TB designed the study; SF, SS, JG, TB, HD, MG, CSK, DV, RB, BK, GW collected data; SS extracted and compiled the data; all authors discussed the data; SF, SS, TB drafted the manuscript; all authors jointly discussed, reviewed and amended the manuscript.

Abstract

Background: Patch test (PT) readings are recommended after 48h and 72h (D3). An additional day 7 (D7) reading has been suggested by some, although data on efficient patient selection is scarce.

Objective: Investigation of positive D7 reactions regarding (i) allergens in the baseline series and additional PT series of the German Contact Dermatitis Research Group (DKG), and (ii) characteristics of the patients tested.

Methods: Retrospective, multicentre analysis of 190 allergens derived from 17 DKG test series in 4687 patients with an additional D7 reading. Patients were patch tested with the baseline series and additional series, if required. Occurrence of novel D7 reactions as well as increasing skin reactions from D3 to D7 were analysed separately.

Results: Depending on the allergen tested, waiving D7 readings would have missed 4.4-26.8% of positive PT results. Patch test series with the highest number of novel D7 reactions were baseline series, metal series, and leather/shoe series. New positive reactions on D7 were associated with age over 50 years and with a negative irritant control containing sodium lauryl sulfate. Of note, application of the PT allergens for 48h instead of 24h was positively associated with late PT reactions.

Conclusion: Within the most frequently tested allergens, without late readings, on average 11.7% of sensitizations would have been missed. Novel late reacting allergens were identified. This study comprehensively dissects patient-, allergen- and test-dependent parameters in support for D7 readings. We propose to always consider late readings individually based on effort-benefit considerations.

Introduction

The gold standard for diagnosing contact allergy is patch testing. In current national and international patch test (PT) guidelines, reading the test on day 3 (D3) or D4 is regarded obligatory, and a late reading on D7 is recommended [1-3]. Previous studies revealed that 6.3% to 15.0% of the reactions would go undiagnosed without a D7 reading [4-6]. However, it is still unknown whether special subgroups of patients exist who would particularly benefit from an additional late PT reading. On the other hand, it is well known that some allergens obviously are more prone to elicit late reactions than others: an additional reading on D7 is recommended especially for corticosteroids, antibiotics (e.g. neomycin), formaldehyde/formaldehyde releasers/formaldehyde resins, p-phenylenediamine and (dental) metals [1, 2]. However, reading PT additionally on D7 requires more patient visits and staff time, and is therefore often omitted. Against this background, we performed a retrospective multicentre study investigating the outcome of D7 readings in consecutive patients of the Information Network of Departments of Dermatology (IVDK), in order to identify patient groups and allergens, in which the benefit of a D7 reading outweighs the additional effort in routine patch testing.

Patients and methods

Clinical data were collected from the IVDK during the years 2010-19. Its structure and operating procedures have been described elsewhere [7]. Data are subjected to standardized quality control and analysed according to international standards [8]. Patch testing and evaluation of PT reactions were performed according to guidelines of the German Contact Dermatitis Research Group (DKG) [1, 2]. For the present data analysis, PT reactions on day 3 (72h, D3) and day 7 (168h, D7) were considered. In a few exceptional cases, when a PT reading was performed on D4 instead of D3, this reading was selected instead. A total of 102,253 patients were patch tested during the study period in 58 departments of dermatology joining the IVDK. An additional D7 reading was not done routinely in all patients. In order to avoid a selection bias, which could be introduced by selective late readings, we only used data from those periods and those IVDK departments, in which at least 66% of the patch-tested patients were read on D3 and D7. Finally, 4687 patients patch-tested in eight departments of dermatology qualified for this analysis. Patch test preparations were purchased from Almirall Hermal, Reinbek, Germany (until 2013), SmartPractice Europe, Greven, Germany (from 2014 on), and Chemotechnique, Vellinge, Sweden. Finn-Chambers® (8 mm inner diameter) on Scanpor® (Smart-Practice, Greven, Germany) were used in 87.2% of the patients, in the remainder allergEAZE® Test chambers were used. PT exposure time was 24h in 68.1%, and 48h in 31.9% of the patients. Readings coded as +, ++ or +++, i.e. positive reactions with erythema, infiltration, papules and/or (coalescing) vesicles were rated as positive. Sodium lauryl sulfate (SLS) was patch-tested in 4669 of the 4687 patients, and irritant reactions were scored as established [9].

Statistical methods

In order to analyse PT reaction patterns, doubtful and irritant reactions were grouped as non-allergic reactions for sorting purposes: +++ > ++ > + > non-allergic reaction > negative reaction. According to this ranking, D3 to D7 reaction patterns were grouped as increase (crescendo), plateau, decrease (decrescendo), or negative at both readings. Two models of logistic regression analyses were computed for 44 substances patch-tested in $\geq 80\%$ of the patients tested with SLS, in order to disentangle patient characteristics (clinical findings) from test parameters and allergen attributes on D7 reactions. Target variables were (I) a novel positive reaction on D7, and (II) the

occurrence of an increasing reaction pattern. In both cases, independent (explanatory) variables were sex, age ($< / \geq 50$ years), presence of co-factors in the aetiology of the skin disease (such as exposure to heat, cold, dust, wet work, glove occlusion), PT application time, and reactivity to SLS on D3. In a first exploratory model calculated for the 20 most frequently positive allergens, further potentially influencing factors (occupational dermatitis, past or present atopic dermatitis, allergic rhinitis, and allergic asthma) were considered. As they did not affect the risk estimates (data not shown in detail), they were excluded from our final regression models. Results of logistic regression analyses are presented as Odds Ratio (OR) estimates with profile-likelihood confidence intervals (95%). Relative risk estimates for novel D7 reactions or increasing reaction patterns of single PT preparations were calculated in relation to the median increase of 44 substances tested in $\geq 80\%$ of the patients (table S1). Data were managed and analysed using the statistical analysis software SAS[®], version 9.4 (SAS Institute, Cary, NC, USA).

Results

Novel positive reactions on day 7 were found in 95% of the most frequently tested allergens

A description of the study group of 4687 patients with a routine D3 and D7 PT reading, the MOAHLFA index, is given in table 1. In 1813 patients (38.7%), co-factors like wet work, glove occlusion, or in rare cases mechanical stress, exposure to heat, dust, etc. were considered important for the development of the skin disease. To avoid a selection bias, our first analysis focussed onto all allergens tested in $\geq 80\%$ of the 4687 patients, resulting in 44 allergens being investigated (table 2 and supplement). With these 44 allergens, 1948/4687 patients (41.6%) had a positive PT on D3, and 2113/4687 (45.1%) on D3 and/or D7. Thus, 165 of the patients (3.5%) demonstrated a first positive PT on D7. This represents an increase of 11.7% of positive PTs, which is determined by the D7 reading in 42 of the 44 allergens analysed. Only for cetostearyl alcohol and triclosan, no novel positive PTs were detected on D7 (table S1). All other tested substances benefited from an additional D7 reading. The highest increase of first positive D7 readings was seen for preservatives, namely bronopol (+25.0%), chlorhexidine (+33.3%), chloroacetamide (+33.3%), and sorbic acid (+26.1%), in addition to mercaptobenzothiazole (+26.7%), epoxy resin (+22.9%), and butylhydroxytoluene (BHT) (+30.0%) (table 2). The relative risk to develop a positive D7 reaction was more than doubled for these substances compared to the median increase of all 44 substances (relative risk ≥ 2.0).

The most tested metals (nickel, chromium, and cobalt) showed an increase in positive findings with the additional D7 reading between 12.9-14.3%. Nevertheless, notable differences were found in the metal series (table S2, #17). For gold in particular, the number of positive findings doubled by a D7 reading. No such effect was seen for copper and tin. Despite the significant increase of late reactions to mercaptobenzothiazole, PTs with the closely related mercapto mix [including morpholinylmercaptobenzothiazole (MOR), n-cyclohexyl-2-benzothiazyl sulfonamide (CBS), and dibenzothiazyl disulfide (MBTS)] showed only a slight increase of +7.3% with an additional D7 reading. However, the single substances MOR, CBS, and MBTS also revealed increases of +12.0-20.0% positive reactions with an additional late reading (tables S2, #8).

Patch test series for metals, leather and shoes, and baseline series reveal most frequent late reactions

We calculated the number of patients needed to undergo testing with the different PT series for one novel positive reaction on D7 (rightmost column in table 3). The highest number of first positive D7 readings was detected in the DKG test series “(Dental) Metals” with an increase of +36.7% (table 3 and supplement tables S2, #17). In this test series, 22 patients were identified with first D7 reactions in addition to 60 regular D3 reactions out of 560 tested patients. Detailed analysis of the tested allergens in this series demonstrated the highest increase for sodium aurothiosulfate. Another substantial increase was seen for amalgam. With regards to other full series, “Leather and Shoes” ranked second with +22.4% novel D7 reactions. This increase was mainly due to late reactions of benzisothiazolinone, ammoniated mercury, and mercapto-benzothiazole (tables S2, #12). Further, formaldehyde resins also showed a delayed reaction pattern. The DKG series „Additional Fragrances and Essential Oils“ showed an increase of positive PT results on D7 of +16.9%. Many patients showed late reactions to essential oils (tables 3 and S2, #44). In contrast, other fragrances to be declared or breakdown series of fragrance mixes elicited new late reactions only occasionally. The series „Resins and Adhesives“ revealed +10.9% positive reactions by D7 readings. Highest increases were seen for 2,4,6-tris(dimethylaminomethyl)phenol (tris-DMP) and phenol formaldehyde resin (Novolak) (tables S2, #28). Out of the tested (meth-)acrylates, only a slight increase of novel late reactions was seen for 2-hydroxyethyl methacrylate (HEMA), ethylenglycol dimethacrylate, hydroxyethyl acrylate, and methylmethacrylate (MMA). According to the pronounced increase of epoxy resin sensitizations with D7 readings (table 2 and tables S2, #1), we found an increase in positive PT reactions for further substances with epoxy groups (glycidyl ethers, tables S2, #28).

Exemplarily for some rare allergens, D3 readings of tris-DMP or vanillin detected only one patient out of 281 or 1071 tested, respectively. With the additional D7 reading, the number of positively tested individuals raised to four. Despite the low total numbers, these effects are noteworthy and lead to underestimation of specific contact allergies. A likewise substantial rise was seen for neomycin sulfate (tables S2, #1), phenol formaldehyde resin (Novolak) (tables S2, #28 & #12), 7-Ethylbicyclooxazolidine (tables S2, #46 & #37) and for more than the half of the essential oils (tables S2, #44). Interestingly, a negligible effect was seen for D7 readings in patients tested with ten corticosteroids (tables S2, #22): Only one of 401 patients tested showed a novel late reaction to triamcinolone acetonide (1% pet), 17 patients reacted already on D3 (table 3).

Increasing reaction strengths from day 3 to day 7 add colophony, methylisothiazolinone, and IPPD to the watchlist

A second data analysis focused on increased reaction patterns from D3 to D7 to the 44 allergens mentioned above, including clinically irrelevant reaction patterns such as negative on D3 to questionable result on D7, or + to ++ increases. With this analysis, we identified a few additional test compounds such as colophony, methylisothiazolinone, and N-Isopropyl-N-phenyl-p-phenylene diamine (IPPD) that followed an increasing test reaction pattern on D7 without reaching the criterion of unambiguous positive PT results (table S3). Hence, since increasing test reactions from D3 to D7 do not implicit negative PT results on D3, we propose that these substances should be monitored closely in future studies on delayed PT reactions.

Delayed skin reactivity is associated with increased age, longer PT application and negativity of the irritant control

To investigate patients' and test characteristics as promoting factors for D7 reactions independent of the allergens, logistic regression analyses were calculated with PT results of the 44 most frequently tested allergens in patients simultaneously tested with the irritant control SLS. In a first analysis that aimed on the clinical finding of novel D7 reactions, we compared the subgroup of patients with at least one positive reaction earliest on D7 and no positive reaction on D3 (n=164) to the subgroup of patients with at least one positive PT on D3 that did not persist until D7 (n=734). Here, PT application time of 48h (compared to 24h) was a significant independent promotor of *de novo* positive D7 reactions (OR 2.9 [1.9 – 4.5], table 4). In contrast, involvement of co-factors (OR 0.6 [0.4 – 0.9]) and SLS reactivity on D3 (OR 0.4 [0.3 – 0.7]) were negatively associated with a late response. In a second logistic regression analysis, we analysed risk factors for increasing reactions, independent of a positive result (n=186 patients). The subgroup of patients with non-increasing reaction patterns between D3 and D7 only (plateau or decrease) served as controls (n=2070). Here, age ≥ 50 years was an independent risk factor (OR 1.4 [1.0 – 1.9]), whereas skin reactivity to SLS was an independent, protective factor for increasing reactions (OR 0.3 [0.2 – 0.5], table 4).

Discussion

In contrast to most published studies on the benefit of D7 PT readings, we not only focussed on single allergens, but also took testing procedures and patient characteristics into consideration. In brief, we found that sex had no influence, PT exposure for 48h was associated with an increased likelihood of *de novo* D7 reactions, whereas irritant skin responses to SLS were associated with reduced occurrence. Thus, our study investigated not only 190 of the most frequently tested allergens, but also assembled a bigger picture of individual characteristics and specific testing procedures with higher probabilities for positive late reactions in PTs.

From earlier studies, it was known that neomycine, metals, formaldehyde/ formaldehyde releasers/ formaldehyde resins, p-phenylenediamine, methylisothiazolinone and mercaptobenzothiazole tend to elicit late reactions [1, 2, 4, 10-13]. We could confirm this for these allergens, but not for corticosteroids – contradictory to some earlier reports [4, 11] while in line with others [10]. In addition, we could identify the highest risk for novel D7 reactions for preservatives as late reacting allergens, which was not described before except for some formaldehyde releasers. The highest risk for novel D7 reactions was found for allergens rarely causing positive PT reactions, which are rather weak to moderate sensitizers, such as mercaptobenzothiazole, bronopol, BHT, chlorhexidine, chloracetamide, or sorbic acid. With regard to the molecular weight of the allergens, no correlation with D7 reactions could be established. Due to the investigation of rare allergens, it was possible to identify 2,4,6-Tris(dimethylaminomethyl)phenol, 7-Ethylbicyclo-oxazolidine and essential oils as allergens with delayed PT reactivity. However, also allergens with higher sensitizing potency were confirmed with increased late reactions such as epoxy resin [20].

As allergens are tested in blocks, i.e. test series, we conclude that a late reading on D7 is particularly helpful when baseline series, metal series, and leather/shoe series are being tested. Testing the baseline series without D7 reading missed 8.3% of positive reactions. In line with earlier studies, we found a clear increase of positive reactions with an additional D7 reading for metals [10, 14]. Especially for gold, the increase was evident but even so for amalgam. Gold is already known to elicit late reactions in patch tests [15]. One hypothesis discusses the slow penetration of metal salts through the stratum corneum [16]. Delayed reactions to gold are rather

common, but, however, did very rarely show clinical relevance [17, 18]. Summarizing our results on metals, the readings for the metals benefited very differently from D7 readings, and no additional advantage of late readings was seen at all for e.g. copper and tin. Therefore, even within a chemically related group, no generalized statement can be made on a delayed D7 response. Of note, PTs with metal salts result in a quite high number of irritant or questionable results on D3, thus, late readings help to differentiate irritation from allergic reactions. In the DKG PT series „Leather and Shoes“, the high rate of novel positive PT reactions on D7 was primarily due to substances with already known late reactivity, e.g. benzisothiazolinone [4], ammoniated mercury [10, 13], mercaptobenzisothiazole [5, 11, 19], and phenol formaldehyde resin (Novolak) [11]. Epoxy resin and p.-tert. butylcatechol, which is chemically closely related to phenol formaldehyde resin [20], were also mentioned as active sensitizers [21, 22]. In a study with p-phenylene diamine (PPD) 1% pet. and lower, all late reactions which indicated active sensitization occurred on day 14 or later [21, 23]. Reactions on D7 are primarily assessed as late reactions [2]. We did not re-test patients with de novo positive reactions on D7 because this was not the focus of our study and therefore, active sensitization cannot be ruled out with certainty in individual cases. However, based on the current literature, we consider this less likely.

Recent work supports the idea that various contact allergens activate different immunological cascades with distinct T-cell responses [24, 25]. In addition, direct anti-inflammatory properties of individual allergens may play a role in delayed skin reactions. Different substance properties such as lipophilia, solubility and protein reactivity are also relevant. Additionally, the vehicle used in the test preparation influences the absorption into the skin [26]. Summarizing our results and considerations with focus on the allergens themselves, it remains difficult to either predict or to draw broader conclusions, on which allergens will present with delayed PT reactions. Most likely, this depends on multiple factors such as molecular weight, polarity, vehicle, anti-inflammatory properties of the allergen, tested concentration, and duration of test application. This seems to be the most convincing explanation for the differences that we even observe between chemically closely related compounds.

Focusing onto the patient characteristics with D7 skin reactions, our study group was characterized by a high share of occupational hand dermatitis patients (table 1) and we therefore included the importance of co-factors for the aetiology of the skin disease, which are mostly occlusion due to

gloves or wetness, into the logistic regression models to consider them as confounding factors. Hence, as a practical consequence of our study, we recommend a reading on D7 especially for aged patients (50+), while patients with “sensitive skin”, as indicated by an irritant reaction to SLS 0.25% aq., are less prone to have late PT reaction patterns to allergens. Theoretical explanations for this age dependency range from age-related decrease of antigen-presenting cells causing a delayed response in PTs [27] to accumulated exposure and low-grade sensitization to various compounds with increasing age [28]. Likewise, a long allergen abstinence with a resulting decrease of allergen-specific T-cell reactivity may also be of relevance [29, 30]. Since SLS 0.25% aq. is included in the baseline series in Austria, Switzerland and Germany, this parameter is readily available on D3, when the necessity of a late reading is considered by the allergist. However, the pathophysiology of irritant skin reactions is not completely understood. It is well established that patients with SLS positivity present with more irritant reactions during PTs, despite the lack of an association with atopic skin diathesis and atopic diseases [31-33]. Importantly, the SLS response is a snapshot of the patient’s skin reactivity at the time of the PT, and a positive reaction suggests increased "irritability" of the skin. It may be hypothesized that a negative irritant control in turn suggests intact and resilient skin, and therefore allergen penetration may be delayed, resulting in likewise delayed skin reactions.

Another influencing factor besides the age-depend activity of the immune system may be a possible influence by immunomodulatory drugs that are more frequently used in older patients. Since all study patients were tested according to current guidelines, prednisolone of 20 mg or equivalent needed to be discontinued one week before PT. However, there is no scientific evidence so far that immunomodulatory drugs such as ciclosporine or dupilumab delay PT reactions [34, 35]. Current data rather points towards milder or false negative reactions, if testing is performed during continued immunomodulatory medication [3, 34, 36].

Lastly, a patch test application of no more than 24h reduces the frequency of doubtful and irritant reactions on D3 [37, 38], but we could show that it also diminishes the number of late reactions, and hence may bear the risk of not diagnosing contact sensitization. For PPD, a PT application time of 48h has been described with delayed PT reactions [23]. Optimal application times of PTs have been fiercely debated in the past: Concordant results for 24h and 48h PT application time were described in 74%-86% of cases [37, 39, 40]. Correspondingly, the total positive rate of metal

salts such as nickel decreased significantly by only 24h instead of 48h PT application time [37, 39, 40]. However, since these studies did not include readings on D7, prospective studies with PT exposure times of 24h vs. 48h with late readings are recommended.

Another important test-dependent parameter for late reactions may also be the concentration of the PT allergen, since lower PT concentrations in PT test formulations were found associated with delayed test positivity [15, 41, 42]. However, this parameter was not included in our analysis, as the allergens presented were not systematically tested in different concentrations. Another limitation of our study is the varying number of patients tested for each allergen, although no other study investigated such a high number of 190 different allergens. Thus, also rarer allergens were included with partly unexpected findings. However, for the majority of the allergens, an increase in new first-time positive reactions was detected on D7. Without D7 reading, out of the most frequently tested substances, clinicians could have missed as much as 11.7% of positive results. If there is a strong clinical suspicion of contact allergy, a D7 reading should be strongly considered, if the PT findings are inconclusive at D3. This is especially true for older patients with SLS negativity, if the PT application time was 48h.

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Tables

Table 1.

MOAHLFA Index of the study group (n=4687 patients).

	n	%
Male	1784	38.1
Occupational dermatitis	1753	37.4
Atopic dermatitis	1276	27.2
Hand dermatitis	2157	46.0
Leg dermatitis	167	3.6
Face dermatitis	508	10.8
Age $\geq$ 40 years	3462	73.9

Table 2.

Allergen test preparations with an increased risk for D7 reactions.

Forty-four test preparations were tested in $\geq 80\%$ of the study group (n=4687 patients). Only those 20 allergens with an increased risk above average (≥ 1.1) for late reactions are presented here in alphabetical order. Increase of new positive D7 readings in relation to D3 positive readings was calculated [%; First positive on D7]. Details of all 44 allergens can be found in the supplement (table S1).

HICC, Hydroxyisohexyl 3-cyclohexene carboxaldehyde

Substance	Conc.	tested [n]	Positive on D3		First positive on D7		
			Pos [n]	Positive % [95% CI]	[n]	[%]	Relative Risk estimate
Benzophenone 4	10% pet.	3880	31	0.8 [0.5-1.1]	4	+12.9	1.1
Benzyl alcohol	1% pet.	3823	5	0.1 [0.0-0.3]	1	+20.0	1.7
Bronopol	0.5% pet.	4411	24	0.5 [0.3-0.8]	6	+25.0	2.1
Butylhydroxytoluene (BHT)	2% pet.	3820	10	0.3 [0.1-0.5]	3	+30.0	2.6
Chlorhexidine digluconate	0.5% aq.	4005	12	0.3 [0.2-0.5]	4	+33.3	2.9
Chloroacetamide	0.2% pet.	3822	12	0.3 [0.2-0.5]	4	+33.3	2.9
Cobalt (II)-chloride	1% pet.	4586	268	5.8 [5.2-6.6]	35	+13.1	1.1
Colophony (Rosin)	20% pet.	4625	177	3.8 [3.3-4.4]	25	+14.1	1.2
Epoxy resin	1% pet.	4443	70	1.6 [1.2-2.0]	16	+22.9	2.0
Formaldehyde	1% aq.	4636	39	0.8 [0.6-1.1]	5	+12.8	1.1
HICC #	5% pet.	4636	91	2.0 [1.6-2.4]	13	+14.3	1.2
Lanolin alcohols	30% pet.	4582	52	1.1 [0.8-1.5]	8	+15.4	1.3
Mercaptobenzothiazole	2% pet.	3746	30	0.8 [0.5-1.1]	8	+26.7	2.3
Methylchloroisothia- zolinone/ Methyliso- thiazolinone (MCI/MI)	0.01% aq.	4629	158	3.4 [2.9-4.0]	21	+13.3	1.1

Nickel (II)-sulfate hexahydrate	5% pet.	4522	637	14.1 [13.1-15.1]	91	+14.3	1.2
Paraben mix	16% pet.	4614	32	0.7 [0.5-1.0]	4	+12.5	1.1
Potassium dichromate	0.5% pet.	4601	225	4.9 [4.3-5.6]	29	+12.9	1.1
Sorbic acid	2% pet.	3797	23	0.6 [0.4-0.9]	6	+26.1	2.2
tert.-Butylhydroquinone	1% pet.	3825	58	1.5 [1.2-2.0]	11	+19.0	1.6
Ylang ylang oil	10% pet.	4602	90	2.0 [1.6-2.4]	13	+14.4	1.2

Table 3.

Results of the patch test series of the German Contact Dermatitis Research Group (DKG), which were tested in more than 300 patients of the study group.

In the last column, the number of patients needed to be tested with this specific test series for finding the first individual with a late reaction is calculated [n tested / n first positive on D7]. Detailed test results of all 190 allergens in each respective test series can be found in the supplement (Tables S2).

		Positive on D3	First positive on D7		Patients needed to find one novel D7 reaction
Test series according to DKG	tested [n]	Pos [n]	Pos [n]	Pos [%]	[n]
(Dental) Metals	560	60	22	+36.7%	25
Leather and Shoes	391	67	15	+22.4%	26
Additional Fragrances and Essential Oils	1072	77	13	+16.9%	82
Preservatives	3810	448	51	+11.4%	75
Resins and Adhesives	529	101	11	+10.9%	48
Rubber Additives	2566	307	31	+10.1%	83
Disinfectants	1759	184	16	+8.7%	110
Baseline series	4687	1978	165	+8.3%	28
Ointment Bases	3838	386	31	+8.0%	124
Additional Fragrances to be Declared	1089	50	4	+8.0%	272

Industrial Biocides	404	88	7	+8.0%	58
Breakdown of Fragrance mix I	774	71	5	+7.0%	155
Metal Working Fluids	423	96	6	+6.3%	71
Textile and Leather Dyes	353	33	2	+6.1%	177
Corticosteroids	401	17	1	+5.9%	401
Plant Constituents	336	42	2	+4.8%	168
Breakdown of Fragrance mix II	733	43	2	+4.7%	367

Table 4.

Results of two multivariate logistic regression analyses of 4669 patients tested with the most frequent 44 substances (tested in $\geq 80\%$ of the study group) and sodium lauryl sulfate (SLS). Significant odds ratios are illustrated in bold. For details, see text.

Explanatory factors	OR [95% CI] for novel D7 reaction	OR [95% CI] for increasing reaction strength D3 $\rightarrow$ D7
Female sex	1.375 [0.951 - 2.010]	1.208 [0.874 - 1.687]
Age ≥ 50 years	1.195 [0.841 - 1.706]	1.404 [1.031 - 1.924]
Presence of Cofactors (e.g. occlusion)	0.603 [0.388 - 0.930]	0.740 [0.503 - 1.074]
Patch Test Application Time 48h	2.918 [1.902 - 4.510]	1.261 [0.869 - 1.814]
Irritant reaction to PT with SLS 0.25% aq.	0.443 [0.270 - 0.721]	0.313 [0.195 - 0.493]

SUPPLEMENT

Table S1.

Frequency of positive reactions on Day 3 (D3) and Day 7 (D7) to 44 allergens which were tested in $\geq 80\%$ of the study Group (4687 patients).

HICC, Hydroxyisohexyl 3-cyclohexene carboxaldehyde

			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7		
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%	Risk
Amerchol L-101	50% pet.	3722	67	1.8 [1.4-2.3]	73	2.0 [1.5-2.5]	6	+9.0	0.8
Balsam of Peru (Myroxolon pereirae)	25% pet.	4636	233	5.0 [4.4-5.7]	249	5.4 [4.7-6.1]	16	+6.9	0.6
Benzophenone 4	10% pet.	3880	31	0.8 [0.5-1.1]	35	0.9 [0.6-1.3]	4	+12.9	1.1
Benzyl alcohol	1% pet.	3823	5	0.1 [0.0-0.3]	6	0.2 [0.1-0.3]	1	+20.0	1.7
Bromonitropropanediol	0.5% pet.	4411	24	0.5 [0.3-0.8]	30	0.7 [0.5-1.0]	6	+25.0	2.1
Butylhydroxy anisole (BHA)	2% pet.	3735	17	0.5 [0.3-0.7]	19	0.5 [0.3-0.8]	2	+11.8	1.0
Butylhydroxy toluene (BHT)	2% pet.	3820	10	0.3 [0.1-0.5]	13	0.3 [0.2-0.6]	3	+30.0	2.6
Cetostearyl alcohol	20% pet.	4619	20	0.4 [0.3-0.7]	20	0.4 [0.3-0.7]	0	0	0.0
Chlorhexidine digluconate	0.5% aq.	4005	12	0.3 [0.2-0.5]	16	0.4 [0.2-0.6]	4	+33.3	2.9
Chloroacetamide	0.2% pet.	3822	12	0.3 [0.2-0.5]	16	0.4 [0.2-0.7]	4	+33.3	2.9
Cobalt (II)-chloride	1% pet.	4586	268	5.8 [5.2-6.6]	303	6.6 [5.9-7.4]	35	+13.1	1.1
Cocamidopropyl betaine	1% aq.	3800	38	1.0 [0.7-1.4]	39	1.0 [0.7-1.4]	1	+2.6	0.2
Coconut diethanolamide	0.5% pet.	3823	22	0.6 [0.4-0.9]	23	0.6 [0.4-0.9]	1	+4.5	0.4
Colophony (Rosin)	20% pet.	4625	177	3.8 [3.3-4.4]	202	4.4 [3.8-5.0]	25	+14.1	1.2
Compositae Mix II	5% pet.	4197	77	1.8 [1.5-2.3]	82	2.0 [1.6-2.4]	5	+6.5	0.6
DMDM Hydantoin	2% aq.	3793	25	0.7 [0.4-1.0]	27	0.7 [0.5-1.0]	2	+8.0	0.7
Epoxy resin	1% pet	4443	70	1.6 [1.2-2.0]	86	1.9 [1.6-2.4]	16	+22.9	2.0
Formaldehyde	1% aq.	4636	39	0.8 [0.6-1.1]	44	0.9 [0.7-1.3]	5	+12.8	1.1
Fragrance mix I	8% pet.	4575	252	5.5 [4.9-6.2]	274	6.0 [5.3-6.7]	22	+8.7	0.7
Fragrance mix II	14% pet.	4606	154	3.3 [2.8-3.9]	164	3.6 [3.0-4.1]	10	+6.5	0.6
HICC #	5% pet.	4636	91	2.0 [1.6-2.4]	104	2.2 [1.8-2.7]	13	+14.3	1.2
Imidazolidinyl Urea (Germall 115)	2% pet.	3854	12	0.3 [0.2-0.5]	13	0.3 [0.2-0.6]	1	+8.3	0.7

Iodopropynylbutyl carbamate (IPBC)	0.2% pet.	4129	42	1.0 [0.7-1.4]	47	1.1 [0.8-1.5]	5	+11.9	1.0
Jasmine absolute	5% pet.	4599	52	1.1 [0.8-1.5]	58	1.3 [1.0-1.6]	6	+11.5	1.0
Lanolin alcohols	30% pet.	4582	52	1.1 [0.8-1.5]	60	1.3 [1.0-1.7]	8	+15.4	1.3
Mercapto mix (CBS, MBTS, MOR)	2% pet.	4634	41	0.9 [0.6-1.2]	44	0.9 [0.7-1.3]	3	+7.3	0.6
Mercaptobenzothiazole	2% pet.	3746	30	0.8 [0.5-1.1]	38	1.0 [0.7-1.4]	8	+26.7	2.3
Methylisothiazolinone	0.05% aq.	4120	185	4.5 [3.9-5.2]	204	5.0 [4.3-5.7]	19	+10.3	0.9
Methylchloroisothiazolinone /Methylisothiazolinone (MCI/MI)	0.01% aq.	4629	158	3.4 [2.9-4.0]	179	3.9 [3.3-4.5]	21	+13.3	1.1
Nickel (II)-sulfate hexahydrate	5% pet.	4522	637	14.1 [13.1-15.1]	728	16.1 [15.0-17.2]	91	+14.3	1.2
N-Isopropyl-N'-phenyl-p-phenylenediamine (IPPD)	0.1% pet.	4634	46	1.0 [0.7-1.3]	49	1.1 [0.8-1.4]	3	+6.5	0.6
Oil of turpentine	10% pet.	4517	30	0.7 [0.4-0.9]	33	0.7 [0.5-1.0]	3	+10.0	0.9
Paraben mix	16% pet.	4614	32	0.7 [0.5-1.0]	36	0.8 [0.5-1.1]	4	+12.5	1.1
Potassium dichromate	0.5% pet.	4601	225	4.9 [4.3-5.6]	254	5.5 [4.9-6.2]	29	+12.9	1.1
Propolis	10% pet.	4639	139	3.0 [2.5-3.5]	149	3.2 [2.7-3.8]	10	+7.2	0.6
Propylene glycol	20% aq.	3822	48	1.3 [0.9-1.7]	53	1.4 [1.0-1.8]	5	+10.4	0.9
Sandalwood oil	10% pet.	4602	37	0.8 [0.6-1.1]	40	0.9 [0.6-1.2]	3	+8.1	0.7
Sorbic acid	2% pet.	3797	23	0.6 [0.4-0.9]	29	0.8 [0.5-1.1]	6	+26.1	2.2
tert-Butylhydroquinone	1% pet.	3825	58	1.5 [1.2-2.0]	69	1.8 [1.4-2.3]	11	+19.0	1.6
Thiuram mix	1% pet.	4623	158	3.4 [2.9-4.0]	170	3.7 [3.2-4.3]	12	+7.6	0.7
Triclosan	2% pet.	3796	3	0.1 [0.0-0.2]	3	0.1 [0.0-0.2]	0	0	0
Triethanolamine	2.5% pet.	3836	33	0.9 [0.6-1.2]	34	0.9 [0.6-1.2]	1	+3.0	0.3
Ylang ylang oil	10% pet.	4602	90	2.0 [1.6-2.4]	103	2.2 [1.8-2.7]	13	+14.4	1.2
Zinc diethyldithiocarbamate (ZDEC)	1% pet.	4637	36	0.8 [0.5-1.1]	40	0.9 [0.6-1.2]	4	+11.1	1.0

Tables S2.

Patch test results of all DKG test series read on Day 3 (D3) and Day 7 (D7) in the study group (sorted according to their ranking presented in table 3).

DKG, German Contact Dermatitis Research Group; N.A., not applicable; Φ tested in parallel to baseline series in selected patients and centers

Test series according to DKG (Dental) Metals DKG test series No. #17			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Amalgam (with zinc)	5 % pet.	556	15	2.7 [1.5 -4.4]	27	4.9 [3.2 -7.0]	12	+80.0
Amalgam alloy metals (Si, Cu, Sn, Zn)	20 % pet.	556	8	1.4 [0.6 -2.8]	9	1.6 [0.7 -3.1]	1	+12.5
Ammoniated mercury	1 % pet.	556	17	3.1 [1.8 -4.9]	20	3.6 [2.2 -5.5]	3	+17.6
Ammonium tetrachloro platinate	0.25 % pet.	556	4	0.7 [0.2 -1.8]	6	1.1 [0.4 -2.3]	2	+50.0
Copper-II-sulfate hexahydrate	1 % aq.	559	1	0.2 [0.0 -1.0]	1	0.2 [0.0 -1.0]	0	0
Palladium chloride	1 % pet.	556	34	6.1 [4.3 -8.4]	40	7.2 [5.2 -9.7]	6	+17.6
Sodium thiosulfate aurate	0.25 % pet.	554	6	1.1 [0.4 -2.3]	15	2.7 [1.5 -4.4]	9	+150.0
Stannous chloride	0.5 % pet.	557	7	1.3 [0.5 -2.6]	7	1.3 [0.5 -2.6]	0	0

Test series according to DKG Leather and shoes DKG test series No. #12			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
1,2-Benzisothiazolin-3-one, sodium salt	0.1 % pet.	386	13	3.4 [1.8 -5.7]	16	4.1 [2.4 -6.6]	3	+23.1
1,3-Diphenylguanidine (DPG)	1 % pet.	389	7	1.8 [0.7 -3.7]	7	1.8 [0.7 -3.7]	0	0
4,4'-Diaminodiphenylmethane	0.5 % pet.	384	5	1.3 [0.4 -3.0]	6	1.6 [0.6 -3.4]	1	+20.0
Acid Yellow 36 (CI 13065)	1 % pet.	163	2	1.2 [0.1 -4.4]	2	1.2 [0.1 -4.4]	0	0
Ammoniated mercury	1 % pet.	389	13	3.3 [1.8 -5.6]	18	4.6 [2.8 -7.2]	5	+38.5
Bismark brown R	0.5 % pet.	158	1	0.6 [0.0 -3.5]	1	0.6 [0.0 -3.5]	0	0
Chlorocresol	1 % pet.	387	3	0.8 [0.2 -2.2]	4	1.0 [0.3 -2.6]	1	+33.3
Chloroacetamide	0.2 % pet.	387	0	0.0 [0.0 -0.9]	1	0.3 [0.0 -1.4]	1	N.A.
Dibutyl thiourea	1 % pet.	328	2	0.6 [0.1 -2.2]	2	0.6 [0.1 -2.2]	0	0
Diphenyl thiourea	1 % pet.	328	0	0.0 [0.0 -1.1]	0	0.0 [0.0 -1.1]	0	0
Disperse orange 3 (CI 11005)	1 % pet.	162	5	3.1 [1.0 -7.1]	5	3.1 [1.0 -7.1]	0	0
Ethylene diamine-di-HCl	1 % pet.	378	2	0.5 [0.1 -1.9]	2	0.5 [0.1 -1.9]	0	0
Glutardialdehyde (Glutaral)	0.3 % pet.	386	1	0.3 [0.0 -1.4]	2	0.5 [0.1 -1.9]	1	+100.0
Melamin formaldehyde resin	7 % pet.	388	4	1.0 [0.3 -2.6]	5	1.3 [0.4 -3.0]	1	+25.0
Mercaptobenzothiazole	2 % pet.	299	5	1.7 [0.5 -3.9]	8	2.7 [1.2 -5.2]	3	+60.0
Methylmethacrylate (MMA)	2 % pet.	125	2	1.6 [0.2 -5.7]	2	1.6 [0.2 -5.7]	0	0
Monobenzene	1 % pet.	328	2	0.6 [0.1 -2.2]	2	0.6 [0.1 -2.2]	0	0
N-Isopropyl-N'-phenyl-p- phenylene diamine (IPPD)	0.1 % pet.	387	6	1.6 [0.6 -3.3]	6	1.6 [0.6 -3.3]	0	0
Octyl isothiazolinone	0.025 % pet.	137	1	0.7 [0.0 -4.0]	1	0.7 [0.0 -4.0]	0	0
p-Aminoazobenzene (CI 11000)	1 % pet.	63	1	1.6 [0.0 -8.5]	1	1.6 [0.0 -8.5]	0	0
Phenol formaldehyde resin (Novolak)	5 % pet.	387	5	1.3 [0.4 -3.0]	9	2.3 [1.1 -4.4]	4	+80.0
Phenyl glycidylether	0.25 % pet.	385	4	1.0 [0.3 -2.6]	4	1.0 [0.3 -2.6]	0	0
p-tert-Butylphenol	1 % pet.	87	1	1.1 [0.0 -6.2]	1	1.1 [0.0 -6.2]	0	0
p-tert-Butylphenol formaldehyde resin (PTBFR)	1 % pet.	386	1	0.3 [0.0 -1.4]	1	0.3 [0.0 -1.4]	0	0
Tricresyl phosphate	5 % pet.	380	0	0.0 [0.0 -1.0]	0	0.0 [0.0 -1.0]	0	0
Urea formaldehyde resin	10 % pet.	387	1	0.3 [0.0 -1.4]	2	0.5 [0.1 -1.9]	1	+100.0

Test series according to DKG Additional Fragrances and Ess. Oils DKG test series No. #44			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Benzaldehyde	5 % pet.	1071	0	0.0 [0.0 -0.3]	0	0.0 [0.0 -0.3]	0	0
Cedarwood oil	10 % pet.	1069	3	0.3 [0.1 -0.8]	5	0.5 [0.2 -1.1]	2	+66.7
Clove oil	2 % pet.	116	3	2.6 [0.5 -7.4]	3	2.6 [0.5 -7.4]	0	0
Eucalyptus oil	2 % pet.	1072	2	0.2 [0.0 -0.7]	3	0.3 [0.1 -0.8]	1	+50.0
Jasmine Absolute	5 % pet.	1067	12	1.1 [0.6 -2.0]	13	1.2 [0.7 -2.1]	1	+8.3
Laurel leaf oil	2 % pet.	1072	8	0.7 [0.3 -1.5]	12	1.1 [0.6 -1.9]	4	+50.0
Lemon oil	2 % pet.	1071	1	0.1 [0.0 -0.5]	1	0.1 [0.0 -0.5]	0	0
Lemongrass oil	2 % pet.	1072	19	1.8 [1.1 -2.8]	20	1.9 [1.1 -2.9]	1	+5.3
Majantol	5 % pet.	1068	6	0.6 [0.2 -1.2]	6	0.6 [0.2 -1.2]	0	0
Menthol	1 % pet.	1063	0	0.0 [0.0 -0.3]	1	0.1 [0.0 -0.5]	1	0
Narcissus absolute	2 % pet.	796	7	0.9 [0.4 -1.8]	8	1.0 [0.4 -2.0]	1	+14.3
Narcissus poeticus absolute	2 % pet.	267	0	0.0 [0.0 -1.4]	0	0.0 [0.0 -1.4]	0	0
Neroli oil	5 % pet.	954	7	0.7 [0.3 -1.5]	10	1.0 [0.5 -1.9]	3	+42.9
Oil of patchouli	10 % pet.	269	0	0.0 [0.0 -1.4]	0	0.0 [0.0 -1.4]	0	0
Orange oil	2 % pet.	1072	1	0.1 [0.0 -0.5]	1	0.1 [0.0 -0.5]	0	0
Patchouli oil	10 % pet.	802	7	0.9 [0.4 -1.8]	7	0.9 [0.4 -1.8]	0	0
Peppermint oil	2 % pet.	1072	3	0.3 [0.1 -0.8]	5	0.5 [0.2 -1.1]	2	+66.7
Salicyl aldehyde	2 % pet.	1072	11	1.0 [0.5 -1.8]	12	1.1 [0.6 -1.9]	1	+9.1
Sandalwood oil	10 % pet.	1068	5	0.5 [0.2 -1.1]	6	0.6 [0.2 -1.2]	1	+20.0
Vanillin	10 % pet.	1071	1	0.1 [0.0 -0.5]	4	0.4 [0.1 -1.0]	3	+300.0
Ylang ylang oil	10 % pet.	1069	31	2.9 [2.0 -4.1]	35	3.3 [2.3 -4.5]	4	+12.9

Test series according to DKG Preservatives DKG test series No. #38			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Benzyl alcohol	1 % pet.	3792	5	0.1 [0.0 -0.3]	6	0.2 [0.1 -0.3]	1	+20.0
Bronopol	0.5 % pet.	3789	19	0.5 [0.3 -0.8]	24	0.6 [0.4 -0.9]	5	+26.3
Chlorhexidine digluconate	0.5 % aq.	3798	11	0.3 [0.1 -0.5]	15	0.4 [0.2 -0.7]	4	+36.4
Chloroacetamide	0.2 % pet.	3793	12	0.3 [0.2 -0.6]	16	0.4 [0.2 -0.7]	4	+33.3
Diazolidinyl urea	1 % pet.	1863	3	0.2 [0.0 -0.5]	4	0.2 [0.1 -0.5]	1	+33.3
Diazolidinyl urea	2 % pet.	1933	10	0.5 [0.2 -0.9]	10	0.5 [0.2 -0.9]	0	0
DMDM Hydantoin	2 % aq.	3793	25	0.7 [0.4 -1.0]	27	0.7 [0.5 -1.0]	2	+8.0
Imidazolidinyl Urea (Germall 115)	2 % pet.	3793	12	0.3 [0.2 -0.6]	13	0.3 [0.2 -0.6]	1	+8.3
Iodopropynylbutyl carbamate (IPBC)	0.2 % pet.	3790	41	1.1 [0.8 -1.5]	46	1.2 [0.9 -1.6]	5	+12.2
Methylisothiazolinone	0.05 % aq.	3772	171	4.5 [3.9 -5.2]	188	5.0 [4.3 -5.7]	17	+9.9
Methyldibromo glutaronitrile	0.3 % pet.	2438	117	4.8 [4.0 -5.7]	127	5.2 [4.4 -6.2]	10	+8.5
Paraben mix	16 % pet.	3781	26	0.7 [0.4 -1.0]	30	0.8 [0.5 -1.1]	4	+15.4
Polyaminopropyl biguanide	2.5 % aq.	315	5	1.6 [0.5 -3.7]	5	1.6 [0.5 -3.7]	0	0
Quaternium 15	1 % pet.	1685	8	0.5 [0.2 -0.9]	11	0.7 [0.3 -1.2]	3	+37.5
Quaternium 15	2 % pet.	2107	14	0.7 [0.4 -1.1]	15	0.7 [0.4 -1.2]	1	+7.1
Sodium benzoate	2 % pet.	2442	2	0.1 [0.0 -0.3]	3	0.1 [0.0 -0.4]	1	+50.0
Sodium benzoate	5 % pet.	1352	2	0.1 [0.0 -0.5]	3	0.2 [0.0 -0.6]	1	+50.0
Sodium disulfide	1 % pet.	1939	34	1.8 [1.2 -2.4]	37	1.9 [1.3 -2.6]	3	+8.8
Sorbic acid	2 % pet.	3796	23	0.6 [0.4 -0.9]	29	0.8 [0.5 -1.1]	6	+26.1
Triclosan	2 % pet.	3795	3	0.1 [0.0 -0.2]	3	0.1 [0.0 -0.2]	0	0

Test series according to DKG Resins and Adhesives DKG test series No. #28			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
1,4-Butanediol diglycidylether	0.25 % pet.	515	8	1.6 [0.7 -3.0]	11	2.1 [1.1 -3.8]	3	+37.5
1,6-Hexanediol diglycidylether	0.25 % pet.	515	15	2.9 [1.6 -4.8]	16	3.1 [1.8 -5.0]	1	+6.7
2,4,6-Tris(dimethylamino- methyl)phenol	0.5 % pet.	281	1	0.4 [0.0 -2.0]	4	1.4 [0.4 -3.6]	3	+300.0
2-Hydroxypropyl methacrylate (HPMA)	2 % pet.	518	14	2.7 [1.5 -4.5]	14	2.7 [1.5 -4.5]	0	0
2-Hydroxyethyl methacrylate (HEMA)	1 % pet.	522	14	2.7 [1.5 -4.5]	15	2.9 [1.6 -4.7]	1	+7.1
4,4'-Diaminodiphenylmethane	0.5 % pet.	516	11	2.1 [1.1 -3.8]	13	2.5 [1.3 -4.3]	2	+18.2
4,4'-Dihydroxydiphenyle	0.1 % pet.	456	0	0.0 [0.0 -0.8]	0	0.0 [0.0 -0.8]	0	0
Benzoyl peroxide	1 % pet.	520	22	4.2 [2.7 -6.3]	24	4.6 [3.0 -6.8]	2	+9.1
BIS-GMA	2 % pet.	518	7	1.4 [0.5 -2.8]	7	1.4 [0.5 -2.8]	0	0
Butyl glycidylether	0.25 % pet.	515	4	0.8 [0.2 -2.0]	4	0.8 [0.2 -2.0]	0	0
Cresyl glycidylether	0.25 % pet.	514	9	1.8 [0.8 -3.3]	10	1.9 [0.9 -3.5]	1	+11.1
Diethylenetriamine	1 % pet.	515	5	1.0 [0.3 -2.3]	6	1.2 [0.4 -2.5]	1	+20.0
Ethyl-2-cyanoacrylate	10 % pet.	60	0	0.0 [0.0 -6.0]	0	0.0 [0.0 -6.0]	0	0
Ethylenglycol dimethacrylate	2 % pet.	518	11	2.1 [1.1 -3.8]	12	2.3 [1.2 -4.0]	1	+9.1
Hydroquinone	1 % pet.	346	3	0.9 [0.2 -2.5]	3	0.9 [0.2 -2.5]	0	0
Hydroxyethyl acrylate	0.1 % pet.	521	11	2.1 [1.1 -3.7]	13	2.5 [1.3 -4.2]	2	+18.2
Isobornyl acrylate	0.1 % pet.	61	1	1.6 [0.0 -8.8]	1	1.6 [0.0 -8.8]	0	0
Isophoronediamine (IPD)	0.5 % pet.	514	4	0.8 [0.2 -2.0]	5	1.0 [0.3 -2.3]	1	+25.0
Methylmethacrylate (MMA)	2 % pet.	519	12	2.3 [1.2 -4.0]	13	2.5 [1.3 -4.2]	1	+8.3
M-Xylidenediamine	0.1 % pet.	517	10	1.9 [0.9 -3.5]	12	2.3 [1.2 -4.0]	2	+20.0
Phenol formaldehyde resin (Novolak)	5 % pet.	518	8	1.5 [0.7 -3.0]	14	2.7 [1.5 -4.5]	6	+75.0
Phenyl glycidylether	0.25 % pet.	516	11	2.1 [1.1 -3.8]	14	2.7 [1.5 -4.5]	3	+27.3
p-tert-Butylcatechol	0.25 % pet.	524	6	1.1 [0.4 -2.5]	7	1.3 [0.5 -2.7]	1	+16.7
P-tert-butylphenyl glycidylether	0.25 % pet.	427	6	1.4 [0.5 -3.0]	7	1.6 [0.7 -3.3]	1	+16.7
Triethyleneglycol dimethacrylate (TEGDMA)	2 % pet.	520	13	2.5 [1.3 -4.2]	13	2.5 [1.3 -4.2]	0	0
Trimethylhexane-1,6-diamine	0.5 % pet.	514	0	0.0 [0.0 -0.7]	0	0.0 [0.0 -0.7]	0	0

Trimethylolpropane triglycidylether	0.25 % pet.	516	5	1.0 [0.3 -2.2]	5	1.0 [0.3 -2.2]	0	0
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Test series according to DKG Rubber Additives DKG test series No. #8			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
1,3-Diphenylguanidine (DPG)	1 % pet.	2558	27	1.1 [0.7 -1.5]	29	1.1 [0.8 -1.6]	2	+7.4
4,4'-Dihydroxydiphenyle	0.1 % pet.	1043	0	0.0 [0.0 -0.4]	0	0.0 [0.0 -0.4]	0	0
Benzoyl peroxide	1 % pet.	492	23	4.7 [3.0 -6.9]	25	5.1 [3.3 -7.4]	2	+8.7
Cyclohexylthiophthalimide	0.5 % pet.	2557	15	0.6 [0.3 -1.0]	17	0.7 [0.4 -1.1]	2	+13.3
Dibenzothiazyldisulfide (MBTS)	1 % pet.	2561	11	0.4 [0.2 -0.8]	13	0.5 [0.3 -0.9]	2	+18.2
Dibutyl thiourea	1 % pet.	2558	5	0.2 [0.1 -0.5]	5	0.2 [0.1 -0.5]	0	0
Dipentamethylen thiuramdisulfide	0.25 % pet.	2553	39	1.5 [1.1 -2.1]	43	1.7 [1.2 -2.3]	4	+10.3
Diphenyl thiourea	1 % pet.	2557	2	0.1 [0.0 -0.3]	3	0.1 [0.0 -0.3]	1	+50.0
Ethylene diamine-di-HCl	1 % pet.	2526	8	0.3 [0.1 -0.6]	9	0.4 [0.2 -0.7]	1	+12.5
Mercaptobenzothiazole	2 % pet.	2003	22	1.1 [0.7 -1.7]	29	1.4 [1.0 -2.1]	7	+31.8
Methenamine	1 % pet.	2532	5	0.2 [0.1 -0.5]	7	0.3 [0.1 -0.6]	2	+40.0
Monobenzone	1 % pet.	2558	13	0.5 [0.3 -0.9]	14	0.5 [0.3 -0.9]	1	+7.7
Morpholinylmercaptobenzothi azole	0.5 % pet.	2559	25	1.0 [0.6 -1.4]	30	1.2 [0.8 -1.7]	5	+20.0
N,N'-Diphenyl-p-phenylene diamine (DPPD)	0.25 % pet.	2555	22	0.9 [0.5 -1.3]	25	1.0 [0.6 -1.4]	3	+13.6
N-Cyclohexyl-2-benzothiazyl sulfenamide	1 % pet.	2562	25	1.0 [0.6 -1.4]	28	1.1 [0.7 -1.6]	3	+12.0
N-Isopropyl-N'-phenyl-p- phenylenediamine (IPPD)	0.1 % pet.	2536	31	1.2 [0.8 -1.7]	32	1.3 [0.9 -1.8]	1	+3.2
p-tert-Butylcatechol	0.25 % pet.	2557	21	0.8 [0.5 -1.3]	28	1.1 [0.7 -1.6]	7	+33.3
Tetraethylthiuramdisulfide (Disulfiram)(TETD)	0.25 % pet.	2550	99	3.9 [3.2 -4.7]	104	4.1 [3.3 -4.9]	5	+5.1
Tetramethylthiuramdisulfide (TMTD)	0.25 % pet.	2527	62	2.5 [1.9 -3.1]	65	2.6 [2.0 -3.3]	3	+4.8
Tetramethylthiurammonosulfi de (TMTM)	0.25 % pet.	2555	78	3.1 [2.4 -3.8]	83	3.2 [2.6 -4.0]	5	+6.4
Zinc dibenzylidithiocarbamate	1 % pet.	2513	4	0.2 [0.0 -0.4]	5	0.2 [0.1 -0.5]	1	+25.0
Zinc dibutylidithiocarbamate (ZDBC)	1 % pet.	2557	5	0.2 [0.1 -0.5]	6	0.2 [0.1 -0.5]	1	+20.0

Zinc diethyldithiocarbamate (ZDEC)	1 % pet.	2541	27	1.1 [0.7 -1.5]	30	1.2 [0.8 -1.7]	3	+11.1
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Test series according to DKG Disinfectants DKG test series No. #5			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Benzalkonium chloride	0.1 % pet.	1735	11	0.6 [0.3 -1.1]	12	0.7 [0.4 -1.2]	1	+9.1
Chlorhexidine digluconate	0.5 % aq.	1741	6	0.3 [0.1 -0.7]	7	0.4 [0.2 -0.8]	1	+16.7
Glutardialdehyde (Glutaral)	0.3 % pet.	1691	35	2.1 [1.4 -2.9]	42	2.5 [1.8 -3.3]	7	+20.0
Glyoxal trimer dihydrate	1 % pet.	1755	13	0.7 [0.4 -1.3]	16	0.9 [0.5 -1.5]	3	+3.8
Polyaminopropyl biguanide	2.5 % aq.	159	2	1.3 [0.2 -4.5]	2	1.3 [0.2 -4.5]	0	+23.1
Povidone iodine	10 % aq.	1749	132	7.5 [6.4 -8.9]	137	7.8 [6.6 -9.2]	5	0

Test series according to DKG Baseline series DKG test series No. #1			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
2-Hydroxyethyl methacrylate (HEMA)	1 % pet.	1667	27	1.6 [1.1 -2.3]	28	1.7 [1.1 -2.4]	1	+3.7
Ammoniated mercury Φ	1 % pet.	951	30	3.2 [2.1 -4.5]	38	4.0 [2.8 -5.4]	8	+26.7
Balsam of Peru (Myroxolon pereirae)	25 % pet.	4636	233	5.0 [4.4 -5.7]	249	5.4 [4.7 -6.1]	16	+6.9
Benzocaine Φ	5 % pet.	1002	2	0.2 [0.0 -0.7]	2	0.2 [0.0 -0.7]	0	0
Bronopol	0.5 % pet.	4411	24	0.5 [0.3 -0.8]	30	0.7 [0.5 -1.0]	6	+25.0
Bufexamac Φ	5 % pet.	1349	10	0.7 [0.4 -1.4]	12	0.9 [0.5 -1.5]	2	+20.0
Cetostearyl alcohol	20 % pet.	4619	20	0.4 [0.3 -0.7]	20	0.4 [0.3 -0.7]	0	0
Cobalt (II)-chloride, 6*H ₂ O	1 % pet.	4586	268	5.8 [5.2 -6.6]	303	6.6 [5.9 -7.4]	35	+13.1
Colophony (Rosin)	20 % pet.	4625	177	3.8 [3.3 -4.4]	202	4.4 [3.8 -5.0]	25	+14.1
Compositae Mix	5 % pet.	448	13	2.9 [1.6 -4.9]	14	3.1 [1.7 -5.2]	1	+7.7
Compositae Mix II	5 % pet.	4197	77	1.8 [1.5 -2.3]	82	2.0 [1.6 -2.4]	5	+6.5
Epoxy resin	1 % pet.	4443	70	1.6 [1.2 -2.0]	86	1.9 [1.6 -2.4]	16	+22.9
Formaldehyde	1 % aq.	4636	39	0.8 [0.6 -1.1]	44	0.9 [0.7 -1.3]	5	+12.8
Fragrance mix I	8 % pet.	4575	252	5.5 [4.9 -6.2]	274	6.0 [5.3 -6.7]	22	+8.7
Fragrance Mix II	14 % pet.	4606	154	3.3 [2.8 -3.9]	164	3.6 [3.0 -4.1]	10	+6.5
HICC #	5 % pet.	4636	91	2.0 [1.6 -2.4]	104	2.2 [1.8 -2.7]	13	+14.3
Iodopropynylbutyl carbamate (IPBC)	0.2 % pet.	4129	42	1.0 [0.7 -1.4]	47	1.1 [0.8 -1.5]	5	+11.9
Jasmine absolute	5 % pet.	4599	52	1.1 [0.8 -1.5]	58	1.3 [1.0 -1.6]	6	+11.5
Lanolin alcohols	30 % pet.	4582	52	1.1 [0.8 -1.5]	60	1.3 [1.0 -1.7]	8	+15.4
Mercapto mix (CBS, MBTS, MOR)	1 % pet.	4634	41	0.9 [0.6 -1.2]	44	0.9 [0.7 -1.3]	3	+7.3
Mercaptobenzothiazole	1 % pet.	891	9	1.0 [0.5 -1.9]	10	1.1 [0.5 -2.1]	1	+11.1
Mercaptobenzothiazole	2 % pet.	3746	30	0.8 [0.5 -1.1]	38	1.0 [0.7 -1.4]	8	+26.7
Methylisothiazolinone	0.05 % aq.	4120	185	4.5 [3.9 -5.2]	204	5.0 [4.3 -5.7]	19	+10.3
Methylchlorisothiazolinone / Methylisothiazolinone (MCI/MI)	100 ppm aq.	4629	158	3.4 [2.9 -4.0]	179	3.9 [3.3 -4.5]	21	+13.3
Methyldibromo glutaronitrile	0.2 % pet.	1963	58	3.0 [2.3 -3.8]	61	3.1 [2.4 -4.0]	3	+5.2
Methyldibromo glutaronitrile	0.3 % pet.	2656	128	4.8 [4.0 -5.7]	140	5.3 [4.5 -6.2]	12	+9.4
Neomycin sulfate Φ	20 % pet.	126	2	1.6 [0.2 -5.6]	9	7.1 [3.3 -13.1]	7	+350

Nickel (II)-sulfate hexahydrate	5 % pet.	4522	637	14.1 [13.1 - 15.1]	728	16.1 [15.0 -17.2]	91	+14.3
N-Isopropyl-N'-phenyl-p-phenylene diamine (IPPD)	0.1 % pet.	4634	46	1.0 [0.7 -1.3]	49	1.1 [0.8 -1.4]	3	+6.5
Oil of turpentine	10 % pet.	4517	30	0.7 [0.4 -0.9]	33	0.7 [0.5 -1.0]	3	+10.0
Paraben mix	16 % pet.	4614	32	0.7 [0.5 -1.0]	36	0.8 [0.5 -1.1]	4	+12.5
Potassium dichromate	0.5 % pet.	4601	225	4.9 [4.3 -5.6]	254	5.5 [4.9 -6.2]	29	+12.9
p-Phenylenediamine	1 % pet.	2241	98	4.4 [3.6 -5.3]	107	4.8 [3.9 -5.7]	9	+9.2
Propolis	10 % pet.	4639	139	3.0 [2.5 -3.5]	149	3.2 [2.7 -3.8]	10	+7.2
p-tert-Butylphenol formaldehyde resin (PTBFR)	1 % pet.	1675	7	0.4 [0.2 -0.9]	8	0.5 [0.2 -0.9]	1	+14.3
Sandalwood oil	10 % pet.	4602	37	0.8 [0.6 -1.1]	40	0.9 [0.6 -1.2]	3	+8.1
Sorbitan sesquioleate (SSQ)	20 % pet.	3032	25	0.8 [0.5 -1.2]	27	0.9 [0.6 -1.3]	2	+8.0
Thiuram mix	1 % pet.	4623	158	3.4 [2.9 -4.0]	170	3.7 [3.2 -4.3]	12	+7.6
Ylang ylang oil	10 % pet.	4602	90	2.0 [1.6 -2.4]	103	2.2 [1.8 -2.7]	13	+14.4
Zinc diethyldithiocarbamate (ZDEC)	1 % pet.	4637	36	0.8 [0.5 -1.1]	40	0.9 [0.6 -1.2]	4	+11.1

Test series according to DKG Ointment Bases DKG test series No. #18			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Amerchol L-101	50 % pet.	3722	67	1.8 [1.4 -2.3]	73	2.0 [1.5 -2.5]	6	+9.0
Benzophenone 4	10 % pet.	3821	30	0.8 [0.5 -1.1]	34	0.9 [0.6 -1.2]	4	+13.3
Butylhydroxyanisole (BHA)	2 % pet.	3735	17	0.5 [0.3 -0.7]	19	0.5 [0.3 -0.8]	2	+11.8
Butylhydroxytoluene (BHT)	2 % pet.	3820	10	0.3 [0.1 -0.5]	13	0.3 [0.2 -0.6]	3	+30.0
Cetostearyl alcohol	20 % pet.	3812	20	0.5 [0.3 -0.8]	20	0.5 [0.3 -0.8]	0	0
Cocamidopropyl betaine	1 % aq.	3785	38	1.0 [0.7 -1.4]	39	1.0 [0.7 -1.4]	1	+2.6
Coconut diethanolamide	0.5 % pet.	3823	22	0.6 [0.4 -0.9]	23	0.6 [0.4 -0.9]	1	+4.5
Decyl glucoside	5 % pet.	1681	23	1.4 [0.9 -2.0]	23	1.4 [0.9 -2.0]	0	0
Ethylhexylglycerin	5 % pet.	2197	4	0.2 [0.0 -0.5]	5	0.2 [0.1 -0.5]	1	+25.0
Hydroquinone	1 % pet.	2713	15	0.6 [0.3 -0.9]	17	0.6 [0.4 -1.0]	2	+13.3
Lauryl polyglucose (Lauryl glucoside)	3 % pet.	1682	8	0.5 [0.2 -0.9]	8	0.5 [0.2 -0.9]	0	0
Octyl gallate	0.3 % pet.	3826	59	1.5 [1.2 -2.0]	65	1.7 [1.3 -2.2]	6	+10.2
Polyethylene glycol-400	100%	1884	1	0.1 [0.0 -0.3]	1	0.1 [0.0 -0.3]	0	0
Polyethylene glycol ointment DAB 8	100%	1936	3	0.2 [0.0 -0.5]	3	0.2 [0.0 -0.5]	0	0
Propylene glycol	20 % aq.	3822	48	1.3 [0.9 -1.7]	53	1.4 [1.0 -1.8]	5	+10.4
Sorbitan sesquioleate (SSQ)	20 % pet.	2796	24	0.9 [0.6 -1.3]	26	0.9 [0.6 -1.4]	2	+8.3
Tert-Butylhydroquinone	1 % pet.	3825	58	1.5 [1.2 -2.0]	69	1.8 [1.4 -2.3]	11	+19.0
Triethanolamine	2.5 % pet.	3814	33	0.9 [0.6 -1.2]	34	0.9 [0.6 -1.2]	1	+3.0

Test series according to DKG Additional Fragrances to be Declared DKG test series No. #43			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Amyl cinnamic alcohol	1 % pet.	1075	0	0.0 [0.0 -0.3]	0	0.0 [0.0 -0.3]	0	0
Anisyl alcohol	1 % pet.	1081	0	0.0 [0.0 -0.3]	0	0.0 [0.0 -0.3]	0	0
Benzyl alcohol	1 % pet.	1075	2	0.2 [0.0 -0.7]	3	0.3 [0.1 -0.8]	1	+50.0
Benzyl benzoate	1 % pet.	1077	1	0.1 [0.0 -0.5]	1	0.1 [0.0 -0.5]	0	0
Benzyl cinnamate	5 % pet.	1083	0	0.0 [0.0 -0.3]	0	0.0 [0.0 -0.3]	0	0
Benzyl salicylate	1 % pet.	1076	0	0.0 [0.0 -0.3]	0	0.0 [0.0 -0.3]	0	0
D - limonene	2 % pet.	966	0	0.0 [0.0 -0.4]	0	0.0 [0.0 -0.4]	0	0
Dipentene (D,1-Limonene)	2 % pet.	122	0	0.0 [0.0 -3.0]	0	0.0 [0.0 -3.0]	0	0
Gamma-methyl ionone	1 % pet.	1079	1	0.1 [0.0 -0.5]	1	0.1 [0.0 -0.5]	0	0
Lilial	10 % pet.	1083	6	0.6 [0.2 -1.2]	9	0.8 [0.4 -1.6]	3	+50.0
Linalool (linalyl alcohol)	10 % pet.	700	2	0.3 [0.0 -1.0]	2	0.3 [0.0 -1.0]	0	0
Linalool (stabilized)	10 % pet.	384	2	0.5 [0.1 -1.9]	2	0.5 [0.1 -1.9]	0	0
Methyl heptincarbonate	1 % pet.	122	1	0.8 [0.0 -4.5]	1	0.8 [0.0 -4.5]	0	0
Methyl-2-octynoate	0.2 % pet.	262	0	0.0 [0.0 -1.4]	0	0.0 [0.0 -1.4]	0	0
Treemoss	1 % pet.	943	34	3.6 [2.5 -5.0]	36	3.8 [2.7 -5.2]	2	+5.9
Treemoss absolute	1 % pet.	136	4	2.9 [0.8 -7.4]	5	3.7 [1.2 -8.4]	1	+25.0

Test series according to DKG Industrial Biocides DKG test series No. #37			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
(Nitrobutyl)morpholine	1 % pet.	394	7	1.8 [0.7 -3.6]	8	2.0 [0.9 -4.0]	1	+14.3
1,2-Benzisothiazolin-3-one, sodium salt	0.1 % pet.	398	17	4.3 [2.5 -6.8]	19	4.8 [2.9 -7.4]	2	+11.8
4,4-Dimethyloxazolidine/ (Bioban CS 1135)	0.1 % pet.	395	7	1.8 [0.7 -3.6]	9	2.3 [1.0 -4.3]	2	+28.6
7-Ethylbicylo-oxazolidine	1 % pet.	395	1	0.3 [0.0 -1.4]	4	1.0 [0.3 -2.6]	3	+300.0
Benzyl hemiformal	1 % pet.	386	12	3.1 [1.6 -5.4]	14	3.6 [2.0 -6.0]	2	+16.7
Bromonitropropanediol	0.5 % pet.	396	4	1.0 [0.3 -2.6]	7	1.8 [0.7 -3.6]	3	+75.0
Chlorocresol	1 % pet.	398	1	0.3 [0.0 -1.4]	1	0.3 [0.0 -1.4]	0	0
Chloroxylenol	1 % pet.	395	0	0.0 [0.0 -0.9]	1	0.3 [0.0 -1.4]	1	N.A.
Iodopropynylbutyl carbamate (IPBC)	0.2 % pet.	401	11	2.7 [1.4 -4.9]	12	3.0 [1.6 -5.2]	1	+9.1
Methylisothiazolinone	0.05 % aq.	393	30	7.6 [5.2 -10.7]	32	8.1 [5.6 -11.3]	2	+6.7
Methyldibromo glutaronitrile	0.3 % pet.	294	30	10.2 [7.0 -14.2]	33	11.2 [7.9 -15.4]	3	+10.0
Methylene-bis(methyloxazolidine)	1 % pet.	392	8	2.0 [0.9 -4.0]	9	2.3 [1.1 -4.3]	1	+12.5
Octylisothiazolinone	0.025 % pet.	393	3	0.8 [0.2 -2.2]	3	0.8 [0.2 -2.2]	0	0
Polyaminopropyl biguanide	1 % pet.	54	0	0.0 [0.0 -6.6]	0	0.0 [0.0 -6.6]	0	0
Sodium-2-pyridinethiol-1-oxide	0.1 % aq.	393	1	0.3 [0.0 -1.4]	1	0.3 [0.0 -1.4]	0	0

Test series according to DKG Breakdown of Fragrance mix I DKG test series No. #33			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Amyl cinnamal	1 % pet.	753	1	0.1 [0.0 -0.7]	1	0.1 [0.0 -0.7]	0	0
Cinnamic alcohol (cinnamyl alcohol)	1 % pet.	766	6	0.8 [0.3 -1.7]	6	0.8 [0.3 -1.7]	0	0
Cinnamic aldehyde (cinnamal)	1 % pet.	766	13	1.7 [0.9 -2.9]	13	1.7 [0.9 -2.9]	0	0
Eugenol	1 % pet.	766	7	0.9 [0.4 -1.9]	7	0.9 [0.4 -1.9]	0	0
Geraniol	1 % pet.	767	7	0.9 [0.4 -1.9]	7	0.9 [0.4 -1.9]	0	0
Hydroxycitronellal	1 % pet.	765	23	3.0 [1.9 -4.5]	23	3.0 [1.9 -4.5]	0	0
Isoeugenol	1 % pet.	738	19	2.6 [1.6 -4.0]	22	3.0 [1.9 -4.5]	3	+15.8
Oak moss absolute	1 % pet.	770	29	3.8 [2.5 -5.4]	31	4.0 [2.8 -5.7]	2	+6.9
Sorbitan sesquioleate (SSO)	20 % pet.	771	13	1.7 [0.9 -2.9]	15	1.9 [1.1 -3.2]	2	+15.4

Test series according to DKG Metal Working Fluids DKG test series No. #46			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
(Nitrobutyl)morpholine	1 % pet.	408	6	1.5 [0.5 -3.2]	8	2.0 [0.9 -3.8]	2	+33.3
1,2-Benzisothiazolin-3-one, sodium salt	0.1 % pet.	413	13	3.1 [1.7 -5.3]	15	3.6 [2.0 -5.9]	2	+15.4
1,3,5-Tris(2-hydroxyethyl)- hexahydrotriazin	1 % pet.	408	6	1.5 [0.5 -3.2]	7	1.7 [0.7 -3.5]	1	+16.7
2-(2-Aminoethoxy)ethanol (Diglycolamine)	1 % pet.	407	1	0.2 [0.0 -1.4]	1	0.2 [0.0 -1.4]	0	0
2-Phenoxyethanol	1 % pet.	409	1	0.2 [0.0 -1.4]	1	0.2 [0.0 -1.4]	0	0
4,4-Dimethyloxazolidine	1 % pet.	408	6	1.5 [0.5 -3.2]	8	2.0 [0.9 -3.8]	2	+33.3
7-Ethylbicyclooxazolidine	1 % pet.	407	2	0.5 [0.1 -1.8]	6	1.5 [0.5 -3.2]	4	+200.0
Abietic acid	10 % pet.	412	18	4.4 [2.6 -6.8]	19	4.6 [2.8 -7.1]	1	+5.6
Benzyl hemiformal	1 % pet.	406	9	2.2 [1.0 -4.2]	12	3.0 [1.5 -5.1]	3	+33.3
Diethanolamine (DEA)	2 % pet.	407	4	1.0 [0.3 -2.5]	4	1.0 [0.3 -2.5]	0	0
Glyoxal trimer dihydrate	1 % pet.	410	3	0.7 [0.2 -2.1]	3	0.7 [0.2 -2.1]	0	0
Iodopropynylbutyl carbamate (IPBC)	0.2 % pet.	420	10	2.4 [1.1 -4.3]	12	2.9 [1.5 -4.9]	2	+20.0
Methylisothiazolinone	0.05 % aq.	419	33	7.9 [5.5 - 10.9]	34	8.1 [5.7 - 11.2]	1	+3.0
Methylene- bis(methyloxazolidine)	1 % pet.	408	9	2.2 [1.0 -4.1]	10	2.5 [1.2 -4.5]	1	+11.1
Monoethanolamine (MEA)	2 % pet.	404	14	3.5 [1.9 -5.7]	14	3.5 [1.9 -5.7]	0	0
Morpholinylmercaptobenzothiaz ole	0.5 % pet.	417	5	1.2 [0.4 -2.8]	6	1.4 [0.5 -3.1]	1	+20.0
Octylisothiazolinone	0.025 % pet.	406	6	1.5 [0.5 -3.2]	7	1.7 [0.7 -3.5]	1	+16.7
p-tert-Butylphenol	1 % pet.	408	1	0.2 [0.0 -1.4]	1	0.2 [0.0 -1.4]	0	0
Sodium-2-Pyridinethiol-1-oxide	0.1 % aq.	407	2	0.5 [0.1 -1.8]	2	0.5 [0.1 -1.8]	0	0
Triethanolamine (TEA) (Trolamine)	2.5 % pet.	418	5	1.2 [0.4 -2.8]	5	1.2 [0.4 -2.8]	0	0

Test series according to DKG Textile and Leather Dyes DKG test series No. #24			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Acid Yellow 36 (CI 13065)	1 % pet.	352	4	1.1 [0.3 -2.9]	4	1.1 [0.3 -2.9]	0	0
Bismark brown R	0.5 % pet.	345	1	0.3 [0.0 -1.6]	1	0.3 [0.0 -1.6]	0	0
Disperse blue 106	0.3 % pet.	127	1	0.8 [0.0 -4.3]	1	0.8 [0.0 -4.3]	0	0
Disperse blue 124	0.3 % pet.	127	2	1.6 [0.2 -5.6]	2	1.6 [0.2 -5.6]	0	0
Disperse blue 3 (CI 61505)	1 % pet.	352	2	0.6 [0.1 -2.0]	2	0.6 [0.1 -2.0]	0	0
Disperse orange 3 (CI 11005)	1 % pet.	347	11	3.2 [1.6 -5.6]	11	3.2 [1.6 -5.6]	0	0
Disperse red 1 (CI 11110)	1 % pet.	352	2	0.6 [0.1 -2.0]	2	0.6 [0.1 -2.0]	0	0
Disperse red 11 (CI 62015)	1 % pet.	349	0	0.0 [0.0 -1.1]	0	0.0 [0.0 -1.1]	0	0
Disperse red 17 (CI 11210)	1 % pet.	352	3	0.9 [0.2 -2.5]	4	1.1 [0.3 -2.9]	1	+33.3
Disperse yellow 3 (CI 11855)	1 % pet.	352	3	0.9 [0.2 -2.5]	3	0.9 [0.2 -2.5]	0	0
Disperse yellow 9 (CI 10375)	1 % pet.	352	0	0.0 [0.0 -1.0]	1	0.3 [0.0 -1.6]	1	N.A.
Naphthol AS (CI 37505)	1 % pet.	352	0	0.0 [0.0 -1.0]	1	0.3 [0.0 -1.6]	1	N.A.

Test series according to DKG Corticosteroids DKG test series No. #22			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Amcinonide	0.1 % pet.	399	2	0.5 [0.1 -1.8]	2	0.5 [0.1 -1.8]	0	0
Betamethasone-17-valerate	0.12 % pet.	399	2	0.5 [0.1 -1.8]	2	0.5 [0.1 -1.8]	0	0
Budesonide	0.1 % pet.	399	5	1.3 [0.4 -2.9]	5	1.3 [0.4 -2.9]	0	0
Clobetasol-17-propionate	0.25 % pet.	278	3	1.1 [0.2 -3.1]	3	1.1 [0.2 -3.1]	0	0
Clobetasol-17-propionate	1 % pet.	121	0	0.0 [0.0 -3.0]	0	0.0 [0.0 -3.0]	0	0
Dexamethasone-21-Phosphate, Disodium salt	1 % pet.	399	3	0.8 [0.2 -2.2]	3	0.8 [0.2 -2.2]	0	0
Hydrocortisone (Cortisol)	1 % pet.	399	1	0.3 [0.0 -1.4]	1	0.3 [0.0 -1.4]	0	0
Hydrocortisone-17-butyrate	0.1 % pet.	398	1	0.3 [0.0 -1.4]	1	0.3 [0.0 -1.4]	0	0
Prednisolone	1 % pet.	400	1	0.3 [0.0 -1.4]	1	0.3 [0.0 -1.4]	0	0
Tixocortol-pivalate	1 % pet.	399	7	1.8 [0.7 -3.6]	7	1.8 [0.7 -3.6]	0	0
Triamcinolone-acetonide	0.1 % pet.	169	1	0.6 [0.0 -3.3]	1	0.6 [0.0 -3.3]	0	0
Triamcinolone-acetonide	1 % pet.	230	0	0.0 [0.0 -1.6]	1	0.4 [0.0 -2.4]	1	N.A.

Test series according to DKG Plant Constituents DKG test series No. #15			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Achillea millefolium	1 % pet.	332	8	2.4 [1.0 -4.7]	9	2.7 [1.2 -5.1]	1	+12.5
Anthemis nobilis (Roman chamomile)	1 % pet.	292	2	0.7 [0.1 -2.5]	2	0.7 [0.1 -2.5]	0	0
Anthemis nobilis (Roman chamomile)	1.2 % pet.	24	1	4.2 [0.1 -21.1]	1	4.2 [0.1 -21.1]	0	0
Arnica montana	0.5 % pet.	332	1	0.3 [0.0 -1.7]	1	0.3 [0.0 -1.7]	0	0
Atranorin	0.1 % pet.	326	2	0.6 [0.1 -2.2]	2	0.6 [0.1 -2.2]	0	0
Atranorin	0.1 % pet.	326	2	0.6 [0.1 -2.2]	2	0.6 [0.1 -2.2]	0	0
Chamomilla recutita	1 % pet.	294	0	0.0 [0.0 -1.2]	1	0.3 [0.0 -1.9]	1	N.A.
Chamomilla romana	1 % pet.	15	1	6.7 [0.2 -31.9]	2	13.3 [1.7 -40.5]	1	+100.0
Dipentene (D,1- Limonene)	2 % pet.	15	0	0.0 [0.0 -21.8]	0	0.0 [0.0 -21.8]	0	0
Parthenolide	0.1 % pet.	329	22	6.7 [4.2 -9.9]	25	7.6 [5.0 -11.0]	3	+13.6
Primin	100 ppm pet.	324	0	0.0 [0.0 -1.1]	1	0.3 [0.0 -1.7]	0	N.A.
Sesquiterpenlactone mix	0.1 % pet.	327	25	7.6 [5.0 -11.1]	25	7.6 [5.0 -11.1]	0	0
Sorbitan sesquioleate (SSO)	20 % pet.	292	3	1.0 [0.2 -3.0]	3	1.0 [0.2 -3.0]	0	0
Tanacetum vulgare (Rainfarn)	1 % pet.	331	19	5.7 [3.5 -8.8]	20	6.0 [3.7 -9.2]	1	+5.3
Usnic acid	0.1 % pet.	325	4	1.2 [0.3 -3.1]	4	1.2 [0.3 -3.1]	0	0

Test series according to DKG Breakdown of Fragrance mix II DKG test series No. #41			Positive PT on D3		Positive PT on D3 and/or D7		First positive on D7	
Substance	Conc.	tested [n]	Pos [n]	Positive % [95% CI]	Pos [n]	Positive % [95% CI]	[n]	%
Hexyl cinnamal	10 % pet.	732	4	0.5 [0.1 -1.4]	6	0.8 [0.3 -1.8]	2	+50.0
Citral	2 % pet.	732	23	3.1 [2.0 -4.7]	23	3.1 [2.0 -4.7]	0	0
Citronellol	1 % pet.	731	4	0.5 [0.1 -1.4]	4	0.5 [0.1 -1.4]	0	0
Coumarin	5 % pet.	731	1	0.1 [0.0 -0.8]	1	0.1 [0.0 -0.8]	0	0
Farnesol	5 % pet.	730	15	2.1 [1.2 -3.4]	15	2.1 [1.2 -3.4]	0	0

Table S3.

Patch test results and reaction dynamics of 44 allergens tested in $\geq 80\%$ of the study group (4687 patients). The sum of “not-negative reactions” on D3 and/or D7 per substance (non-allergic + positive reactions) served as denominator for the calculation of the relative amount of increased (crescendo) reactions [%]. The relative risk estimate for these increases were calculated in relation to the median of the 44 substances concerned, namely 11.0%.

HICC, Hydroxyisohexyl 3-cyclohexene carboxaldehyde

		Patch test result on D3 and/or D7			Increase of reaction intensity from D3 → D7 Examples: o negative → positive o negative → ir/? o ir/? → positive o + → ++ or +++ o ++ → +++		
Substance	tested [n]	Pos [n]	ir/? [n]	not-negative [n]	[n] increase	[%]	Relative risk estimate
Amerchol L-101	3722	73	130	203	14	+6.9	0.6
Balsam of Peru (Myroxolon pereirae)	4636	249	201	450	28	+6.2	0.6
Benzophenone 4	3880	35	114	149	15	+10.1	0.9
Benzyl alcohol	3823	6	21	27	3	+11.1	1.0
Bromonitropropanediol	4411	30	28	58	8	+13.8	1.2
Butylhydroxyanisole (BHA)	3735	19	29	48	6	+12.5	1.1
Butylhydroxytoluene (BHT)	3820	13	35	48	5	+10.4	0.9
Cetostearyl alcohol	4619	20	41	61	1	+1.6	0.1
Chlorhexidine digluconate	4005	16	30	46	6	+13.0	1.2
Chloroacetamide	3822	16	13	29	7	+24.1	2.2
Cobalt (II)-chloride	4586	303	246	549	68	+12.4	1.1
Cocamidopropyl betaine	3800	39	203	242	2	+0.8	0.1
Coconut diethanolamide	3823	23	72	95	2	+2.1	0.2
Colophony (Rosin)	4625	202	55	257	55	+21.4	1.9
Compositae Mix II	4197	82	37	119	12	+10.1	0.9
DMDM Hydantoin	3793	27	18	45	7	+15.6	1.4
Epoxy resin	4443	86	27	113	31	+27.4	2.5
Formaldehyde	4636	44	57	101	17	+16.8	1.5
Fragrance mix I	4575	274	179	453	42	+9.3	0.8
Fragrance mix II	4606	164	125	289	24	+8.3	0.8
HICC	4636	104	38	142	22	+15.5	1.4
Imidazolidinyl Urea (Germall 115)	3854	13	17	30	3	+10.0	0.9

Iodopropynylbutyl carbamate (IPBC)	4129	47	143	190	10	+5.3	0.5
Jasmine absolute	4599	58	64	122	10	+8.2	0.7
Lanolin alcohols	4582	60	53	113	15	+13.3	1.2
Mercapto mix (CBS, MBTS, MOR)	4634	44	20	64	7	+11.0	1.0
Mercaptobenzothiazole	3746	38	13	51	14	+27.5	2.5
Methylisothiazolinone	4120	204	32	236	38	+16.1	1.5
Methylchloroisothiazolinone / Methylisothiazolinone (MCI/MI)	4629	179	32	211	34	+16.1	1.5
Nickel (II)-sulfate hexahydrate	4522	728	132	860	160	+18.6	1.7
N-Isopropyl-N'-phenyl-p- phenylenediamine (IPPD)	4634	49	38	87	13	+14.9	1.4
Oil of turpentine	4517	33	30	63	6	+9.5	0.9
Paraben mix	4614	36	106	142	7	+4.9	0.4
Potassium dichromate	4601	254	198	452	66	+14.6	1.3
Propolis	4639	149	180	329	15	+4.6	0.4
Propylene glycol	3822	53	85	138	8	+5.8	0.5
Sandalwood oil	4602	40	48	88	10	+11.4	1.0
Sorbic acid	3797	29	44	73	8	+11.0	1.0
tert-Butylhydroquinone	3825	69	166	235	22	+9.4	0.8
Thiuram mix	4623	170	56	226	23	+10.2	0.9
Triclosan	3796	3	21	24	3	+12.5	1.1
Triethanolamine	3836	34	77	111	6	+5.4	0.5
Ylang ylang oil	4602	103	68	171	23	+13.5	1.2
Zinc diethyldithiocarbamate (ZDEC)	4637	40	24	64	9	+14.1	1.3