

North American Contact Dermatitis Group Patch Test Results: 2015–2016

Joel G. DeKoven, MD, MHSc,* Erin M. Warshaw, MD,†‡ Kathryn A. Zug, MD,§ Howard I. Maibach, MD,|| Donald V. Belsito, MD,¶|| Denis Sasseville, MD,# James S. Taylor, MD,** Joseph F. Fowler, Jr, MD,†† C. G. Toby Mathias, MD,‡‡ James G. Marks, MD,§§ Melanie D. Pratt, MD,|||| Matthew J. Zirwas, MD,¶¶ and Vincent A. DeLeo, MD##

Background: Patch testing is an important diagnostic tool for the assessment of allergic contact dermatitis (ACD).

Objective: This study documents the North American Contact Dermatitis Group (NACDG) patch testing results from January 1, 2015, to February 28, 2017.

Methods: At 13 centers in North America, patients were tested in a standardized manner with a screening series of 70 allergens. Data were manually verified and entered into a central database. Descriptive frequencies were calculated, and trends were analyzed using χ^2 test.

Results: A total of 5597 patients were tested. There were 3725 patients (66.6%) who had at least 1 positive reaction, and 2798 patients (50.2%) were ultimately determined to have a primary diagnosis of ACD. A total of 572 patients (10.2%) had occupationally related skin disease. There were 10,983 positive allergic reactions. Nickel remained the most commonly detected allergen (17.5%). Methylisothiazolinone, which was added to the screening series for the 2013–2014 cycle, had the second highest positive reaction rate of allergens tested (13.4%). Compared with the previous reporting periods (2013–2014) and (2005–2014), positive reaction rates for the top 35 screening allergens statistically increased for only 1 allergen: hydroxyethyl methacrylate (3.4%; risk ratios, 1.24 [confidence interval, 1.00–1.54] and 1.46 [confidence interval, 1.23–1.73]). Three newly added allergen preparations—ammonium persulfate (1.7%), chlorhexidine (0.8%), and hydroquinone (0.3%)—all had a reaction rate of less than 2%. Twenty-three percent of the tested patients had at least 1 relevant allergic reaction to an allergen not on the NACDG series; 12% of these were occupationally related. T.R.U.E. Test (SmartPractice Denmark, Hillerød, Denmark) would have hypothetically missed one quarter to almost 40% of reactions detected by the NACDG screening series.

Conclusions: These results confirm that the epidemic of sensitivity to methylisothiazolinone has continued in North America. Patch testing with allergens beyond a screening tray is necessary for a complete evaluation of occupational and nonoccupational ACD.

The North American Contact Dermatitis Group (NACDG) is a group of dermatologists in Canada and the United States who evaluate patients with suspected allergic contact dermatitis (ACD) using a standardized set of allergens. The composition of the

NACDG “screening series” changes slightly every 2-year cycle, and periodically, we publish our epidemiologic data.^{1–9} This article summarizes results from 2015 to 2016.

This material, in part, is the result of work supported with resources and the use of facilities at the Minneapolis Veterans Affairs Health Care System.

The views expressed in this article are those of the authors and do not necessarily represent the position or policy of the Department of Veterans Affairs or the US Government.

Dr. J.S.T. is a consultant for Johnson & Johnson, Monsanto, Equinox Group, and Kao Brands; is a stockholder for Johnson & Johnson, Express Scripts, Opko Health, Allergan, Astra Zeneca, and Merck; is an author for Decision Support in Medicine; and has a nondependent child who is employed by Pfizer. Dr. M.J.Z. is part owner of AsepticMD; is a speaker, consultant, and investigator for Regeneron/Sanofi; is a speaker for Genentech/Novartis; is a consultant for Fit Bit, L’Oreal, and Menlo; and is an investigator for Leo, Janssen, Incyte, Foamix, DS Biopharma, and UCB. Drs. J.G.D., E.M.W., K.A.Z., H.I.M., D.V.B., D.S., J.F.F.Jr, C.G.T.M., J.G.M., M.D.P., and V.A.D., have no conflicts of interest to disclose.

DOI: 10.1097/DER.0000000000000417

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From the *Division of Dermatology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; †Department of Dermatology, Minneapolis Veterans Affairs Medical Center; ‡Department of Dermatology, University of Minnesota, Minneapolis, MN; §Dartmouth-Hitchcock Medical Center, Lebanon, NH; ||Department of Dermatology, University of California San Francisco, San Francisco, CA; ¶Department of Dermatology, Columbia University, New York, NY; #Division of Dermatology, Royal Victoria Hospital, McGill University, Montreal, Quebec, Canada; **Department of Dermatology, Cleveland Clinic, Cleveland, OH; ††University of Louisville, Louisville, KY; ‡‡Department of Dermatology, University of Cincinnati, Cincinnati, OH; §§Department of Dermatology, Pennsylvania State University, State College, PA; ||||Division of Dermatology, University of Ottawa, Ottawa, Ontario, Canada; ¶¶Ohio State University, Columbus, OH; and ##Department of Dermatology, Keck School of Medicine, Los Angeles, CA.

Address reprint requests to Joel G. DeKoven, MD, MHSc, M1-736, 2075 Bayview Ave, Toronto, Ontario, Canada M4N 3M5. E-mail: joel.dekoven@utoronto.ca.

MATERIALS AND METHODS

Between January 1, 2015, and February 28, 2017, the NACDG consisted of 13 dermatologists in North America. Patients were patch tested with a screening series of 70 allergens (allergEAZE; SmartPractice, Calgary, Alberta, Canada). Other allergens were tested as determined by each individual physician, based on factors including patient history, location of dermatitis, and occupation. Recent NACDG reports⁶⁻⁹ described data collection methods in detail and remain unchanged for this reporting cycle. Patch testing was performed with a standardized technique using Finn chambers (SmartPractice, Phoenix, AZ) on Scanpor tape (Norgesplaster Alpha AS, Vennessla, Norway). At the first and second readings, patch tests were graded as +/- (weak/doubtful), + (mild), ++ (strong), or +++ (very strong) on the basis of degrees of induration, papules, vesicles, and/or spreading. A final determination of "allergic/positive" or "not allergic" was determined by each investigator based on the temporal pattern (crescendo/decrecendo), patch test appearance, and known characteristics of that allergen. For example, a weak/doubtful (macular erythema) reaction to a formaldehyde-releasing agent could be determined to be an allergic/positive reaction in the setting of multiple or stronger reactions to related formaldehyde-releasing allergens.

The clinical relevance of the positive patch-test reaction was determined using the patient's history and clinical skin examination. Current relevance was defined as "definite" (use test with the suspected item containing the putative allergen was positive, or a patch test to the object or product was positive), "probable" (the allergen could be verified as present in known skin contactants, and the clinical presentation was consistent), or "possible" (the patient was exposed to circumstances in which skin contact with materials known to contain the allergen was likely to occur). Past relevance was also indicated. For each positive allergen, the source of exposure was coded using a 3-digit code.^{8,9} Occupation and industry were

TABLE 2. Race and Occupation of Patch-Tested Patients

Characteristic	n (%)
Race (N = 5597)	
White	4628 (82.7)
Asiatic	446 (8.0)
Other/not specified	247 (4.4)
Black	189 (3.4)
Hispanic	87 (1.6)
Occupation (N = 5456*)	
Not working†	2372 (43.5)
Managerial or professional	1412 (25.9)
Technical, sales, or administrative support	702 (12.9)
Service	389 (7.1)
Operators, fabricators, and laborers	271 (4.9)
Precision production, craft, and repair	259 (4.7)
Farming, forestry, and fishing	33 (0.6)
Military	18 (0.3)

*Excludes 141 individuals missing industry/occupation codes.

†Retired, homemaker, student, or unemployed/looking for work.

coded by an occupational expert using the US 2000 Census Bureau Codes based on answers to a series of 5 standardized questions collected for each patient.^{10,11} These questions were set to determine employment status at the time when the skin condition started or became significantly worse, type of industry/business, principal product or service produced, title of job, and most important job duties. Up to 3 final diagnoses and up to 3 sites of dermatitis could be coded for each patient. Reporting of these latter 2 characteristics was based on the total number of a specific diagnosis (or site) divided by the number of patients.

Quality control checks were performed by 1 individual who manually checked all required fields. At a central location, all data were manually entered into a computerized database and checked for quality assurance (Access, 2003; Microsoft Corporation, Redmond, WA). All analyses were performed using SAS 9.2 (Statistical Analysis System; SAS Institute Incorporated, Cary, NC) according to recommended guidelines.¹² Pearson χ^2 test was used to compare frequencies between periods. A significance level of 0.05 was used for all analyses. Because this was an exploratory analysis, no adjustments for multiple comparisons were performed. The significance-prevalence index number (SPIN)¹³ was calculated as in the previous data cycle report.⁹ Demographic data were displayed according to MOAHLFAP (male, occupational, atopic, hand, leg, foot, age > 40 years, percent positive) guidelines.^{12,14}

During this period, the NACDG screening series consisted of 70 allergens/allergen mixes. Compared with the previous period (2013–2014; 70 allergens), there were several changes:

(1) the addition of 3 allergens, namely, ammonium persulfate 2.5% in petrolatum (pet), chlorhexidine 1% aqueous (aq), and hydroquinone 1% in pet, and (2) the removal of 3 allergens: glutaraldehyde 1% in pet, ethyl-2-cyanoacrylate 10% in pet, and *Jasminum officinale* oil 2% in pet.

TABLE 1. MOAHLFAP^{12,14} Characteristics

Characteristic	n (%)
Male	1567 (28.0)
Occupational*	572 (10.2)
Atopic triad	
Hay fever†	1788 (31.9)
Eczema	1682 (30.1)
Asthma†	887 (15.8)
Hand‡	1230 (22.0)
Leg‡	207 (3.7)
Face‡	946 (16.9)
Age > 40 y	3780 (67.5)
Positivity rate (≥ 1 allergic reactions)	3725 (66.6)

*Excludes uncertain.

†Not part of MOAHLFAP.

‡Primary site: when primary sites of lips, nose, eyelids, and eyes are added to the face, the total for the face is 1773 (31.6%).

RESULTS

Patient Characteristics

Demographics of patch-tested patients are summarized in Tables 1 and 2. Most were white (82.7%) and female (72.0%). The average age was 49 years (range, 2–95 years; median, 50 years). Sites of dermatitis and final diagnoses are shown in Table 3. The most common primary sites of dermatitis were hands, scattered/generalized pattern, and face; 50.2% had a final primary diagnosis of ACD.

Of the 5597 patients tested, 66.6% (n = 3725) had at least 1 positive reaction; 29.9% (n = 1675) showed 3 or more positive reactions (Table 4).

TABLE 3. Body Sites of Dermatitis and Final Diagnoses

Characteristic	Primary, n (%)	Total of Up to 3 Listed, n (%) [*]
Dermatitis site†	n = 5591‡	n = 5597
Hand	1230 (22.0)	1440 (25.7)
Scattered generalized	995 (17.8)	1358 (24.3)
Face	946 (16.9)	1329 (23.7)
Eyelids	535 (9.6)	695 (12.4)
Trunk	307 (5.5)	691 (12.3)
Lips	274 (4.9)	368 (6.6)
Arm	230 (4.1)	739 (13.2)
Scalp	225 (4.0)	377 (6.7)
Leg	207 (3.7)	535 (9.6)
Foot	120 (2.1)	279 (5.0)
Neck	118 (2.1)	504 (9.0)
Anal/genital	113 (2.0)	159 (2.8)
Other	102 (1.8)	134 (2.4)
Ears	66 (1.2)	130 (2.3)
Most exposed areas	64 (1.1)	72 (1.3)
Only under clothing	38 (0.7)	41 (0.7)
Eyes	16 (0.3)	36 (0.6)
Erythroderma	3 (0.1)	5 (0.1)
Nose	2 (0.0)	12 (0.2)
Final diagnoses	N = 5578§	N = 5597
Allergic	2798 (50.2)	3251 (58.1)
Other dermatitis	813 (14.6)	905 (16.2)
Atopic dermatitis	672 (12.0)	984 (17.6)
Other dermatoses	447 (8.0)	566 (10.1)
Irritant	446 (8.0)	820 (14.7)
Psoriasis	150 (2.7)	226 (4.0)
Nummular dermatitis	67 (1.2)	84 (1.5)
Seborrheic dermatitis	59 (1.1)	82 (1.5)
Photodermatitis	55 (1.0)	73 (1.3)
Pompholyx	31 (0.6)	37 (0.7)
Contact urticaria	21 (0.4)	31 (0.6)
Stasis dermatitis	19 (0.3)	24 (0.4)

^{*}Total of percentages may exceed 100% because up to 3 sites/diagnoses per patient could be listed.

†Total of any of up to 3 sites or up to 3 diagnoses listed.

‡Excludes 6 patients with no primary site listed.

§Excludes 19 patients with no primary diagnosis.

TABLE 4. Number of Positive Patch Test Reactions per Patient

No. Positive Reactions to NACDG Screening Series	No. Patients	% (n = 5597)
0	1872	33.4
1	1121	20.0
2	929	16.6
3	607	10.8
4	386	6.9
5	237	4.2
6	160	2.9
7	112	2.0
8	66	1.2
9	38	0.7
10+	69	1.2

Occupation

Among all tested patients, 10.2% (n = 572) had ACD that was determined to be related to their occupation (Table 1). Of those with reported occupational data (n = 5456), 43.5% (n = 2372) were not working (Table 2). Major occupational groups included professional specialties (n = 834 [15.3%]), executive/administrative/managerial positions (n = 578 [10.6%]), clerical support (n = 320 [5.9%]), and sales (n = 239 [4.4%]). Of the 1066 patients with a relevant irritant identified (19.0% of the patch-tested population), 37.7% (n = 402) were deemed occupationally related. Of the 1262 patients who had relevant non-NACDG allergens identified, 11.9% (n = 150) were related to their occupation.

Allergen Frequencies

Of the 10,983 positive allergic reactions, the top 10 most frequent allergens (and their respective prevalence rates) were nickel sulfate (17.5%), methylisothiazolinone (MI) (13.4%), fragrance mix I (11.3%), formaldehyde 2% (8.4%), methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) (7.3%), *Myroxylon pereirae* (7.0%), neomycin (7.0%), bacitracin (6.9%), formaldehyde 1% (6.4%), and *p*-phenylenediamine (6.4%). The performance of the new allergens in order of frequency was as follows: ammonium persulfate (1.7%), chlorhexidine (0.8%), and hydroquinone (0.3%) (Table 5).

Prevalence Rates for Allergens in the 2015–2016 Period as Compared With 2013–2014

As shown in Table 6, positive reaction rates significantly increased for 7 of the top 35 allergens: MI, formaldehyde 2%, propylene glycol (PG) 100%, hydroxyethyl methacrylate (HEMA), colophonium (rosin), propolis, and ethyl acrylate. Statistically significant decreases were seen for 5 of the top 35 allergens NACDG allergens: nickel sulfate, neomycin sulfate, lanolin alcohol (Amerchol-L101), quaternium-15, and diphenylguanidine.

TABLE 5. Strength of Reactions/Clinical Relevance

Substance	n	Positive Reactions	Second Read Code* (%)					Relevance (%)			
			+++	++	+	+/-		Definite	Probable	Possible	Past
Nickel sulfate hexahydrate, 2.5% pet	5585	976	198 (20.3)	360 (36.9)	366 (37.5)	50 (5.1)		12 (1.2)	155 (15.9)	316 (32.4)	367 (37.6)
MI, 0.2% aq	5591	747	200 (26.8)	244 (32.7)	246 (32.9)	55 (7.4)		51 (6.8)	374 (50.1)	254 (34.0)	19 (2.5)
Fragrance mix, 8.0% pet	5595	632	80 (12.7)	166 (26.3)	325 (51.4)	57 (9.0)		8 (1.3)	183 (29)	348 (55.1)	27 (4.3)
Formaldehyde, 2.0% aq	5590	470	49 (10.4)	184 (39.1)	217 (46.2)	19 (4.0)		5 (1.1)	108 (23)	260 (55.3)	9 (1.9)
MCI/MI, 0.01% aq = 100 ppm aq	5593	407	39 (9.6)	143 (35.1)	197 (48.4)	25 (6.1)		37 (9.1)	194 (47.7)	126 (31.0)	17 (4.2)
<i>M. perillae</i> resin (balsam of Peru), 25.0% pet	5595	392	33 (8.4)	73 (18.6)	225 (57.4)	54 (13.8)		2 (0.5)	104 (26.5)	251 (64.0)	11 (2.8)
Neomycin sulfate, 20.0% pet	5591	390	47 (12.1)	85 (21.8)	205 (52.6)	52 (13.3)		20 (5.1)	45 (11.5)	39 (10.0)	164 (42.1)
Bacitracin, 20.0% pet	5589	386	82 (21.2)	126 (32.6)	157 (40.7)	20 (5.2)		22 (5.7)	92 (23.8)	46 (11.9)	122 (31.6)
Formaldehyde, 1.0% aq	5590	357	34 (9.5)	115 (32.2)	176 (49.3)	32 (9.0)		2 (0.6)	78 (21.8)	208 (58.3)	8 (2.2)
4-Phenylenediamine base, 1.0% pet	5594	356	115 (32.3)	99 (27.8)	130 (36.5)	11 (3.1)		4 (1.1)	134 (37.6)	91 (25.6)	83 (23.3)
Cobalt (II) chloride hexahydrate, 1.0% pet	5594	345	74 (21.4)	107 (31.0)	152 (44.1)	10 (2.9)		4 (1.2)	18 (5.2)	126 (36.5)	123 (35.7)
Fragrance mix II, 14.0% pet	5594	299	16 (5.4)	75 (25.1)	178 (59.5)	29 (9.7)		7 (2.3)	104 (34.8)	152 (50.8)	17 (5.7)
Carba mix, 3.0% pet	5590	257	11 (4.3)	59 (23.0)	160 (62.3)	26 (10.1)		16 (6.2)	54 (21.0)	122 (47.5)	25 (9.7)
Lanolin alcohol (Amerchol-L101), 50.0% pet	5591	231	19 (8.2)	34 (14.7)	134 (58.0)	44 (19.0)		8 (3.5)	85 (36.8)	95 (41.1)	12 (5.2)
PG, 100.0%	5593	222	9 (4.1)	53 (23.9)	140 (63.1)	19 (8.6)		12 (5.4)	132 (59.5)	65 (29.3)	2 (0.9)
Iodopropenyl butylcarbamate, 0.5% pet	5592	219	9 (4.1)	35 (16.0)	132 (60.3)	42 (19.2)		3 (1.4)	80 (36.5)	91 (41.6)	2 (0.9)
Cinnamal (cinnamic aldehyde), 1.0% pet	5594	210	11 (5.2)	44 (21.0)	120 (57.1)	33 (15.7)		4 (1.9)	60 (28.6)	131 (62.4)	5 (2.4)
Quaternium-15, 2.0% pet	5592	204	30 (14.7)	47 (23.0)	113 (55.4)	14 (6.9)		1 (0.5)	36 (17.6)	124 (60.8)	7 (3.4)
Oleamidopropyl dimethylamine, 1.0% aq	5593	198	2 (1.0)	48 (24.2)	128 (64.6)	19 (9.6)		4 (2.0)	32 (16.2)	127 (64.1)	3 (1.5)
Methyldibromo glutaronitrile/phenoxethanol (Euxyl K 400), 2.0% pet	5592	195	12 (6.2)	46 (23.6)	119 (61)	16 (8.2)		1 (0.5)	45 (23.1)	46 (23.6)	30 (15.4)
Thiuram mix, 1.0% pet	5592	191	45 (23.6)	61 (31.9)	73 (38.2)	11 (5.8)		7 (3.7)	47 (24.6)	83 (43.5)	24 (12.6)
2-Hydroxyethyl methacrylate, 2.0% pet	5594	188	48 (25.5)	64 (34.0)	70 (37.2)	6 (3.2)		1 (0.5)	46 (24.5)	60 (31.9)	36 (19.1)
PG, 30.0% aq	5594	155	3 (1.9)	23 (14.8)	94 (60.6)	35 (22.6)		5 (3.2)	114 (73.5)	29 (18.7)	0 (0.0)
Colophonium (rosin), 20.0% pet	5592	140	33 (23.6)	38 (27.1)	60 (42.9)	8 (5.7)		3 (2.1)	23 (16.4)	53 (37.9)	35 (25.0)
Diphenylguanidine, 1.0% pet	5592	139	3 (2.2)	30 (21.6)	95 (68.3)	10 (7.2)		10 (7.2)	16 (11.5)	68 (48.9)	15 (10.8)
Dimethylaminopropylamine, 1.0% aq	5593	131	10 (7.6)	28 (21.4)	74 (56.5)	17 (13.0)		5 (3.8)	49 (37.4)	63 (48.1)	1 (0.8)
Propolis, 10.0% pet	5592	129	19 (14.7)	32 (24.8)	64 (49.6)	12 (9.3)		5 (3.9)	15 (11.6)	59 (45.7)	7 (5.4)
Compositae mix, 6.0% pet	5594	121	16 (13.2)	35 (28.9)	57 (47.1)	10 (8.3)		2 (1.7)	18 (14.9)	69 (57.0)	6 (5.0)
Decyl glucoside, 5.0% pet	5592	118	11 (9.3)	26 (22.0)	62 (52.5)	17 (14.4)		11 (9.3)	29 (24.6)	62 (52.5)	8 (6.8)
Tixocortol-21-pivalate 1.0% pet	5591	117	32 (27.4)	47 (40.2)	34 (29.1)	3 (2.6)		4 (3.4)	62 (53.0)	20 (17.1)	22 (18.8)
Bisphenol A epoxy resin, 1.0% pet	5595	102	30 (29.4)	28 (27.5)	41 (40.2)	3 (2.9)		3 (2.9)	30 (29.4)	15 (14.7)	29 (28.4)
Ammonium persulfate, 2.5% pet	5594	97	18 (18.6)	24 (24.7)	51 (52.6)	4 (4.1)		1 (1.0)	25 (25.8)	28 (28.9)	18 (18.6)
Potassium dichromate, 0.25% pet	5595	93	14 (15.1)	29 (31.2)	49 (52.7)	1 (1.1)		4 (4.3)	10 (10.8)	43 (46.2)	12 (12.9)
Ethyl acrylate, 0.1% pet	5590	93	7 (7.5)	30 (32.3)	50 (53.8)	6 (6.5)		1 (1.1)	26 (28.0)	33 (35.5)	14 (15.1)
Benzophenone-4, 10.0% pet	5592	93	1 (1.1)	20 (21.5)	61 (65.6)	11 (11.8)		3 (3.2)	12 (12.9)	45 (48.4)	8 (8.6)
Cocamidopropyl betaine, 1.0% aq	5592	89	1 (1.1)	6 (6.7)	55 (61.8)	26 (29.2)		5 (5.6)	45 (50.6)	34 (38.2)	2 (2.2)
Benzocaine, 5.0% pet	5583	81	10 (12.3)	30 (37)	38 (46.9)	1 (1.2)		7 (8.6)	9 (11.1)	10 (12.3)	20 (24.7)
Methyl methacrylate, 2.0% pet	5594	78	6 (7.7)	34 (43.6)	31 (39.7)	7 (9.0)		0 (0.0)	25 (32.1)	24 (30.8)	14 (17.9)

Amidamine (stearamidopropyl dimethylamine), 0.1% aq	5594	74	1 (1.4)	9 (12.2)	39 (52.7)	24 (32.4)	2 (2.7)	13 (17.6)	53 (71.6)	3 (4.1)
2-Bromo-2-nitropropane-1,3-diol (bronopol), 0.5% pet	5593	73	5 (6.8)	22 (30.1)	39 (53.4)	7 (9.6)	0 (0.0)	10 (13.7)	44 (60.3)	3 (4.1)
Ylang-ylang oil, 2.0% pet	5594	71	14 (19.7)	23 (32.4)	26 (36.6)	8 (11.3)	2 (2.8)	11 (15.5)	49 (69.0)	3 (4.2)
4- <i>tert</i> -Butylphenol formaldehyde resin, 1.0% pet	5592	69	15 (21.7)	23 (33.3)	30 (43.5)	1 (1.4)	1 (1.4)	7 (10.1)	22 (31.9)	14 (20.3)
Ethylene diamine dihydrochloride, 1.0% pet	5593	67	12 (17.9)	31 (46.3)	22 (32.8)	2 (3.0)	0 (0.0)	10 (14.9)	10 (14.9)	10 (14.9)
Diazolidinyl urea (Germal II), 1.0% pet	5593	67	12 (17.9)	10 (14.9)	37 (55.2)	7 (10.4)	5 (7.5)	13 (19.4)	33 (49.3)	6 (9.0)
<i>M. alternifolia</i> (tea tree leaf oil), oxidized 5.0% pet	5593	66	10 (15.2)	30 (45.5)	23 (34.8)	3 (4.5)	7 (10.6)	20 (30.3)	19 (28.8)	8 (12.1)
Imidazolidinyl urea, 2.0% pet	5594	59	9 (15.3)	15 (25.4)	31 (52.5)	4 (6.8)	2 (3.4)	11 (18.6)	37 (62.7)	2 (3.4)
Tosylamide/formaldehyde resin, 10.0% pet	5592	53	5 (9.4)	16 (30.2)	28 (52.8)	4 (7.5)	0 (0.0)	4 (7.5)	13 (24.5)	12 (22.6)
Black rubber mix, pet 0.6%	5595	51	12 (23.5)	10 (19.6)	27 (52.9)	2 (3.9)	0 (0.0)	9 (17.6)	15 (29.4)	7 (13.7)
Cocamide DEA (coconut diethanolamide), 0.5% pet	5594	49	1 (2.0)	15 (30.6)	25 (51.0)	7 (14.3)	2 (4.1)	11 (22.4)	25 (51)	2 (4.1)
Budesonide, 0.1% pet	5593	47	13 (27.7)	13 (27.7)	17 (36.2)	4 (8.5)	0 (0.0)	18 (38.3)	11 (23.4)	12 (25.5)
Chlorhexidine digluconate, 1.0% aq	5594	46	4 (8.7)	9 (19.6)	25 (54.3)	8 (17.4)	2 (4.3)	10 (21.7)	9 (19.6)	8 (17.4)
DMDM hydantoin (Germal 115), 1.0% pet	5593	45	9 (20.0)	6 (13.3)	25 (55.6)	5 (11.1)	0 (0.0)	9 (20.0)	26 (57.8)	4 (8.9)
Carvone, 5.0% pet	5594	43	3 (7.0)	8 (18.6)	29 (67.4)	3 (7.0)	0 (0.0)	5 (11.6)	26 (60.5)	3 (7.0)
Lidocaine HCl, 15.0% pet	5593	42	8 (19.0)	17 (40.5)	13 (31.0)	4 (9.5)	7 (16.7)	12 (28.6)	6 (14.3)	7 (16.7)
Disperse blue mix 124/106, 1.0% pet	5594	41	7 (17.1)	9 (22.0)	19 (46.3)	6 (14.6)	0 (0.0)	9 (22.0)	13 (31.7)	7 (17.1)
Tocopherol (DL- α -tocopherol), 100.0%	5590	38	3 (7.9)	9 (23.7)	18 (47.4)	8 (21.1)	3 (7.9)	13 (34.2)	17 (44.7)	1 (2.6)
Mixed dialkyl thioureas, 1.0% pet	5594	36	19 (52.8)	11 (30.6)	4 (11.1)	2 (5.6)	3 (8.3)	7 (19.4)	20 (55.6)	3 (8.3)
Chloroxyleneol (4-chloro-3,5-xylenol), 1.0% pet	5594	36	4 (11.1)	15 (41.7)	14 (38.9)	3 (8.3)	2 (5.6)	13 (36.1)	12 (33.3)	1 (2.8)
Paraben mix, 12.0% pet	5593	34	2 (5.9)	6 (17.6)	22 (64.7)	3 (8.8)	4 (11.8)	11 (32.4)	13 (38.2)	0 (0.0)
<i>Mentha piperita</i> oil (peppermint oil), 2.0% pet	5591	33	4 (12.1)	9 (27.3)	17 (51.5)	3 (9.1)	2 (6.1)	7 (21.2)	20 (60.6)	1 (3.0)
2-Mercaptobenzothiazole, 1.0% pet	5591	28	4 (14.3)	12 (42.9)	10 (35.7)	1 (3.6)	1 (3.6)	4 (14.3)	15 (53.6)	2 (7.1)
Parthenolide, 0.1% pet	5594	28	5 (17.9)	6 (21.4)	16 (57.1)	1 (3.6)	0 (0.0)	4 (14.3)	13 (46.4)	1 (3.6)
<i>Lavandula angustifolia</i> oil (lavender oil), 2.0% pet	5594	28	4 (14.3)	10 (35.7)	9 (32.1)	5 (17.9)	2 (7.1)	6 (21.4)	17 (60.7)	2 (7.1)
Sesquiterpene lactone mix, 0.1% pet	5595	27	10 (37)	9 (33.3)	7 (25.9)	1 (3.7)	0 (0.0)	11 (40.7)	9 (33.3)	1 (3.7)
Benzophenone-3 (oxybenzone or 2-hydroxy-4-methoxy-benzophenone), 10.0% pet§§	5595	24	3 (12.5)	4 (16.7)	11 (45.8)	6 (25.0)	4 (16.7)	5 (20.8)	11 (45.8)	1 (4.2)
Ethylhexylglycerin, 5.0% pet	5595	16	1 (6.2)	7 (43.8)	7 (43.8)	0 (0.0)	2 (12.5)	5 (31.2)	6 (37.5)	1 (6.2)
Hydroquinone, 1.0% pet	5594	14	3 (21.4)	2 (14.3)	9 (64.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (21.4)	7 (50.0)
Clobetasol-17-propionate, 1.0% pet	5593	13	1 (7.7)	3 (23.1)	7 (53.8)	2 (15.4)	1 (7.7)	7 (53.8)	2 (15.4)	3 (23.1)
Hydrocortisone-17-butyrate, 1.0% pet	5593	9	0 (0.0)	2 (22.2)	6 (66.7)	1 (11.1)	0 (0.0)	3 (33.3)	5 (55.6)	0 (0.0)
Desoximetasone, 1.0% pet	5588	8	1 (12.5)	1 (12.5)	3 (37.5)	3 (37.5)	2 (25.0)	2 (25.0)	4 (50.0)	0 (0.0)

*Discrepancies in positive reaction numbers and second read code tally may differ by up to 5 because of coding variances.

TABLE 6. Comparison of Current Positive Rates With Those in the Previous Study Years

Patch Test Allergen	2015–2016		2013–2014		2015–2016		2009–2010		2007–2008		2005–2006		2015–2016	
	n*	Pos, %	Pos%	Pos%	vs 2013–2014	Pos%	Pos%	Pos%	Pos%	Pos%	Pos%	vs 2005–2014	Pos%	vs 2005–2014
Nickel sulfate hexahydrate, 2.5% pet	5585	17.5	0.0006, 0.87 (0.80, 0.94)	20.1	18.5	15.5	19.5	19.0	0.0471, 0.94 (0.88, 1.00)	0.0001, 1.24 (1.12, 1.38)	0.1569, 1.06 (0.98, 1.15)	0.0064, 1.20 (1.05, 1.37)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)
MI, 0.2% aq	5591	13.4	0.0001, 1.24 (1.12, 1.38)	10.9	—	—	—	—	0.0001, 1.24 (1.12, 1.38)	0.1569, 1.06 (0.98, 1.15)	0.0064, 1.20 (1.05, 1.37)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)
Fragrance mix, 8.0% pet	5595	11.3	0.4179, 0.96 (0.86, 1.07)	11.9	12.1	8.5	9.4	11.5	0.0001, 1.24 (1.12, 1.38)	0.1569, 1.06 (0.98, 1.15)	0.0064, 1.20 (1.05, 1.37)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)
Formaldehyde, 2.0% aq	5590	8.4	0.0064, 1.20 (1.05, 1.37)	7.0	—	—	—	—	0.0064, 1.20 (1.05, 1.37)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
MC/MI, 0.01% aq = 100 ppm aq	5593	7.3	0.0552, 1.15 (1.00, 1.33)	6.3	5.0	2.5	3.6	2.8	0.0552, 1.15 (1.00, 1.33)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
<i>M. perillae</i> resin (balsam of Peru), 25.0% pet	5595	7.0	0.7746, 0.98 (0.85, 1.13)	7.2	7.9	7.2	11.0	11.9	0.7746, 0.98 (0.85, 1.13)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Neomycin sulfate, 20.0% pet	5591	7.0	0.0072, 0.83 (0.73, 0.95)	8.4	9.1	8.7	10.1	10.0	0.0072, 0.83 (0.73, 0.95)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Bacitracin, 20.0% pet	5589	6.9	0.3529, 0.94 (0.82, 1.08)	7.4	7.8	8.3	7.9	9.2	0.3529, 0.94 (0.82, 1.08)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Formaldehyde, 1.0% aq	5590	6.4	0.1060, 1.13 (0.97, 1.32)	5.6	6.6	5.8	7.7	9.0	0.1060, 1.13 (0.97, 1.32)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
4-Phenylenediamine base, 1.0% pet	5594	6.4	0.1867, 0.91 (0.79, 1.05)	7.0	6.3	5.5	5.3	5.0	0.1867, 0.91 (0.79, 1.05)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Cobalt (II) chloride hexahydrate, 1.0% pet	5594	6.2	0.0128, 0.83 (0.72, 0.96)	7.4	7.3	6.2	8.2	8.4	0.0128, 0.83 (0.72, 0.96)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Fragrance mix II, 14.0% pet	5594	5.3	0.4606, 0.94 (0.80, 1.10)	5.7	5.2	4.7	3.6	—	0.4606, 0.94 (0.80, 1.10)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Carba mix, 3.0% pet	5590	4.6	0.6010, 0.95 (0.80, 1.13)	4.8	4.7	4.6	4.5	3.9	0.6010, 0.95 (0.80, 1.13)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Lanolin alcohol (Amerchol-L101), 50.0% pet†	5591	4.1	0.0036, 0.77 (0.65, 0.92)	5.3	4.6	—	—	—	0.0036, 0.77 (0.65, 0.92)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
PG, 100.0%	5593	4.0	0.0015, 1.39 (1.13, 1.71)	2.8	—	—	—	—	0.0015, 1.39 (1.13, 1.71)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Iodopropynyl butylcarbamate, 0.5% pet	5592	3.9	0.0518, 0.83 (0.69, 0.99)	4.7	4.2	4.3	3.1	2.4	0.0518, 0.83 (0.69, 0.99)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Cinnamal (cinnamic aldehyde), 1.0% pet	5594	3.8	0.2887, 0.90 (0.74, 1.09)	4.2	3.9	2.3	2.4	3.1	0.2887, 0.90 (0.74, 1.09)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Quaternium-15, 2.0% pet	5592	3.6	0.0027, 0.75 (0.62, 0.90)	4.8	6.5	5.8	8.6	10.3	0.0027, 0.75 (0.62, 0.90)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Methyldibromo glutaronitrile/phenoxethanol (Euxyl K 400), 2.0% pet	5592	3.5	0.5766, 0.94 (0.77, 1.15)	3.7	3.7	3.8	5.5	5.8	0.5766, 0.94 (0.77, 1.15)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Oleamidopropyl dimethylamine, 1.0% aq	5593	3.5	0.9641, 1.00 (0.82, 1.22)	3.5	2.4	1.8	—	—	0.9641, 1.00 (0.82, 1.22)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Thiuram mix, 1.0% pet	5592	3.4	0.4550, 1.08 (0.88, 1.33)	3.2	2.9	3.1	3.4	3.9	0.4550, 1.08 (0.88, 1.33)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
2-HEMA, 2.0% pet	5594	3.4	0.0498, 1.24 (1.00, 1.54)	2.7	2.0	2.0	2.4	—	0.0498, 1.24 (1.00, 1.54)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
PG, 30.0% aq	5594	2.8	0.0665, 1.25 (0.98, 1.59)	2.2	2.6	3.2	2.1	2.9	0.0665, 1.25 (0.98, 1.59)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Colophonium (rosin), 20.0% pet	5592	2.5	0.0304, 1.33 (1.03, 1.73)	1.9	2.3	2.7	2.8	2.2	0.0304, 1.33 (1.03, 1.73)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Diphenylguanidine, 1.0% pet	5592	2.5	0.0001, 0.66 (0.53, 0.82)	3.8	—	—	—	—	0.0001, 0.66 (0.53, 0.82)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Dimethylaminopropylamine, 1.0% aq	5593	2.3	0.0627, 1.28 (0.98, 1.67)	1.8	1.5	2.0	—	—	0.0627, 1.28 (0.98, 1.67)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Propolis, 10.0% pet	5592	2.3	0.0213, 1.37 (1.04, 1.80)	1.7	1.8	2.1	4.9	—	0.0213, 1.37 (1.04, 1.80)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Compositae mix, 6.0% pet	5594	2.2	0.1006, 1.26 (0.96, 1.66)	1.7	1.9	1.9	1.4	1.2	0.1006, 1.26 (0.96, 1.66)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Tixocortol-21-pivalate, 1.0% pet	5591	2.1	0.9917, 1.00 (0.77, 1.30)	2.1	2.3	2.0	2.5	2.7	0.9917, 1.00 (0.77, 1.30)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Decyl glucoside, 5.0% pet	5592	2.1	0.1694, 1.21 (0.92, 1.59)	1.7	1.6	1.5	—	—	0.1694, 1.21 (0.92, 1.59)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Bisphenol A epoxy resin, 1.0% pet	5595	1.8	0.9967, 1.00 (0.75, 1.33)	1.8	1.5	1.6	1.7	—	0.9967, 1.00 (0.75, 1.33)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Potassium dichromate, 0.25% pet	5595	1.7	0.0690, 0.77 (0.58, 1.02)	2.2	1.6	2.3	4.1	4.8	0.0690, 0.77 (0.58, 1.02)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Ethyl acrylate, 0.1% pet	5590	1.7	0.0242, 1.45 (1.04, 2.02)	1.1	0.9	0.7	1.2	0.9	0.0242, 1.45 (1.04, 2.02)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Benzophenone-4, 10.0% pet	5592	1.7	0.1456, 0.81 (0.61, 1.07)	2.0	—	—	—	—	0.1456, 0.81 (0.61, 1.07)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Ammonium persulfate, 2.5% pet	5594	1.7	—	—	—	—	—	—	—	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Cocamidopropyl betaine, 1.0% aq	5592	1.6	0.9790, 1.00 (0.74, 1.35)	1.6	1.4	1.4	1.1	1.8	0.9790, 1.00 (0.74, 1.35)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Benzocaine, 5.0% pet	5583	1.5	0.4815, 0.90 (0.66, 1.22)	1.6	1.4	1.8	1.3	1.9	0.4815, 0.90 (0.66, 1.22)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)
Methyl methacrylate, 2.0% pet	5594	1.4	0.7130, 1.06 (0.76, 1.47)	1.3	0.9	0.8	1.2	1.0	0.7130, 1.06 (0.76, 1.47)	0.0000, 1.78 (1.59, 1.99)	0.0000, 0.77 (0.69, 0.85)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)	0.0000, 0.75 (0.68, 0.83)

Amidamine (stearamidopropyl dimethylamine), 0.1% aq	5594	1.3	0.5365, 1.11 (0.79, 1.56)	1.2	1.2	0.3	1.6	2.0	0.8082, 1.03 (0.80, 1.33)
2-Bromo-2-nitropropane-1,3-diol (bronopol), 0.5% pet	5593	1.3	0.0026, 0.63 (0.47, 0.85)	2.1	1.6	1.0	3.1	3.4	0.0000, 0.58 (0.45, 0.74)
Ylang-ylang oil, 2.0% pet	5594	1.3	0.7801, 1.05 (0.75, 1.48)	1.2	0.7	1.3	1.4	1.5	0.8725, 1.02 (0.79, 1.32)
Ethylendiamine dihydrochloride, 1.0% pet	5593	1.2	0.9638, 1.01 (0.71, 1.43)	1.2	1.3	1.4	1.5	1.9	0.1141, 0.82 (0.63, 1.06)
4-tert-Butylphenol formaldehyde resin, 1.0% pet	5592	1.2	0.2626, 1.23 (0.85, 1.77)	1.0	1.1	1.5	1.2	1.3	0.9519, 1.01 (0.78, 1.31)
Diazolidinyl urea (Germall II), 1.0% pet	5593	1.2	0.0988, 0.76 (0.55, 1.05)	1.6	2.1	2.2	3.1	3.7	0.0000, 0.47 (0.37, 0.60)
<i>M. alternifolia</i> (tea tree leaf oil), oxidized 5.0% pet	5593	1.2	0.1944, 1.28 (0.88, 1.87)	0.9	0.8	1.0	1.4	1.4	0.6507, 1.07 (0.82, 1.40)
Imidazolidinyl urea, 2.0% pet	5594	1.1	0.0199, 0.67 (0.48, 0.94)	1.6	1.6	2.2	2.4	2.9	0.0000, 0.49 (0.37, 0.64)
Black rubber mix, pet 0.6%	5595	0.9	0.4901, 0.87 (0.59, 1.28)	1.0	1.2	0.7	1.0	1.0	0.4890, 0.90 (0.67, 1.22)
Tosylamide/formaldehyde resin, 10.0% pet	5592	0.9	0.7197, 1.08 (0.72, 1.61)	0.9	1.2	0.9	1.0	1.3	0.4801, 0.90 (0.67, 1.21)
Cocamide DEA (coconut diethanolamide), 0.5% pet	5594	0.9	0.9322, 1.02 (0.68, 1.54)	0.9	0.8	0.9	1.2	1.0	0.5138, 0.91 (0.67, 1.24)
DMDM hydantoin (Germall 115), 1.0% pet	5593	0.8	0.2841, 0.80 (0.53, 1.20)	1.0	1.6	1.0	2.7	2.6	0.0000, 0.45 (0.33, 0.61)
Budesonide, 0.1% pet	5593	0.8	0.9109, 0.98 (0.65, 1.48)	0.9	0.8	0.8	0.9	1.5	0.3415, 0.86 (0.63, 1.18)
Lidocaine HCl, 15.0% pet	5593	0.8	0.1681, 0.75 (0.50, 1.13)	1.0	0.8	0.7	0.9	1.1	0.3045, 0.85 (0.61, 1.18)
Chlorhexidine digluconate, 1.0% aq	5594	0.8	—	—	—	—	—	—	—
Carvone, 5.0% pet	5594	0.8	0.6655, 1.10 (0.70, 1.72)	0.7	0.6	1.1	—	—	0.8386, 0.96 (0.67, 1.37)
Tocopherol (DL- α -tocopherol), 100.0%	5590	0.7	0.5818, 1.14 (0.70, 1.85)	0.6	0.7	1.0	1.0	0.7	0.4189, 0.87 (0.61, 1.23)
Disperse blue mix 124/106, 1.0% pet†	5594	0.7	0.1677, 0.75 (0.50, 1.14)	1.0	1.0	1.0	—	—	0.0560, 0.73 (0.52, 1.03)
Mixed dialkyl thioureas, 1.0% pet	5594	0.6	0.0263, 0.62 (0.41, 0.95)	1.0	0.7	1.0	0.9	1.0	0.0199, 0.69 (0.49, 0.98)
Paraben mix, 12.0% pet	5593	0.6	0.9649, 0.99 (0.61, 1.62)	0.6	1.4	0.8	1.1	1.2	0.0007, 0.59 (0.41, 0.84)
Chloroxenol (4-chloro-3,5-xylenol), 1.0% pet	5594	0.6	0.1794, 1.43 (0.84, 2.43)	0.5	0.5	0.5	0.4	0.5	0.1818, 1.32 (0.91, 1.92)
<i>M. piperita</i> oil (peppermint oil), 2.0% pet	5591	0.6	0.8016, 1.07 (0.64, 1.78)	0.6	0.4	0.6	—	—	0.6095, 1.12 (0.74, 1.69)
2-Mercaptobenzothiazole, 1.0% pet	5591	0.5	0.9348, 0.98 (0.57, 1.68)	0.5	0.5	0.7	1.0	0.9	0.0391, 0.69 (0.46, 1.03)
Sesquiterpene lactone mix, 0.1% pet	5595	0.5	0.0143, 0.55 (0.34, 0.89)	0.9	0.7	0.6	0.6	0.7	0.0550, 0.70 (0.47, 1.05)
Parthenolide, 0.1% pet	5594	0.5	0.0352, 0.60 (0.37, 0.97)	0.8	—	—	—	—	0.0352, 0.60 (0.37, 0.97)
<i>L. angustifolia</i> oil (lavender oil), 2.0% pet	5594	0.5	0.2289, 1.44 (0.79, 2.63)	0.3	0.4	0.2	—	—	0.0898, 1.56 (0.97, 2.51)
Benzophenone-3 (oxybenzone or 2-hydroxy-4-methoxy-benzophenone), 10.0% pet	5595	0.4	0.1505, 0.68 (0.40, 1.16)	0.6	0.8	0.9	—	—	0.0028, 0.55 (0.35, 0.86)
Ethylhexylglycerin, 5.0% pet	5595	0.3	0.6901, 1.16 (0.55, 2.45)	0.2	—	—	—	—	0.6901, 1.16 (0.55, 2.45)
Hydroquinone, 1.0% pet	5594	0.3	—	—	—	—	—	—	—
Hydrocortisone-17-butyrate, 1.0% pet	5593	0.2	0.4068, 1.57 (0.53, 4.68)	0.1	0.4	0.7	0.5	0.6	0.0000, 0.35 (0.18, 0.69)
Clobetasol-17-propionate, 1.0% pet	5593	0.2	0.1797, 1.89 (0.72, 4.97)	0.1	0.3	0.3	0.6	0.8	0.0213, 0.57 (0.32, 1.02)
Desoximetasone, 1.0% pet	5588	0.1	0.7763, 1.16 (0.40, 3.34)	0.1	0.2	0.2	0.2	—	0.5524, 0.80 (0.37, 1.73)

*N = number tested to specific allergen;

†09–10 cycle Lanolin alcohol tested at 30% concentration.

‡07–08 cycle tested disperse blue 106 (not the 106/124 mix).

Prevalence Rates for Allergens in the 2015–2016 Period as Compared With 2005–2014

When the positive reaction rates of each allergen in 2015–2016 were compared with the pooled prevalence rates for allergens that had been tested in each 2-year cycle over the previous 10 years (2005–2014), 3 allergens of the top 35 had statistically significantly higher rates in 2015–2016: MCI/MI, cinnamal (cinnamic aldehyde), and ethyl acrylate. In addition, the following 5 allergens that had been added to the screening series at some point in the 2005–2014 period showed statistically higher rates in 2015–2016: MI, formaldehyde 2% aq, PG 100%, HEMA, and decyl glucoside.

A total of 8 allergens that had been tested in each 2-year cycle over the previous 10 years had statistically significantly lower rates in 2015–2016 as compared with the 2005–2014 period: nickel, *M. pereirae*, neomycin, bacitracin, cobalt, quaternium-15, methyl-dibromo glutaronitrile phenoxyethanol, and potassium dichromate. Lanolin alcohol (Amerchol-L101), added in the 2011–2012 cycle, also demonstrated this trend.

Detection Rate of NACDG Screening Series

There were 1262 (22.5%) of 5597 patients who had a relevant allergen not on the NACDG screening series; 11.9% of these non-NACDG allergens were occupationally related ($n = 150$). Specific names of non-NACDG allergens are not collected in the database. The most common sources of non-NACDG allergens were personal care products/cosmetics, medications, and clothing/protective equipment (Table 7).

Hypothetical Detection Rate of the T.R.U.E. Test Versus the NACDG

Screening Series

During this data period, there were 3 distinct allergens on the 36-panel T.R.U.E. Test (SmartPractice Denmark, Hillerød, Denmark) that were not on the NACDG screening series (thimerosal, gold, and quinoline mix). Using a liberal calculation (assuming that individual components of a mix would have been detected with a mix and vice versa; eg, benzocaine, an NACDG allergen, would have been detected by the caine mix of the T.R.U.E. Test; sesquiterpene lactone mix and compositae mix NACDG allergens would have been detected by parthenolide of the T.R.U.E. Test), there were 36

NACDG allergens that would have been theoretically detected by the current 36-panel T.R.U.E. Test. The liberal hypothetical detection rate of the T.R.U.E. Test allergens would be 74.0% (8130/10,983). Using a conservative calculation (assuming that individual components of a mix would not have been detected with a mix and vice versa; eg, MI, an NACDG allergen, would not have been detected by MCI/MI of the T.R.U.E. Test), the conservative hypothetical detection rate of the T.R.U.E. Test allergens would be 61.6% (6764/10,983). Importantly, these calculations do not include the 22.5% of patients who had clinically relevant reactions to allergens not present on the NACDG standard series.

SPINs for NACDG Allergens

The SPIN calculations¹³ and order ranking for this reporting period are listed in Table 8. Significance-prevalence index number is a weighted calculation that for each allergen incorporates a composite measure of clinical relevance combined with prevalence, allowing for the identification of “hot allergens.” It is determined by the following equation: $SPIN = (\text{proportion of population allergic}) \times (1 \times \text{percentage with definite relevance} + 0.66 \times \text{percentage with probable relevance} + 0.33 \times \text{percentage with possible relevance}) \times 100$. For the second consecutive 2-year reporting cycle, MI occupied the no. 1 position.

Past Clinical Relevance

Although the SPIN calculations attempt to reflect current clinical relevance, a number of patients show reactions to allergens that have past clinical relevance (and therefore could have future relevance). Top members in this group include longer-standing allergens that show a high background prevalence but that were not considered part of the main clinical reason for testing. Almost all are in the top 10 most frequently detected allergens. Allergens with positive reactions having a greater than 20% proportion of past relevance and a prevalence greater than 2% are noted in Table 9.

Common Sources of Irritants

Relevant irritants were identified in 1066 patients (19%) (based on clinical examinations and not irritant patch-test reactions). Among the 1066 with relevant irritants, 402 (37.7%) were occupationally related. The most common sources of identified irritants were cosmetic/personal care products (Table 10).

TABLE 7. Five Most Common Sources of Non-NACDG Allergens

Source	No. Patients	% ($n = 1262$)
Cosmetic, beauty preparation, skin, and health care products	592	47.4
Drugs, medications, and alcoholic beverages	275	22.0
Clothing, wearing apparel, protective equipment, and textiles	151	12.1
Animals, infectious agents, plants, minerals, and persons	121	9.7
Chemicals and chemical products	67	5.4

Doubtful Second Reads and Percent Positive Final Interpretations

There were 2423 doubtful second reads, of which 953 (39.3%) had a final interpretation of “allergic.” The top 35 allergens, as ranked by the number of doubtful second reads, and their respective positive final interpretation rates are shown in Table 11.

DISCUSSION

Many of the current findings are consistent with previous NACDG reports. As compared with the last reporting cycle, the individual

TABLE 8. Significance-Prevalence Index Number*

Rank	Patch Test Allergen	SPIN
1	MI, 0.2% aq	685
2	Fragrance mix I, 8.0% pet	436
3	Nickel sulfate hexahydrate, 2.5% pet	392
4	MCI/MI, 0.01% aq = 100 ppm aq	371
5	Formaldehyde, 2.0% aq	290
6	<i>M. pereirae</i> resin (balsam of Peru), 25.0% pet	274
7	Fragrance mix II, 14.0% pet	223
8	4-Phenylenediamine base, 1.0% pet	220
9	Formaldehyde, 1.0% aq	218
10	Propylene glycol, 100%	217
11	Bacitracin, 20.0% pet	175
12	Lanolin alcohol (Amerchol-L101), 50% pet	171
13	Carba mix, 3.0% pet	164
14	Propylene glycol, 30.0% aq	160
15	Cinnamal (cinnamic aldehyde), 1.0% pet	155
16	Iodopropynyl butylcarbamate, 0.5% pet	154
17	Oleamidopropyl dimethylamine, 1.0% aq	120
18	Quaternium-15, 2.0% pet	117
19	Thiuram mix, 1.0% pet	117
20	Neomycin sulfate, 20.0% pet	112
21	Dimethylaminopropylamine, 1.0% aq	104
22	Cobalt chloride hexahydrate, 1.0% pet	103
23	Tixocortol-21-pivalate, 1.0% pet	92
24	2-HEMA, 2.0% pet	91
25	Decyl glucoside, 5.0% pet	90
26	Cocamidopropyl betaine, 1.0% aq	82
27	Methylidibromo glutaronitrile/phenoxyethanol (Euxyl K 400), 2.0% pet	82
28	Diphenylguanidine, 1.0% pet	77
29	Compositae mix, 6.0% pet	66
30	Colophonium (rosin), 20.0% pet	64
31	Propolis, 10.0% pet	61
32	Ethyl acrylate, 0.1% pet	52
33	Amidoamine (stearamidopropyl dimethylamine), 0.1% aq	50
34	Bisphenol A epoxy resin, 1.0% pet	50
35	Ammonium persulfate, 2.5% pet	48
36	<i>M. alternifolia</i> (tea tree leaf oil), oxidized 5.0% pet	47
37	Benzophenone-4, 10.0% pet	46
38	Ylang-ylang oil, 2.0% pet	45
39	Potassium dichromate, 0.25% pet	44
40	Diazolidinyl urea (Germall II), 1.0% pet	44
41	Methyl methacrylate, 2.0% pet	44
42	Imidazolidinyl urea, 2.0% pet	38
43	2-Bromo-2-nitropropane-1,3-diol (bronopol), 0.5% pet	38
44	Cocamide DEA (coconut diethanolamide), 0.5% pet	31
45	Tocopherol (DL- α -tocopherol), 100.0%	31
46	Lidocaine HCl, 15.0% pet	30
47	Benzocaine, 5.0% pet	29
48	Paraben mix, 12.0% pet	28
49	Budesonide, 0.1% pet	28
50	Chloroxylonol (4-chloro-3,5-xylonol), 1.0% pet	26
51	DMDM hydantoin (Germall 115), 1.0% pet	26
52	Mixed dialkyl thioureas, 1.0% pet	25

(Continued on next column)

TABLE 8. (Continued)

Rank	Patch Test Allergen	SPIN
53	<i>M. piperita</i> oil (peppermint oil), 2.0% pet	24
54	4- <i>tert</i> -Butylphenol formaldehyde resin, 1.0% pet	23
55	Carvone, 5.0% pet	21
56	Chlorhexidine digluconate, 1.0% aq	21
57	<i>L. angustifolia</i> oil (lavender oil), 2.0% pet	21
58	Benzophenone-3 (oxybenzone or 2-hydroxy-4-methoxy-benzophenone), 10.0% pet	20
59	Black rubber mix, 0.6% pet	19
60	Disperse blue mix 124/106, 1.0% pet	18
61	Sesquiterpene lactone mix, 0.1% pet	18
62	Ethylenediamine dihydrochloride, 1.0% pet	18
63	2-Mercaptobenzothiazole, 1.0% pet	15
64	Ethylhexylglycerin, 5.0% pet	13
65	Tosylamide/formaldehyde resin, 10.0% pet	12
66	Parthenolide, 0.1% pet	12
67	Clobetasol-17-propionate, 1.0% pet	11
68	Desoximetasone, 1.0% pet	8
69	Hydrocortisone-17-butyrate, 1.0% pet	6
70	Hydroquinone, 1.0% pet	2

*SPIN is a weighted calculation depending on prevalence and degree of certainty ascribed to relevance.¹³ A corrected version is used here: calculation = (proportion of population allergic) $\times$ (1 $\times$ R_{definite} + 0.66 $\times$ R_{probable} + 0.33 $\times$ R_{possible}) $\times$ 100.

components of MOAHLEAP¹⁴ varied by less than 5%. In the last cycle, 31.0% of the patients were positive to 3 or more allergens, as compared with 29.9% in this cycle. Sites of dermatitis and final diagnoses (Table 3) were relatively similar.⁹ The composition of the top 15 most frequently positive allergens included 2 metals (nickel and cobalt), 2 antibiotics (neomycin and bacitracin), 3 fragrances (fragrance mix I, fragrance mix II, and *M. pereirae*), 4 preservatives (MI, MCI/MI, formaldehyde [1% and 2%], and iodopropynyl butylcarbamate), propylene glycol (100%), *p*-phenylenediamine, lanolin alcohol, and carba mix. As compared with the 2013–2014 cycle, only 1 allergen, quaternium-15, dropped out of the top 15.

Methylisothiazolinone entered the standard series in the 2013–2014 cycle at a concentration of 2000 ppm (0.2% aq), initially yielding a 10.9% positivity rate, now rising to 13.4% in this latest reporting period. For the second consecutive cycle, it continues to sit at no. 1 in the SPIN calculations, a positivity score weighted by relevance, indicating the current importance of including it in any standard screening series. Methylisothiazolinone's SPIN in this 2015–2016 cycle is the highest ever recorded by the NACDG and is more than 50% higher than the no. 2 allergen. Previously, the concentration of MI in the MCI/MI patch test mix was only 25 ppm. Testing MI alone at a higher concentration enabled the detection of contact allergy more reliably. Prospective and retrospective patch-test prevalence studies from a variety of patch test settings have underlined MI's high sensitization rate across different populations.^{15,16} The NACDG has provided an in-depth report and analysis of MI sensitization in North America based on cumulative data from January 1, 2013, to December 31, 2014.¹⁷

TABLE 9. Past Clinical Relevance*

Allergen	Past Clinical Relevance, %	Current Prevalence, %
Neomycin sulfate, 20.0% pet	42.1	7.0
Nickel sulfate hexahydrate, 2.5% pet	37.6	17.5
Cobalt chloride hexahydrate, 1.0% pet	35.7	6.2
Bacitracin, 20.0% pet	31.6	6.9
Colophonium (rosin), 20.0% pet	25.0	2.5
4-Phenylenediamine base, 1.0% pet	23.3	6.4

*Past relevance > 20% and prevalence > 2%.

In September 2014, the European Commission initiated a ban of MCI/MI from leave-on products and restricted its concentration when used as a preservative up to a maximum authorized concentration of 0.0015% in rinse-off cosmetic products.¹⁸ This was followed by a ban of MI in leave-on products in July 2016.¹⁹ A report from the United Kingdom provides preliminary evidence that these restrictions are having their intended effect, with the incidence of patch test positivity declining between 2014 and 2015 for both MI 0.02% aq (9.1%–4.8%) and MCI/MI 0.02% aq (7.9%–3.9%).²⁰

In the 2013–2014 reporting cycle, MCI/MI 0.01% aq was the only allergen that was tested in each cycle from 2005 to 2014 that showed a statistically significant increase in rates from both the previous reporting cycle (2011–2012) and the pooled rates from the previous 10 years (2005–2014; risk ratios [RRs], 1.26 and 2.08, respectively). The doubling of positive reactions to MCI/MI was consistent with the epidemic of allergy to this preservative that has been seen in Europe. Its continued rise in the 2015–2016 cycle from 6.3% to 7.3% may, in part, be due to stronger concomitant reactions noted to MI, allowing for perhaps a more liberal interpretation of weak reactions to MCI/MI, and to the increased use of MI in personal care products during this recent period.

Nickel sulfate retained its position as the most commonly positive allergen in the screening series, reaching a prevalence of 17.5%. Despite being lower than the previous 2 cycles, its level matches the average prevalence in NACDG patch-test data for nickel between 1994 and 2014.²¹ Although nickel is no. 3 in terms of its composite score of prevalence and current clinical significance (ie, SPIN), its total impact should be considered in the context of its high past clinical significance (37.6%) and its varied potential routes of exposure including direct contact, airborne, dietary, and through medical implantation. There remains a strong case for North American countries to follow the lead of the European Union and institute regulations limiting the levels of leachable nickel in items that are likely to have prolonged direct skin contact.

Propylene glycol 100% aq was added to the screening series on the basis of the collective experience of some NACDG members who had found a higher rate of bona fide positive reactions without a significant increase in irritancy. Propylene glycol 100% has shown a relatively low irritancy rate of 1.4% (as compared with 0.7% with the 30% aq concentration).²² In addition, the 2 concentrations were noted in 2015–2016 to have a similar number of doubtful/equivocal

patch-test reactions, whereas PG 100% has been clearly more effective at discerning positive and relevant positive reactions (4.0% vs 2.8%; SPIN, 217 vs 160). In view of the performance of PG 100%, PG 30% was assigned for deletion from the standard series for the NACDG 2017–2018 cycle. One caveat is that, with PG, the possibility of a subsequent negative usage test should always be kept in mind.²³

Formaldehyde 2% aq has been shown in the last 2 cycles and in other jurisdictions to be a worthy screen for formaldehyde with little sacrifice of increased irritancy.^{9,24,25} The NACDG data for the 2015–2016 cycle showed an 8.4% positivity rate for formaldehyde 2% compared with 6.4% for formaldehyde 1%, with a SPIN of 280 versus 218. In this current cycle, formaldehyde 2% yielded 233 (49.5%) of 470 positive reactions read as 2+ or 3+ as compared with formaldehyde 1%, 149/299 (49.8%), for a surfeit of 84 strongly positive reactions, despite an equal proportion of these stronger patch-test reactions. With respect to doubtful second reads, formaldehyde 2% was given an “allergic” interpretation in 19.6% (19 patients), whereas formaldehyde 1% had 40% of doubtful reads (32 patients) interpreted as “allergic.” The NACDG members noted that a clear positive reaction to the 2% formulation allowed for a more liberal interpretation of the 1% concentration. On balance, the utility of testing formaldehyde at 1% aq in addition to 2% aq was determined to be low. Therefore, the 1% concentration will not be included in the 2019–2020 series.

The International Agency for Research on Cancer, a special agency of the World Health Organization, classified formaldehyde as a human carcinogen in 2004, and in 2011, the US Department of Health and Human Services named formaldehyde as a known human carcinogen in its *12th Report on Carcinogens*.²⁶

Although these agencies did not specifically mention formaldehyde-releasing preservatives, several large companies have eliminated this group of preservatives from their products.²⁷ This may account for the observed statistically significant decreases in rates from both the previous reporting cycle (2013–2014) and the pooled rates from the previous 10 years (2005–2014) for the following 3 formaldehyde-releasing preservatives: quaternium-15 (RRs, 0.62 and 0.44), 2-bromo-2-nitro-1,3-propanediol (bronopol) (RRs, 0.47 and 0.45), and imidazolidinyl urea (RRs, 0.48 and 0.37). As part of this downward trend since 2005, dimethylol dimethyl (DMDM) hydantoin (0.33)

TABLE 10. Five Most Common Sources of Irritants

Source	No. Patients (N = 1066)	%
Cosmetic, beauty preparation, skin, and health care products	259	24.3
Animals, infectious agents, plants, minerals, and persons	244	22.9
Sewage, waste, debris, environmental, and miscellaneous consumer	112	10.5
Chemicals and chemical products	106	9.9
Soaps, detergents, cleansers, disinfectants, and laundry aids (non skin)	93	8.7

TABLE 11. Doubtful Second Reads and % Positive Final Interpretations*

Allergen	Doubtful Second Read	+ Final Interpretation	%
Iodopropynyl butylcarbamate, 0.5% pet	158	42	26.6
Fragrance mix, 8.0% pet	133	57	42.9
<i>M. pereirae</i> resin (balsam of Peru), 25.0% pet	126	54	42.9
Methyldibromo glutaronitrile/phenoxyethanol (Euxyl K 400), 2.0% pet	105	16	15.2
Formaldehyde, 2.0% aq	97	19	19.6
PG, 100%	84	19	22.6
Formaldehyde, 1.0% aq	80	32	40.0
PG, 30.0% aq	78	35	44.9
MI, 0.2% aq	78	55	70.5
Carba mix, 3.0% pet	76	26	34.2
Fragrance mix II, 14.0% pet	75	29	38.7
Neomycin sulfate, 20.0% pet	75	52	69.3
Oleamidopropyl dimethylamine, 1.0% aq	73	19	26.0
Nickel sulfate hexahydrate, 2.5% pet	72	50	69.4
Cocamidopropyl betaine, 1.0% aq	70	26	37.1
Lanolin alcohol (Amerchol-L101), 50% pet	62	44	71.0
Diphenylguanidine, 1.0% pet	57	10	17.5
Cinnamal (cinnamic aldehyde), 1.0% pet	56	33	58.9
Amidoamine (stearamidopropyl dimethylamine), 0.1% aq	55	24	43.6
Benzophenone-4, 10% pet	54	11	20.4
Cobalt (II) chloride hexahydrate, 1.0% pet	41	10	24.4
Compositae mix, 6.0% pet	37	10	27.0
Decyl glucoside, 5.0% pet	37	17	45.9
Ammonium persulfate, 2.5% pet	34	4	11.8
Dimethylaminopropylamine, 1.0% aq	32	17	53.1
Bacitracin, 20.0% pet	30	20	66.7
MCI/MI, 0.01% aq	30	25	83.3
4-Phenylenediamine base, 1.0% pet	29	11	37.9
Potassium dichromate, 0.25% pet	28	1	3.6
Propolis, 10.0% pet	28	12	42.9
Colophonium (rosin), 20.0% pet	24	8	33.3
Tocopherol (DL- α -tocopherol), 100.0%	22	8	36.4
Thiuram max, 1.0% pet	18	11	61.1
Quaternium-15, 2.0% pet	18	14	77.8
Chlorhexidine digluconate, 1.0% aq	18	8	44.4

*Lists the most frequent 35 allergens with doubtful second reads.

and diazolidinyl urea (0.37) also showed significantly decreased rates compared with their respective pooled 10-year rates. Considering this trend, it is not always obvious from where the positive patch-test reactions to formaldehyde originate—formaldehyde itself is on very few labels and Material Safety Data Sheets.

Similarly, paraben mix showed a statistically significant decrease in its patch test positivity rate in the 2015–2016 cycle as compared with the 2005–2014 period (RR, 0.59; confidence interval [CI], 0.41–0.84). Parabens are some of the most commonly used preservatives in personal care products. They continue to show the lowest prevalence of positivity (0.6%) of any major preservative on the North American market and, from a contact allergy perspective, are one of the safest groups of preservatives. It has been suggested that the low prevalence of contact allergy to parabens can, in part, be attributed to industry decreasing its use in cosmetic/personal care

products. Interestingly, though, a review of its use in North America shows that more than 10,000 cosmetic/personal care products still contain either methyl paraben, propyl paraben, or both.²⁸ In contrast, a similar review shows that MI is a constituent in less than 2000 such products.²⁹

However, as documented by our data, the use of other preservatives in North America, especially MI, in place of formaldehyde-releasing preservatives and parabens, will continue to impact contact sensitivity rates.

In the 2013–2014 reporting period, HEMA was identified correctly as an allergen that could continue to rise in importance in the future because of increased consumer exposure. In the 2015–2016 cycle, there was a statistically significant increase in prevalence rates from both the previous reporting cycle (3.4%; RR, 1.24; CI, 1.00–1.54) and the pooled rate from the previous 8 years (2007–2014; RR, 1.46; CI, 1.23–1.73).

The source of HEMA-positive patch tests was determined in 69 (63.6%) of 107 patients to be artificial nails (50), nail care products (7), nail polish (7), and nail adhesives (4). At this point, SPIN for HEMA is at 91, but its detection is rising worldwide.

Methacrylates have been identified in North America²² and internationally as an important contact sensitizer in the nail aesthetic industry, and consumers are increasingly being recognized as an at-risk group.^{30–34} In 2017, estimated annual industry statistics indicate that US \$8.53 billion were spent in nail salons in the United States, with more than 56,000 nail salons in operation.³⁵ The North American experience is part of an international phenomenon with billions of dollars being spent in each of multiple jurisdictions such as Germany, Mexico/Central America/South America, Japan, South Africa, India, and Russia.³⁵

Methacrylates are key components in both “gel” nails and “shellac” nail polish, including some home-applied preparations. Ultraviolet curing nail polish available for home use has extended the risk of sensitization.^{36,37} The health implications are of concern, given the use of methacrylates in surgical and dental procedures.

Mild and doubtful reactions are often nonreproducible,³⁸ and differentiation of irritant from allergic reactions is difficult. Our group attempts to discern this through a final interpretation of all reactions as positive, negative, or irritant. For example, a doubtful reaction to fragrance mix I may be determined to be positive on the basis of the patient's reactivity to multiple other fragrance allergens. However, preparations with high mild and doubtful reaction rates often represent “problematic” preparations.³⁹

Herein, we report only the reaction strength of positive reactions. However, using a crude cutoff of 50% or greater for positive reactions graded as doubtful or mild, 47 of the 70 NACDG standard allergens would fall into this category. Although some of these may be due to late reactions often doubtful or mild at the final reading (eg, neomycin, corticosteroids), others warrant careful interpretation. Patch-test reactions determined to be doubtful yet interpreted as allergic can clearly have an impact on final reported results.

There were 2423 doubtful second reads, of which 953 (39.3%) had a final interpretation of “allergic.” Looking at the impact of these doubtful reactions, 8.7% (953/10,983) of the total number of reactions in the 2015–2016 cycle were read as doubtful yet interpreted as “allergic.” Of the top 15 allergens based on the number of doubtful reads, the following had at least 50% of their doubtful reads interpreted as allergic: MI (70.5% [55 patients]), neomycin (69.3% [52 patients]), and nickel (69.4% [50 patients]). The past “reputation” and/or specific characteristics of an allergen may influence final interpretations, for example, MI and nickel having the highest SPIN in the previous 2013–2014 cycle and neomycin being well known for late positive reactions.

Hypothetically, T.R.U.E. Test would have detected 61.6% to 74.0% of reactions found by the NACDG screening series during this data period. Of the top 40 NACDG allergens, the following are not on the T.R.U.E. Test: MI, fragrance mix II, iodopropynyl butylcarbamate, PG, oleamidopropyl dimethylamine, HEMA, dimethylaminopropylamine, propolis, decyl glucoside, ammonium

persulfate, benzophenone-4, ethyl acrylate, cocamidopropyl betaine, methyl methacrylate, and amidoamine. Although not represented in the top 40, other potentially important non-T.R.U.E. Test allergens include ylang-ylang oil, *Melaleuca alternifolia* (tea tree oil), cocamide diethanolamine (DEA), tosylamide formaldehyde resin, lidocaine, mixed dialkyl thioureas, and benzophenone-3.

A customizable screening series such as the NACDG-70 allows for the flexibility of adding or subtracting allergens on an ongoing basis after a careful analysis of current and emerging trends in contact allergy. The NACDG allergens are added and deleted on the basis of new data in the literature and member experience testing with additional allergens. Twenty-three percent of the patients tested during this data period had at least 1 currently relevant reaction to a non-NACDG antigen. This underscores the importance of testing supplemental antigens, personal products, and workplace materials. The American Contact Dermatitis Society recommends a screening panel of 80 allergens,^{40,41} but the current data suggest that even this number may not be sufficient to adequately screen a significant percentage of patients.

Limitations of this study include the following:

- The NACDG data represent a largely referral patient group and thus do not reflect the general population or general dermatology patients.
- Patch testing is both a science and a learned art. Distinctions between positive and irritant reactions, occupational relevance, clinical relevance source codes, and other collected variables are standardized wherever possible. However, relevance judgments are just that—judgments—with minimal data on clinical follow-up and few confirming usage tests.
- The NACDG does not collect data on non-NACDG allergens other than presence and source.
- Although the composition of the group remained the same as the previous cycle, there were some changes in practices (varying patient numbers and changes in practice locations); therefore, comparisons to previous cycles could reflect these changes and not true changes in prevalence rates.

CONCLUSIONS

Appropriate history, skin examination, and patch testing can lead to significant benefits in the diagnosis and management of care for patients with dermatitis. Patch testing remains a critical diagnostic tool. This latest NACDG data summary for 2015–2016 adds to the references available on emerging trends and patterns in the field.

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