

North American Contact Dermatitis Group Patch Test Results: 2011–2012

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

Objective: This study documents the North American Contact Dermatitis Group (NACDG) patch-testing results from January 1, 2011, to December 31, 2012.

Methods: At 12 centers in North America, patients were tested in a standardized manner with a series of 70 allergens. Data were manually verified and entered into a central database. Descriptive frequencies were calculated, and trends analyzed using χ^2 statistics.

Results: Four thousand two hundred thirty-eight patients were tested; of these, 2705 patients (63.8%) had at least 1 positive reaction, and 2029 (48.0%) were ultimately determined to have a primary diagnosis of ACD. Four hundred eight patients (9.6%) had occupationally related skin disease. There were 7532 positive allergic reactions. As compared with previous reporting periods (2009–2010 and 2000–2010), positive reaction rates statistically increased for 6 allergens: methylchloroisothiazolinone/methylisothiazolinone (5.0%; risk ratios [RRs]: 2.01 [1.60–2.52], 1.87 [1.61–2.18]), lanolin alcohol (4.6%; RRs 1.83 [1.45–2.30], 2.10 [1.79–2.47]), cinnamic aldehyde (3.9%; 1.69 [1.32–2.15], 1.53 [1.28–1.82]), glutaral (1.5%; 1.67 [1.13–2.48], 1.31 [1.00–1.71]), paraben mix (1.4%; 1.77 [1.16–2.69], 1.44 [1.09–1.92]), and fragrance mix I (12.1%; RRs 1.42 [1.25–1.61], 1.24 [1.14–1.36]). Compared with the previous decade, positivity rates for all formaldehyde-releasing preservatives significantly decreased (formaldehyde 6.6%; RR, 0.82 [0.73, 0.93]; quaternium-15 6.4% RR 0.75 [0.66, 0.85]; diazolidinyl urea 2.1%; RR, 0.67 [0.54, 0.84]; imidazolidinyl urea 1.6%, 0.60 [0.47, 0.77]; bronopol 1.6%; RR, 0.60 [0.46, 0.77]; DMDM hydantoin 1.6%; RR, 0.59 [0.54, 0.84]). Approximately a quarter of patients had at least 1 relevant allergic reaction to a non-NACDG allergen. In addition, approximately one-fourth to one-third of reactions detected by NACDG allergens would have been hypothetically missed by T.R.U.E. TEST (SmartPractice Denmark, Hillerød, Denmark).

Conclusions: These data document the beginning of the epidemic of sensitivity to methylisothiazolinones in North America, which has been well documented in Europe. Patch testing with allergens beyond a standard screening tray is necessary for complete evaluation of occupational and nonoccupational ACD.

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The North American Contact Dermatitis Group (NACDG) is a group of dermatologists in Canada and United States who evaluate patients with suspected allergic contact dermatitis (ACD) utilizing a standardized set of allergens. Composition of the NACDG “screening series” changes slightly every biyearly cycle. Periodically, these epidemiologic data are published.^{1–11} This article summarizes results from the 2011–2012 cycle.

METHODS AND MATERIALS

Between January 1, 2011, and December 31, 2012, the NACDG consisted of 12 dermatologists practicing in North America. Patients were patch tested with a screening series of 70 allergens (allergEAZE SmartPractice, Calgary, Alberta, Canada). Most recent reports^{10,11} comprehensively described data collection methods that remain unchanged for this reporting cycle. Briefly, patch testing

TABLE 1. MOAHLFAP¹⁶ Characteristics

Characteristic	n (%)
Male	1329 (31.4)
Occupational*	408 (9.6)
Atopic triad	
Hayfever†	1274 (30.1)
Atopic dermatitis	1188 (28.0)
Asthma‡	702 (16.6)
Hand‡	815 (19.2)
Leg‡	166 (3.9)
Face‡	681 (16.1)
Age >40 y	2848 (67.3)
Positivity rate (>1 allergic reaction)	2705 (63.8)

*Excludes uncertain.

†Not part of MOAHLFAP¹⁶ (male, occupational, atopic, hand, leg, foot, age >40 y, percent positive).

‡Primary site; when primary sites of lips, nose, eyelids, and eyes are added to face, total for face = 1293 (30.5%).

was performed with a standardized technique using Finn chambers (SmartPractice, Phoenix, Ariz) on Scanpor tape (Norgesplaster Alpha AS, Vennesla, Norway). At the first and second readings, patch tests were graded as +/– (weak/doubtful), + (mild), ++ (strong), or +++ (very strong) based on degree of induration, presence of papules/vesicles, and/or a spreading reaction. Final determination of “allergic/positive” or “not allergic” was determined by investigators based on the patch-test morphology, the reaction time pattern (crescendo/decrecendo), 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.

Clinical relevance of positive patch-test reactions was determined using the patient's history and clinical skin examination. *Current* relevance was defined as *definite* (use test with the suspected item was positive, or a patch test to the object or product was positive), *probable* (the antigen could be verified as present in known skin contactants and clinical presentation was consistent), or *possible* (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, source of antigen exposure was coded using a 3-digit code.¹² Occupation and industry were coded by an occupational expert using the US 2000 Census Bureau Codes based on answers to 5 standardized questions collected for each patient.¹³ 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, Wash). Analyses were performed using SAS 9.2 (Statistical Analysis

System, SAS Institute Incorporated, Cary, NC) and according to recommended guidelines.¹⁴ Pearson χ^2 test was used to compare frequencies between time periods. A significance level of 0.05 was utilized for all analyses. Because this was an exploratory analysis, no adjustments for multiple comparisons were performed. Significance-Prevalence Index Numbers (SPIN; prevalence weighted by relevance)¹⁵ were calculated as in the last report.¹¹ Demographic data were displayed according to MOAHLFAP guidelines.^{14,16}

During this period, the NACDG screening tray consisted of 70 allergens/allergen mixes. Compared with the previous period (2009–2010; 70 allergens), there were several changes: (1) the concentration of lanolin alcohol was increased from 30% to 50%; (2) glycerol thioglycolate and dimethylol dihydroxyethyleneurea were removed; (3) carmine 2.5% pet and ethyl 2-cyanoacrylate 10% pet were added; and (4) the vehicle for hydrocortisone 7-butyrate was changed from alcohol to petrolatum.

RESULTS

Patient Characteristics

Demographics are summarized in Tables 1, 2, and 3. Most were white (85.2%) and female (68.6%). Average age was 48 years (range, 2–97 years; median, 50 years). Most common body locations were scattered/generalized pattern, hands, and face. Of the 4238 patients tested, 63.7% (n = 2705) had at least 1 positive reaction, and 26.9% (n = 1139) were polysensitized (≥ 3 allergic reactions¹⁷; Table 4); 48.0% had a final primary diagnosis of ACD.

Occupation

Data on occupation were available for 4095, with 41.0% (n = 1602) of these not working (Table 2). Among all patients, 9.6% (n = 408) had dermatitis determined to be related to their occupation (Table 1). Of the 873 patients who had a relevant irritant identified, 38.3% (n = 334) were deemed occupationally related. Of the 1100

TABLE 2. Race and Occupation of Patch-Tested Patients

Characteristic	n (%)
Race (n = 4238)	
White	3612 (85.2)
Black	223 (5.3)
Asiatic	183 (4.3)
Other/not specified	133 (3.1)
Hispanic	87 (2.1)
Occupation (n = 4095*)	
Not working†	1680 (41.0)
Managerial or professional	1175 (28.7)
Technical, sales, administrative support	563 (13.7)
Service	292 (7.1)

*Excludes 143 individuals missing industry/occupation codes.

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

TABLE 3. Body Sites of Dermatitis and Final Diagnoses

Characteristic	Primary, n (%)	Total of Up to 3 Listed,* n (%)†
Dermatitis site‡	n = 4235*	n = 4238
Scattered/generalized	830 (19.6)	1011 (23.9)
Hand	815 (19.2)	993 (23.4)
Face	681 (16.1)	1022 (24.1)
Eyelids	442 (10.4)	580 (13.7)
Trunk	262 (6.1)	585 (13.8)
Arm	218 (5.1)	689 (16.3)
Leg	166 (3.9)	467 (11.0)
Scalp	165 (3.9)	256 (6.0)
Lips	158 (3.7)	215 (5.1)
Foot	113 (2.7)	267 (6.3)
Other	109 (2.6)	120 (2.8)
Anal/genital	78 (1.8)	118 (2.8)
Neck	74 (1.7)	416 (9.8)
Ears	53 (1.3)	100 (2.4)
Most exposed areas	45 (1.1)	61 (1.4)
Only under clothes	14 (0.3)	17 (0.4)
Eyes	10 (0.2)	19 (0.4)
Nose	2 (0.0)	5 (0.1)
Final diagnoses	n = 4224§	n = 4238
ACD	2029 (48.0)	2456 (58.0)
Atopic dermatitis	652 (15.4)	876 (20.7)
Other dermatitis	465 (11.0)	549 (13.0)
Irritant contact dermatitis	369 (8.7)	651 (15.4)
Other dermatoses	318 (7.5)	428 (10.1)
Psoriasis	162 (3.8)	237 (5.6)
Seborrheic dermatitis	70 (1.7)	91 (2.1)
Nummular dermatitis	63 (1.5)	90 (2.1)
Photo dermatitis	31 (0.7)	54 (1.3)
Contact urticaria	31 (0.7)	45 (1.1)
Pompholyx	22 (0.5)	26 (0.6)
Stasis dermatitis	12 (0.3)	22 (0.5)

*Excludes 3 patients with no primary site listed.

†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 14 patients with no primary final diagnosis.

patients who had relevant non-NACDG allergens identified, 13.1% (n = 144) were related to their occupation.

Allergen Frequencies

There were 7532 positive allergic reactions. The top 10 most frequent allergens (with their respective prevalence rates) were nickel sulfate (18.5%), fragrance mix I (12.1%), neomycin (9.1%), *Myroxylon perei* (7.9%), bacitracin (7.8%), cobalt chloride (7.3%), formaldehyde (6.6%), quaternium-15 (6.4%), p-phenylenediamine (6.3%), and fragrance mix II (5.2%). Rates for the new allergens/concentration changes/vehicle changes, in order of frequency, were as follows: lanolin alcohol (4.6%), carmine (3.1%), and ethyl-2-cyanoacrylate (0.3%) and hydrocortisone-17-butyrate (0.3%) (Table 5).

Allergen Prevalence Rates in the 2011–2012 Period Compared with 2009–2010

As shown in Table 6, the positive reaction rates significantly (or borderline significantly) increased for 13 allergens (nickel, fragrance mix I, cobalt, methylchlorisothiazolinone/methylisothiazolinone, lanolin, cinnamic aldehyde, bronopol, dimethylol dimethyl (DMDM) hydantoin, glutaral, paraben mix, black rubber mix, amidoamine, and dibucaine) and significantly decreased for 6 allergens (imidazolidinyl urea, potassium dichromate, ylang ylang oil, mercaptobenzothiazole, jasmine oil, and hydrocortisone-17 butyrate).

Allergen Prevalence Rates in the 2011–2012 Period Compared with 2001–2010

When the positive reaction rates of each antigen in 2011–2012 were compared with the pooled prevalence rates for the previous decade (2001–2010), 10 allergens had statistically significantly higher rates in 2011–2012 (fragrance mix I, p-phenylenediamine, fragrance mix II, methylchlorisothiazolinone/methylisothiazolinone, lanolin alcohol, iodopropynyl butylcarbamate, cinnamic aldehyde, Compositae mix, glutaral, and paraben mix). Twenty-one had statistically lower rates in 2011–2012 (neomycin, *M. perei*, formaldehyde, quaternium-15, methylidibromoglutaronitrile/pheonxyethanol, thiuram mix, diazolidinyl urea, propolis, imidazolidinyl urea, potassium dichromate, bronopol, DMDM hydantoin, ethylenediamine, amidoamine, p-tert butylphenol formaldehyde resin, disperse blue mix 106/124, methyl methacrylate, budesonide, ylang ylang oil, mercaptobenzothiazole, and clobetasol).

Detection Rate of NACDG Screening Series

One thousand one hundred ten (26.2%) of 4238 patients had a relevant allergen not on the screening series; 13% of these non-NACDG allergens were occupationally related (n = 144). Specific names of non-NACDG allergens are not collected in the database. Most common sources of non-NACDG allergens were personal care products, medications, and clothing (Table 7).

TABLE 4. Number of Positive Patch Test Reactions per Patient

No. Positive Reactions to NACDG Screening Allergens	No. Patients	Percentage (n = 4238)
0	1544	36.2
1	880	20.8
2	686	16.2
3	447	10.5
4	265	6.3
5	154	3.6
6	96	2.3
7	68	1.6
8	38	0.9
9	28	0.7
>10	43	1.0

TABLE 5. Positive Reactions

Substance	n	Positive Reactions	Second Read Code* (%)				Relevance (%)			
			+++	++	+	+/-	Definite	Probable	Possible	Past
Nickel sulfate hexahydrate 2.5% pet.	4224	781	232 (29.7)	276 (35.3)	252 (32.3)	18 (2.3)	20 (2.6)	158 (20.2)	332 (42.5)	191 (24.5)
Fragrance mix 8.0% pet.	4232	511	95 (18.6)	140 (27.4)	216 (42.3)	59 (11.5)	12 (2.3)	152 (29.7)	309 (60.5)	11 (2.2)
Neomycin sulfate 20.0% pet.	4229	384	70 (18.2)	94 (24.5)	181 (47.1)	38 (9.9)	14 (3.6)	48 (12.5)	34 (8.9)	233 (60.7)
<i>M. pereirae</i> resin (balsam of Peru) 25.0% pet.	4234	333	37 (11.1)	64 (19.2)	168 (50.5)	63 (18.9)	3 (0.9)	122 (36.6)	173 (52.0)	9 (2.7)
Bacitracin 20.0% pet.	4234	330	97 (29.4)	99 (30.0)	112 (33.9)	21 (6.4)	30 (9.1)	70 (21.2)	38 (11.5)	140 (42.4)
Cobalt (ii) chloride hexahydrate 1.0% pet.	4231	310	91 (29.4)	86 (27.7)	115 (37.1)	15 (4.8)	3 (1.0)	31 (10.0)	133 (42.9)	61 (19.7)
Formaldehyde 1.0% aq.	4237	278	27 (9.7)	96 (34.5)	122 (43.9)	32 (11.5)	3 (1.1)	59 (21.2)	192 (69.1)	11 (4.0)
Quaternium-15 2.0% pet.	4235	273	56 (20.5)	79 (28.9)	111 (40.7)	26 (9.5)	3 (1.1)	72 (26.4)	178 (65.2)	14 (5.1)
4-Phenylenediamine base 1.0% pet.	4223	267	109 (40.8)	44 (16.5)	92 (34.5)	21 (7.9)	9 (3.4)	124 (46.4)	52 (19.5)	50 (18.7)
Fragrance mix II 14.0% pet.	4237	219	17 (7.8)	42 (19.2)	124 (56.6)	35 (16.0)	5 (2.3)	79 (36.1)	122 (55.7)	3 (1.4)
Methylchloroisothiazolinone/methylisothiazolinone 0.01% aq. = 100 ppm aq.	4227	213	28 (13.1)	77 (36.2)	94 (44.1)	14 (6.6)	21 (9.9)	110 (51.6)	68 (31.9)	7 (3.3)
Carba mix 3.0% pet.	4236	201	9 (4.5)	50 (24.9)	114 (56.7)	28 (13.9)	12 (6.0)	62 (30.8)	92 (45.8)	10 (5.0)
Lanolin alcohol (Amerchol L 101) 50% pet.	4235	194	15 (7.7)	43 (22.2)	103 (53.1)	31 (16.0)	11 (5.7)	79 (40.7)	85 (43.8)	7 (3.6)
Iodopropyl butylcarbamate 0.5% pet.	4231	178	7 (3.9)	32 (18.0)	95 (53.4)	44 (24.7)	5 (2.8)	66 (37.1)	90 (50.6)	4 (2.2)
Cinnamal (cinnamic aldehyde) 1.0% pet.	4231	164	12 (7.3)	48 (29.3)	90 (54.9)	13 (7.9)	3 (1.8)	52 (31.7)	101 (61.6)	0 (0.0)
Methyldibromo glutaronitrile/phenoxyethanol 2.0% pet.	4231	157	7 (4.5)	40 (25.5)	89 (56.7)	21 (13.4)	1 (0.6)	40 (25.5)	92 (58.6)	7 (4.5)
Carmine 2.5% pet.	4230	131	1 (0.8)	38 (29.0)	84 (64.1)	7 (5.3)	2 (1.5)	18 (13.7)	51 (38.9)	13 (9.9)
Thiuram mix 1.0% pet.	4236	121	36 (29.8)	30 (24.8)	45 (37.2)	10 (8.3)	7 (5.8)	44 (36.4)	49 (40.5)	9 (7.4)
Propylene glycol 30.0% aq.	4232	112	4 (3.6)	16 (14.3)	68 (60.7)	22 (19.6)	14 (12.5)	51 (45.5)	40 (35.7)	2 (1.8)
Tixocortol-21-pivalate 1.0% pet.	4230	99	29 (29.3)	35 (35.4)	28 (28.3)	6 (6.1)	7 (7.1)	47 (47.5)	18 (18.2)	21 (21.2)
Oleamidopropyl betaine 1.0% aq.	4231	98	4 (4.1)	25 (25.5)	61 (62.2)	8 (8.2)	2 (2.0)	23 (23.5)	58 (59.2)	2 (2.0)
Colophonium (rosin) 20.0% pet.	4236	96	39 (40.6)	22 (22.9)	31 (32.3)	4 (4.2)	2 (2.1)	19 (19.8)	37 (38.5)	24 (25.0)
Diazolidinyl urea 1.0% pet.	4232	90	5 (5.6)	23 (25.6)	53 (58.9)	9 (10.0)	7 (7.8)	23 (25.6)	56 (62.2)	2 (2.2)
2-Hydroxyethyl methacrylate 2.0% pet.	4230	83	27 (32.5)	31 (37.3)	22 (26.5)	3 (3.6)	1 (1.2)	27 (32.5)	23 (27.7)	22 (26.5)
Compositae mix 6.0% pet.	4231	81	8 (9.9)	20 (24.7)	47 (58.0)	6 (7.4)	2 (2.5)	11 (13.6)	32 (39.5)	4 (4.9)
Propolis 10.0% pet.	4231	76	9 (11.8)	27 (35.5)	38 (50.0)	2 (2.6)	2 (2.6)	13 (17.1)	37 (48.7)	3 (3.9)
Imidazolidinyl urea 2.0% pet.	4232	69	5 (7.2)	19 (27.5)	41 (59.4)	4 (5.8)	2 (2.9)	18 (26.1)	46 (66.7)	1 (1.4)
Potassium dichromate 0.25% pet.	4235	68	15 (22.1)	18 (26.5)	33 (48.5)	2 (2.9)	0 (0.0)	13 (19.1)	28 (41.2)	7 (10.3)
2-Bromo-2-nitropropane-1,3-diol (bronopol) 0.5% pet.	4231	67	13 (19.4)	22 (32.8)	24 (35.8)	7 (10.4)	3 (4.5)	24 (35.8)	31 (46.3)	4 (6.0)
DMDM hydantoin 1.0% pet.	4232	67	3 (4.5)	16 (23.9)	40 (59.7)	8 (11.9)	5 (7.5)	28 (41.8)	29 (43.3)	2 (3.0)
Decyl glucoside 5.0% pet.	4231	66	7 (10.6)	15 (22.7)	33 (50.0)	11 (16.7)	3 (4.5)	10 (15.2)	18 (27.3)	10 (15.2)
Shellac 20.0% alc	4231	66	7 (10.6)	10 (15.2)	41 (62.1)	8 (12.1)	4 (6.1)	19 (28.8)	28 (42.4)	4 (6.1)
Glutaral 1.0% pet.	4213	64	12 (18.8)	23 (35.9)	22 (34.4)	5 (7.8)	2 (3.1)	9 (14.1)	10 (15.6)	10 (15.6)
Dimethylaminopropylamine 1.0% aq.	4233	62	10 (16.1)	16 (25.8)	31 (50.0)	4 (6.5)	1 (1.6)	27 (43.5)	30 (48.4)	1 (1.6)
Bisphenol A epoxy resin 1.0% pet.	4235	62	18 (29.0)	24 (38.7)	19 (30.6)	1 (1.6)	4 (6.5)	19 (30.6)	8 (12.9)	15 (24.2)
Cocamidopropyl betaine 1.0% aq.	4232	61	0 (0.0)	12 (19.7)	33 (54.1)	16 (26.2)	2 (3.3)	40 (65.6)	18 (29.5)	0 (0.0)
Benzocaine 5.0% pet.	4236	60	18 (30.0)	13 (21.7)	24 (40.0)	4 (6.7)	3 (5.0)	9 (15.0)	4 (6.7)	24 (40.0)
Paraben mix 12.0% pet.	4231	59	11 (18.6)	13 (22.0)	25 (42.4)	10 (16.9)	7 (11.9)	36 (61.0)	13 (22.0)	1 (1.7)
Ethylenediamine dihydrochloride 1.0% pet.	4232	56	18 (32.1)	22 (39.3)	13 (23.2)	2 (3.6)	1 (1.8)	7 (12.5)	11 (19.6)	17 (30.4)
Majantol 5.0% pet.	4231	53	13 (24.5)	7 (13.2)	28 (52.8)	4 (7.5)	0 (0.0)	10 (18.9)	32 (60.4)	3 (5.7)
Black rubber mix pet. 0.6%	4236	53	16 (30.2)	15 (28.3)	19 (35.8)	2 (3.8)	2 (3.8)	11 (20.8)	16 (30.2)	7 (13.2)
Tosylamide/formaldehyde resin 10.0% pet.	4232	52	5 (9.6)	16 (30.8)	30 (57.7)	1 (1.9)	3 (5.8)	12 (23.1)	12 (23.1)	9 (17.3)
Amidoamine (stearamidopropyl dimethylamine) 0.01% aq.	4231	51	3 (5.9)	7 (13.7)	26 (51.0)	15 (29.4)	0 (0.0)	18 (35.3)	30 (58.8)	0 (0.0)

(Continued on next page)

TABLE 5. (Continued)

Substance	n	Positive Reactions	Second Read Code* (%)				Relevance (%)			
			+++	++	+	+/-	Definite	Probable	Possible	Past
4-tert-Butylphenol formaldehyde resin 1.0% pet.	4235	45	14 (31.1)	11 (24.4)	19 (42.2)	1 (2.2)	1 (2.2)	2 (4.4)	17 (37.8)	11 (24.4)
Disperse blue mix 124/106 1.0% pet.	4228	44	13 (29.5)	12 (27.3)	13 (29.5)	5 (11.4)	0 (0.0)	16 (36.4)	20 (45.5)	3 (6.8)
Dibucaine (cinchocaine-HCl) 2.5% pet.	4230	40	10 (25.0)	14 (35.0)	14 (35.0)	2 (5.0)	5 (12.5)	2 (5.0)	4 (10.0)	23 (57.5)
Ethyl acrylate 0.1% pet.	4230	39	7 (17.9)	8 (20.5)	21 (53.8)	3 (7.7)	1 (2.6)	9 (23.1)	15 (38.5)	6 (15.4)
Methyl methacrylate 2.0% pet.	4236	37	6 (16.2)	17 (45.9)	13 (35.1)	1 (2.7)	1 (2.7)	14 (37.8)	11 (29.7)	9 (24.3)
Cocamide DEA (coconut diethanolamide) 0.5% pet.	4230	36	2 (5.6)	12 (33.3)	18 (50.0)	4 (11.1)	4 (11.1)	11 (30.6)	19 (52.8)	1 (2.8)
<i>Melaleuca alternifolia</i> (tea tree leaf oil), oxidized 5.0% pet.	4231	36	17 (47.2)	8 (22.2)	10 (27.8)	1 (2.8)	4 (11.1)	15 (41.7)	8 (22.2)	3 (8.3)
Benzophenone-3 (oxybenzone or 2-hydroxy-4-methoxy-benzophenone) 10% pet.	4231	35	9 (25.7)	9 (25.7)	12 (34.3)	5 (14.3)	6 (17.1)	14 (40.0)	12 (34.3)	3 (8.6)
Budesonide 0.1% pet.	4232	35	20 (57.1)	7 (20.0)	5 (14.3)	3 (8.6)	3 (8.6)	16 (45.7)	11 (31.4)	4 (11.4)
Lidocaine hydrochloride 15.0% pet.	4230	33	7 (21.2)	12 (36.4)	13 (39.4)	1 (3.0)	7 (21.2)	6 (18.2)	4 (12.1)	9 (27.3)
Tocopherol (DL- α -tocopherol) 100.0%	4230	30	5 (16.7)	15 (50.0)	8 (26.7)	2 (6.7)	8 (26.7)	11 (36.7)	12 (40.0)	0 (0.0)
Ylang-ylang oil 2.0% pet.	4230	30	7 (23.3)	8 (26.7)	14 (46.7)	1 (3.3)	0 (0.0)	8 (26.7)	18 (60.0)	0 (0.0)
Sesquiterpene lactone mix 0.1% pet.	4230	29	13 (44.8)	3 (10.3)	9 (31.0)	4 (13.8)	0 (0.0)	9 (31.0)	12 (41.4)	3 (10.3)
Mixed dialkyl thioureas 1.0% pet.	4231	29	11 (37.9)	7 (24.1)	10 (34.5)	1 (3.4)	7 (24.1)	7 (24.1)	4 (13.8)	4 (13.8)
Carvone 5.0% pet.	4230	25	1 (4.0)	7 (28.0)	14 (56.0)	3 (12.0)	0 (0.0)	14 (56.0)	7 (28.0)	1 (4.0)
Chloroxylenol (4-chloro-3,5-xylene) 1.0% pet.	4230	23	3 (13.0)	8 (34.8)	11 (47.8)	0 (0.0)	2 (8.7)	11 (47.8)	6 (26.1)	0 (0.0)
2-Mercaptobenzothiazole 1.0% pet.	4236	21	8 (38.1)	9 (42.9)	4 (19.0)	0 (0.0)	2 (9.5)	4 (19.0)	15 (71.4)	0 (0.0)
Mercapto mix 1.0% pet.	4236	20	8 (40.0)	3 (15.0)	7 (35.0)	2 (10.0)	2 (10.0)	2 (10.0)	14 (70.0)	0 (0.0)
<i>J. officinale</i> oil (<i>J. grandiflorum</i>) 2.0% pet.	4230	19	2 (10.5)	6 (31.6)	9 (47.4)	2 (10.5)	0 (0.0)	7 (36.8)	9 (47.4)	0 (0.0)
<i>M. piperita</i> oil (peppermint oil) 2.0% pet.	4230	18	3 (16.7)	2 (11.1)	10 (55.6)	3 (16.7)	0 (0.0)	7 (38.9)	5 (27.8)	2 (11.1)
Benzyl alcohol 1.0% pet.	4232	18	0 (0.0)	5 (27.8)	13 (72.2)	0 (0.0)	4 (22.2)	9 (50.0)	3 (16.7)	0 (0.0)
<i>Lavandula angustifolia</i> oil (lavender oil) 2.0% pet.	4229	16	1 (6.2)	3 (18.8)	10 (62.5)	1 (6.2)	2 (12.5)	9 (56.2)	3 (18.8)	2 (12.5)
Ethyl-2-cyanoacrylate 10.0% pet.	4230	14	0 (0.0)	2 (14.3)	8 (57.1)	4 (28.6)	2 (14.3)	5 (35.7)	3 (21.4)	3 (21.4)
Hydrocortisone-17-butyrate 1% pet.	4231	14	3 (21.4)	4 (28.6)	6 (42.9)	1 (7.1)	2 (14.3)	4 (28.6)	6 (42.9)	1 (7.1)
Clobetasol-17-propionate 1.0% pet.	4230	11	2 (18.2)	3 (27.3)	3 (27.3)	3 (27.3)	0 (0.0)	6 (54.5)	4 (36.4)	1 (9.1)
Desoximetasone 1.0% pet.	4230	10	0 (0.0)	2 (20.0)	3 (30.0)	5 (50.0)	0 (0.0)	2 (20.0)	5 (50.0)	1 (10.0)
D-Limonene 2.0% pet.	4230	9	1 (11.1)	3 (33.3)	4 (44.4)	1 (11.1)	0 (0.0)	2 (22.2)	4 (44.4)	1 (11.1)

*Discrepancies in positive reaction numbers and second read code tally may differ by up to <3 because of coding variances.

Hypothetical Detection Rate of T.R.U.E. TEST Versus NACDG Screening Series

During this data period, there were 3 antigens 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 and dibucaine NACDG antigens would have been detected by the caine mix of T.R.U.E. TEST; sesquiterpene lactone mix and Compositae mix NACDG antigens would have been detected by parthenolide of T.R.U.E. TEST), there were 36 NACDG antigens 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 75.1% (5658/7532). Using a conservative calculation (assuming

that individual components of a mix would not have been detected with a mix and vice versa), the conservative hypothetical detection rate of T.R.U.E. TEST allergens would be 69.7% (5251/7532).

SPIN for NACDG Allergens

Significance-Prevalence Index Numbers calculations¹⁵ weight prevalence by relevance. Significance-Prevalence Index Numbers ranking for these data are listed in Table 8.

Common Sources of Irritants

Most common sources of identified irritants were personal care products and soaps (not meant for skin use; eg, laundry detergent, industrial cleansers) (Table 9).

TABLE 6. Comparison of Positive Rates to Previous Study Years

Patch Test Allergen	2011–2012			2001–2010							
	n*	Positive, %	P [RR (95% CI)]	2009–2010		2007–2008		2005–2006		2001–2002	
				Pos, %	Pos, %	Pos, %	Pos, %	Pos, %	Pos, %	Pos, %	P [RR (95% CI)]
Nickel sulfate 2.5% pet.	4224	18.5	0.0003 1.19 (1.08–1.31)	15.5	19.5	19.0	18.7	16.9	0.4427 1.03 (0.96–1.10)		
Fragrance mix I 8% pet.	4232	12.1	<0.0001 1.42 (1.25–1.61)	8.5	9.4	11.5	9.1	10.2	<0.0001 1.24 (1.14–1.36)		
Neomycin 20% pet.	4229	9.1	0.5393 1.04 (0.91–1.20)	8.7	10.1	10.0	10.6	11.4	0.0274 0.89 (0.80–0.99)		
<i>M. perirae</i> 25% pet.	4234	7.9	0.2413 1.09 (0.94–1.27)	7.2	11.0	11.9	10.6	11.5	<0.0001 0.75 (0.67–0.84)		
Bacitracin 20% pet.	4234	7.8	0.3970 0.94 (0.81–1.08)	8.3	7.9	9.2	7.9	7.7	0.3991 0.95 (0.85–1.07)		
Cobalt chloride 1% pet.	4231	7.3	0.0390 1.18 (1.01–1.38)	6.2	8.2	8.4	8.4	7.5	0.3073 0.94 (0.84–1.06)		
Formaldehyde 1% aq.	4237	6.6	0.1479 1.13 (0.96–1.33)	5.8	7.7	9.0	8.7	8.5	0.0016 0.82 (0.73–0.93)		
Quaternium-15 2% pet.	4235	6.4	0.2212 1.11 (0.94–1.31)	5.8	8.6	10.3	8.9	9.3	<0.0001 0.75 (0.66–0.85)		
p-Phenylenediamine 1% pet.	4223	6.3	0.1069 1.15 (0.97–1.36)	5.5	5.3	5.0	4.7	4.8	0.0006 1.25 (1.10–1.42)		
Fragrance mix II 14% pet.	4237	5.2	0.3067 1.10 (0.91–1.33)	4.7	3.6	—	—	—	0.0053 1.26 (1.07–1.48)		
Methylchlorisothiazolinone/ Methylisothiazolinone 100 ppm. aq.	4227	5.0	<0.0001 2.01 (1.60–2.52)	2.5	3.6	2.8	2.2	2.3	<0.0001 1.87 (1.61–2.18)		
Carba mix 3% pet.	4236	4.7	0.7442 1.03 (0.85–1.25)	4.6	4.5	3.9	4.0	4.5	0.1866 1.10 (0.95–1.28)		
Lanolin alcohol (Amerchol L 101), 50% pet.§	4235	4.6	<0.0001 1.83 (1.45–2.30)	2.5	2.1	1.8	2.2	2.3	<0.0001 2.10 (1.79–2.47)		
Iodopropenyl butylcarbamate 0.5% pet.	4231	4.2	0.8345 0.98 (0.80–1.20)	4.3	3.1	2.4	—	—	0.0029 1.30 (1.09–1.54)		
Cinnamic aldehyde 1% pet.	4231	3.9	<0.0001 1.69 (1.32–2.15)	2.3	2.4	3.1	2.4	—	<0.0001 1.53 (1.28–1.82)		
Methyl dibromoglutaronitrile/ phenoxyethanol 2.0% pet.	4231	3.7	0.8071 0.97 (0.79–1.21)	3.8	5.5	5.8	6.1	5.5	<0.0001 0.69 (0.59–0.81)		
Camphor 2.5 Pet	4230	3.1	—	—	—	—	—	—	—		
Thiuram mix 1% pet.	4236	2.9	0.5250 0.92 (0.73–1.18)	3.1	3.4	3.9	4.6	4.6	0.0007 0.73 (0.60–0.88)		
Propylene glycol 30% aq.	4232	2.6	0.1251 0.83 (0.65–1.06)	3.2	2.1	2.9	3.3	4.1	0.1099 0.85 (0.70–1.04)		
Tixocortol-21-pivalate 1% pet.	4230	2.3	0.2777 1.17 (0.88–1.56)	2.0	2.5	2.7	2.7	2.9	0.3858 0.91 (0.74–1.12)		
Oleamidopropyl dimethylamine 0.1% aq.	4231	2.3	0.0869 1.29 (0.96–1.73)	1.8	—	—	—	—	—		
Colophony 20% pet.	4236	2.3	0.2103 0.84 (0.65–1.10)	2.7	2.8	2.2	2.8	2.7	0.1576 0.86 (0.69–1.06)		
Diazolidinyl urea 1% pet.	4232	2.1	0.7982 0.96 (0.72–1.28)	2.2	3.1	3.7	3.5	3.2	0.0003 0.67 (0.54–0.84)		
Hydroxyethyl methacrylate 2% pet.	4230	2.0	0.9015 0.98 (0.73–1.32)	2.0	2.4	—	—	—	0.3347 0.88 (0.69–1.14)		
Compositae mix 6% pet.	4231	1.9	0.9775 1.00 (0.74–1.36)	1.9	1.4	1.2	1.3	1.0	0.0050 1.41 (1.11–1.80)		
Propolis 10% pet.	4231	1.8	0.3241 0.86 (0.63–1.16)	2.1	4.9	—	—	—	<0.0001 0.50 (0.39–0.64)		
Imidazolidinyl urea 2% pet.	4232	1.6	0.0524 0.74 (0.54–1.00)	2.2	2.4	2.9	2.9	3.1	<0.0001 0.60 (0.47–0.77)		
Potassium dichromate 0.25% pet.	4235	1.6	0.0207 0.70 (0.51–0.95)	2.3	4.1	4.8	4.3	4.1	<0.0001 0.41 (0.32–0.52)		
2-Bromo-2-nitro-1, 3-propanediol 0.5% pet.	4231	1.6	0.0167 1.58 (1.08–2.32)	1.0	3.1	3.4	2.3	3.4	<0.0001 0.60 (0.46–0.77)		
DMDM hydantoin 1% pet.	4232	1.6	0.0167 1.58 (1.08–2.32)	1.0	2.7	2.6	2.3	2.8	0.0035 0.59 (0.54–0.89)		
Decyl glucoside 5% pet.	4231	1.6	0.8540 1.03 (0.74–1.45)	1.5	—	—	—	—	—		
Shellac 20% alc.	4231	1.6	0.6163 0.92 (0.66–1.28)	1.7	—	—	—	—	—		
Glutaral 1% pet.	4213	1.5	0.0100 1.67 (1.13–2.48)	0.9	1.1	1.3	1.2	1.3	0.0518 1.31 (1.00–1.71)		
Dimethylaminopropylamine 1% aq.	4233	1.5	0.0598 0.73 (0.53–1.01)	2.0	—	—	—	—	—		
Epoxy resin 1% pet.	4235	1.5	0.6027 0.91 (0.65–1.28)	1.6	1.7	1.8	1.8	2.4	0.0738 0.79 (0.60–1.02)		
Cocamidopropyl betaine 1% aq.	4232	1.4	0.8532 1.03 (0.73–1.47)	1.4	1.1	1.8	1.8	2.9	0.1141 0.81 (0.62–1.05)		
Benzocaine 5% pet.	4236	1.4	0.1489 0.78 (0.56–1.09)	1.8	1.3	1.9	1.7	1.7	0.2359 0.85 (0.65–1.11)		
Paraben mix 12% pet.	4231	1.4	0.0072 1.77 (1.16–2.69)	0.8	1.1	1.2	1.1	0.6	0.0113 1.44 (1.09–1.92)		
Ethylenediamine dihydrochloride 1% pet.	4232	1.3	0.7805 0.95 (0.66–1.36)	1.4	1.5	1.9	2.4	2.8	0.0030 0.66 (0.50–0.87)		

Majantole 5% pet.	4231	1.3	0.5669 0.90 (0.62–1.30)	1.4	—	—	—	—	—
Black rubber mix 0.6% pet.	4236	1.3	0.0090 1.80 (1.15–2.81)	0.7	1.0	1.0	1.0	0.0601 1.33 (0.99–1.79)	—
Tosylamide formaldehyde resin 10% pet.	4232	1.2	0.1483 1.35 (0.90–2.05)	0.9	1.0	1.3	1.7	0.7383 0.95 (0.71–1.27)	1.0
Amidoamine (stearamidopropyl dimethylamine) 0.1% aq.	4231	1.2	<0.0001 3.99 (2.17–7.33)	0.3	1.6	2.0	1.7	0.0494 0.75 (0.56–1.00)	2.4
p-tert-Butylphenol formaldehyde resin 1% pet.	4235	1.1	0.0674 0.70 (0.48–1.03)	1.5	1.2	1.3	1.8	0.0164 0.69 (0.51–0.94)	1.9
Disperse blue mix 106/124 1% pet.†	4228	1.0	0.8517 1.04 (0.69–1.58)	1.0	0.9	2.1	1.9	0.0006 0.59 (0.43–0.80)	3.0
Dibucaine (cinchocaine hydrochloride) 2.5% pet.	4230	0.9	0.0122 1.94 (1.14–3.28)	0.5	1.1	1.1	1.0	0.9927 1.00 (0.71–1.40)	1.0
Ethyl acrylate 0.1% pet.	4230	0.9	0.2471 1.32 (0.82–2.12)	0.7	1.2	0.9	1.1	0.4381 0.88 (0.63–1.23)	1.3
Methyl methacrylate 2% pet.	4236	0.9	0.6702 1.11 (0.70–1.76)	0.8	1.2	1.0	1.6	0.0467 0.71 (0.50–1.00)	1.5
Cocamide DEA 0.5% pet.	4230	0.9	0.7852 0.94 (0.60–1.47)	0.9	1.2	1.0	1.1	0.1661 0.78 (0.55–1.11)	1.2
Tea tree oil, oxidized 5% pet.	4231	0.9	0.4715 0.85 (0.55–1.32)	1.0	1.4	1.4	0.9	0.0722 0.73 (0.51–1.03)	—
2-Hydroxy-4-methoxy-benzophenone (benzophenone-3) 10% pet.‡	4231	0.8	0.6927 0.91 (0.58–1.44)	0.9	0.9	0.7	0.7	0.6576 1.09 (0.76–1.56)	0.6
Budesonide .01% pet.	4232	0.8	0.8483 1.05 (0.65–1.68)	0.8	0.9	1.5	1.8	0.0233 0.67 (0.47–0.95)	1.1
Lidocaine 15% pet.	4230	0.8	0.6565 1.12 (0.68–1.83)	0.7	0.9	1.1	0.6	0.8843 0.97 (0.67–1.41)	0.7
Tocopherol (DL- α -tocopherol) 100.0% pet.	4230	0.7	0.1457 0.71 (0.45–1.13)	1.0	1.0	0.7	1.1	0.0876 0.72 (0.49–1.05)	1.1
Canaga odorata oil (ylang ylang) 2% pet.	4230	0.7	0.0062 0.55 (0.35–0.85)	1.3	1.4	1.5	1.2	0.0009 0.54 (0.37–0.78)	1.2
Sesquiterpene lactone mix 0.1% pet.	4230	0.7	0.6393 1.13 (0.67–1.92)	0.6	0.6	0.7	0.6	0.6088 1.11 (0.75–1.65)	0.6
Mixed dialkyl thioureas, 1.0% pet.	4231	0.7	0.1129 0.69 (0.43–1.10)	1.0	0.9	1.0	1.0	0.1328 0.74 (0.51–1.10)	0.7
Carvone 5% pet.	4230	0.6	0.113 0.54 (0.33–0.88)	1.1	—	—	—	—	—
4-chloro-3,5-xyleneol (PCMX, chloroxyleneol) 1% pet.	4230	0.5	0.8354 1.06 (0.59–1.91)	0.5	0.4	0.5	0.7	0.9821 1.01 (0.65–1.57)	0.6
Mercaptobenzothiazole 1% pet.	4236	0.5	0.0090 0.71 (0.41–1.24)	0.7	1.0	0.9	1.3	0.0034 0.52 (0.33–0.81)	0.8
Mercapto mix 1% pet.	4236	0.5	0.4062 0.78 (0.44–1.40)	0.6	0.6	0.8	0.9	0.0904 0.67 (0.42–1.07)	0.6
Jasminum officinale oil (<i>J. grandiflorum</i>) 2.0% pet.	4230	0.4	0.0028 0.45 (0.26–0.77)	1.0	—	—	—	—	—
<i>M. piperita</i> oil (peppermint oil) 2% pet.	4230	0.4	0.2492 0.70 (0.39–1.28)	0.6	—	—	—	—	—
Benzyl alcohol 1% pet.	4232	0.4	0.0753 2.03 (0.91–4.52)	0.2	0.4	—	—	0.2838 1.38 (0.77–2.48)	—
<i>L. angustifolia</i> oil (lavender oil) 2% pet.	4229	0.4	0.1485 1.81 (0.80–4.09)	0.2	—	—	—	—	—
Ethyl-2-cyanoacrylate, 10.0% pet.	4230	0.3	—	—	—	—	—	—	—
Hydrocortisone-17-butyrate 1% pet.	4231	0.3	0.0182 0.47 (0.25–0.89)	0.7	0.5	0.6	0.5	0.0780 0.61 (0.35–1.06)	0.4
Clobetasol-17-propionate 1% pet.	4230	0.3	0.7141 0.86 (0.39–1.92)	0.3	0.6	0.8	0.7	0.0061 0.43 (0.23–0.80)	—
Desoximetasone 1% pet.	4230	0.2	0.7891 1.13 (0.46–2.78)	0.2	0.2	—	—	0.6931 1.17 (0.54–2.51)	—
D-Limonene 3% pet.	4230	0.2	0.1559 2.29 (0.71–7.43)	0.1	—	—	—	—	—

*Number tested to specific allergen.

†07-08 Cycle tested disperse blue 106 (not the 106/124 mix).

‡07-08 Cycle tested 3% benzophenone (not 100%).

\$09-10 Cycle lanolin alcohol tested at 30% concentration.

aq. Indicates aqueous; pet., petrolatum; CI, confidence interval; DEA, diethanolamine.

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

Source	No. Patients	Percentage (n = 1100)
Cosmetics, beauty preparations, skin and health care products	370	33.6
Drugs, medications, alcoholic beverages	337	30.6
Clothing, wearing apparel, protective equipment, textiles	196	17.8
Animals, infectious agents, plants, minerals, persons	79	7.2
Furniture, fixtures, structures, and surfaces	60	5.5

DISCUSSION

Many current findings are consistent with previous reports. As compared with the last cycle, the individual components of MOAHLFAP¹⁶ varied by less than 5%. Polysensitization rate was 23.4% compared with 26.9% in this cycle. As compared with previous cycles,^{7–11} the ranking of hand dermatitis has decreased.

Composition of the top 15 most frequently positive allergens included 2 metals (nickel and cobalt), 2 antibiotics (neomycin and bacitracin), 4 fragrances (fragrance mix I, fragrance mix II, *M. pereirae*, and cinnamic aldehyde), and 4 preservatives (formaldehyde, quaternium-15, methylchloroisothiazolinone/methylisothiazolinone, iodopropynyl butyl carbamate), as well as paraphenylenediamine, carba mix, and lanolin alcohol. As compared with the 2009–2010 cycle, 3 allergens moved up into the top 15 group; methylchloroisothiazolinone/methylisothiazolinone, iodopropynyl butyl carbamate and lanolin alcohol moved up, whereas methyl dibromoglutaronitrile/phenoxyethanol, propylene glycol, and thiuram mix moved down.

There were statistically significant increases in rates from both the previous reporting cycle (2009–2010) and the pooled rates from the previous decade (2001–2010) for 6 allergens: methylchloroisothiazolinone/methylisothiazolinone (risk ratios [RRs], 2.01, 1.87), lanolin alcohol (RRs, 1.83, 2.10), cinnamic aldehyde (RRs, 1.69, 1.53), glutaral (RRs, 1.67, 1.31), paraben mix (RRs, 1.77, 1.44), and fragrance mix I (RRs, 1.42, 1.24). Doubling of positive reactions to methylchloroisothiazolinone/methylisothiazolinone is consistent with the epidemic of allergy to this preservative seen in Europe^{18–22} and does not account for those reactions to methylisothiazolinone alone that may be missed by testing with this allergen combination^{23,24} and the likely culprit for this increase.²⁵ The 2013–2014 NACDG screening series contains methylisothiazolinone alone, at a concentration of 0.2%. In late 2013, Cosmetics Europe, the European trade association representing the interests of the cosmetics industry in the European Union, issued an industry-wide recommendation to discontinue methylisothiazolinone in leave-on products²⁶; 100 parts per million is allowed in wash-off products. In North

TABLE 8. Significance-Prevalence Index Number

Rank	Patch Test Allergen	SPIN
1	Nickel sulfate 2.5% pet.*	553
2	Fragrance mix I 8% pet.*	506
3	<i>M. pereirae</i> 25% pet.*	334
4	Methylchloroisothiazolinone/methylisothiazolinone 100 ppm aq.*	273
5	Quaternium-15 2% pet.*	256
6	p-Phenylenediamine 1% pet.*	255
7	Formaldehyde 1% aq.*	250
8	Fragrance mix II 14% pet.	231
9	Lanolin alcohol 50% pet.*	217
10	Bacitracin 20% pet.*	210
11	Carba mix 3% pet.*	195
12	Iodopropynyl butyl carbamate 0.5% pet.*	185
13	Cinnamic aldehyde 1% pet.*	168
14	Cobalt chloride 1% pet.*	159
15	Propylene glycol 30% aq.	141
16	Methyl dibromoglutaronitrile/phenoxyethanol 2.0% pet*	136
17	Neomycin 20% pet.*	135
18	Thiuram mix 1% pet.*	125
19	Tixocortol-21-pivalate 1% pet.*	102
20	Diazolidinyl urea 1% pet.*	95
21	Oleamidopropyl dimethylamine 0.1% aq.	85
22	Paraben mix 12% pet.*	83
23–24	DMDM hydantoin 1% pet.*	79
23–24	Cocamidopropylbetaine 1% aq.	79
25	Carmine 2.5% pet	72
26	2-Bromo-2-nitro-1,3-propanediol 0.5% pet.*	69
27	Dimethylaminopropylamine 1% aq.	69
28	Imidazolidinyl urea 2% pet.*	67
29–30	Colophony 20% pet.*	64
29–30	Hydroxyethyl methacrylate 2% pet.	64
31	Shellac 20% alc.	63
32	Propolis 10% pet.	54
33	Amidoamine 0.1% aq.	51
34–35	Compositae mix 6% pet.*	47
34–35	Epoxy resin 1% pet.*	47
36	DL- α -Tocopherol 100%	45
37–38	Cocamide DEA 0.5% pet.	44
37–38	Benzophenone-3 10% pet.	44
39–40	Majantole 5% pet.	42
39–40	Potassium dichromate 0.25% pet.*	42
41	Tea tree oil 5% pet.	41
42–43	Budesonide .01% pet.*	39
42–43	Disperse blue 106/124 mix 1% pet.*	39
44	Decyl glucoside 5% pet.	38
45	Black rubber mix 0.6% pet.*	36
46–47	Methyl methacrylate 2% pet.	34
46–47	Tosylamide formaldehyde resin 10% pet.	34
48	Thioureas 1% pet.	31
49	Lidocaine 15% pet.	30
50	Carvone 5% pet.	28
51	Ethyl acrylate 0.1% pet.	27
52–53	Ylang ylang 2% pet.	26

TABLE 8. (Continued)

Rank	Patch Test Allergen	SPIN
52–53	Glutaraldehyde 1% pet.	26
54–57	Benzocaine 5% pet.*	24
54–57	Sesquiterpene lactone mix 0.1% pet.*	24
54–57	PCMX 1% pet.	24
54–57	Benzyl alcohol 1% pet.	24
58	Mercaptobenzothiazole 1% pet.*	23
59–60	Ethylenediamine 1% pet.*	22
50–60	<i>L. angustifolia</i> oil 2% pet.	22
61	Mercapto mix 1% pet.*	20
62	p-tert-Butylphenol formaldehyde resin 1% pet.*	19
63	Dibucaine 2.5% pet.	17
64	<i>J. grandiflorum</i> 2% pet.	16
65–68	Clobetasol-17-propionate 1% pet.	14
65–68	Ethy-2-cyanoacrylate 10.0% pet	14
65–68	<i>M. piperita</i> oil 2% pet.	14
65–68	Hydrocortisone-17-butyrate 1% pet.*	14
69–70	Desoximetasone 1% pet.	6
69–70	D-Limonene 3% pet.	6

SPIN¹⁵ = a weighted calculation depending upon degree of certainty ascribed to relevance.

Calculation = (proportion of population allergic) * (1 * R_{definite} + 0.66 * R_{probable} + 0.33 * R_{possible}) * 100.

*Represented or partially represented in T.R.U.E. TEST.

aq. indicates aqueous; pet., petrolatum; DEA, diethanolamine; DMDM, dimethylol dimethyl.

America, methylchloroisothiazolinone/methylisothiazolinone is now ranked no. 4 based on SPIN calculations, a positivity score weighted by relevance.

The increase in detection rate for lanolin is likely due to an increase in allergen concentration from 30% to 50% rather than increased sensitivity. Fragrance mix I positivity varied between 8.5% and 11.5% over the last decade; this cycle's rate of 12.1% is the highest recorded for the NACDG. Although statistically significantly higher, positivity rates for glutaral (1.5%) and paraben mix (1.4%) are still low.

There were statistically significant decreases in rates from both the previous reporting cycle (2009–2010) and the pooled rates from the previous decade (2001–2010) for 3 allergens: imidazolidinyl urea (RRs, 0.74, 0.60), potassium dichromate (RRs, 0.70, 0.41), and ylang ylang oil (RRs, 0.55, 0.54). The significant decrease in chromium sensitivity could be explained by possible secondary effects of chromate regulation in other countries^{27–29} and/or decrease in construction or access to health care because of the economic recession. The decrease in ylang ylang oil positivity to 0.7% may be spurious as it has consistently been 1.2% to 1.5% over the last decade; data from future cycles will confirm trends.

Compared with the previous decade, all formaldehyde-releasing preservatives significantly decreased by 18% to 41% (formaldehyde RR, 0.82; quaternium-15 RR, 0.75; diazolidinyl urea RR, 0.67; imidazolidinyl urea RR, 0.60; bronopol RR, 0.60; DMDM hydantoin RR, 0.59). The US Department of Health and Human Services

classified formaldehyde as a carcinogen in 2011,³⁰ and although it did not implicate formaldehyde-releasing preservatives, several large manufacturers have recently eliminated this group of preservatives from products.³¹ Similarly, methyldibromoglutaronitrile is no longer allowed in leave-on or rinse-off products in the European Union. The replacement of these biocides by other preservatives, especially methylisothiazolinone, will likely impact sensitivity rates in the future. There is now discussion in Europe about banning methylisothiazolinone in personal care products. Of the common and effective preservatives, parabens, because of its low sensitization rate,³² remains the preferred choice of the NACDG.

Positivity rates of the 2 new allergens added to this data period were 3.1% for carmine and 0.3% for ethyl cyanoacrylate. Almost two-thirds of reactions to carmine were mild, however, and relevance was low (1.5% definite, 13.7% probable, and 38.9% possible); thus far, only a few case reports have been published of reactions to this allergen.^{33–35} Because of its red color, which can mimic macular erythema, caution should be used with interpreting reactions to this allergen. Although a relatively rare allergen, reactions to ethyl cyanoacrylate were more often relevant (14.3% definite, 35.7% probable, and 21.4% possible).

Prevalence rates of the newer allergens (added in the 2009–2010 cycle) continue to be relatively high for the surfactants oleamidopropyl dimethylamine (2.3%) and dimethylaminopropylamine (1.5%). Like cocamidopropyl betaine and amidoamine, these agents are mild irritants, so macular erythema should be interpreted with caution.^{36,37} Decyl glucoside was an especially important addition; one-third of reactions were strong or very strong, and relevance was good (6.1% definite, 28.8% probable, and 42.4% possible). This surfactant is used in personal care products,³⁸ as well as in methylene bis-benzotriazolyl tetramethylbutylphenol,³⁹ a sunscreen agent not available in the United States, but present on the Canadian market. 1.6% of patients had a positive reaction to shellac, but only 47% of those reactions were currently relevant. Most reported cases of confirmed shellac allergy have been due to eye^{40–42} or lip^{43,44} products. Anecdotal experience indicates that shellac 20% in alcohol may also be an irritant. The remaining newer allergens were flavoring/perfume ingredients; positive rates, and

TABLE 9. Five Most Common Sources of Irritants

Source	No. Patients (n = 873)	Percentage
Cosmetics, beauty preparations, skin and health care products	219	25.1
Soaps, detergents, cleansers, disinfectants, laundry aids (nonskin)	169	19.4
Animals, infectious agents, plants, minerals, persons	108	12.4
Drugs, medications, alcoholic beverages	101	11.6
Clothing, wearing apparel, protective equipment, textiles	48	5.5

respective current relevance rates were as follows: majantole (1.3%, 79.3%), carvone (0.6%, 84.0%), *Jasminum grandiflorum* (0.4%, 84.2%), *Mentha piperita* oil (0.4%, 66.7%), *Lavendula angustifolia* oil (0.4%, 87.5%), and D-limonene (0.2%, 66.6%).

Another noteworthy allergen is benzophenone-3. Although sensitivity was only 0.8%, more than 50% of reactions were strong or very strong, and current relevance was high (91.4%). For these reasons, as well as its common use in products other than sunscreens (such as nail polish, shampoo, and waterless hand cleansers), benzophenones were named 2014 Allergens of the Year by the American Contact Dermatitis Society.⁴⁵

Mild and doubtful reactions are often nonreproducible,^{37,46} 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 based on the patient's reactivity to multiple other fragrance allergens. Nonetheless, preparations with high mild and doubtful reaction rates often represent "problematic" preparations.⁴⁷ Herein, we report reaction strength of positive reactions for interested readers.

Hypothetically, T.R.U.E. TEST would have detected 69.7% to 75.1% of reactions found by the NACDG screening series during this data period. Of the top 40 NACDG allergens, the following antigens are not on T.R.U.E. TEST: fragrance mix II, iodopropenyl butylcarbamate, carmine, propylene glycol, propolis, dimethylaminopropylamine, hydroxyethylmethacrylate, oleamidopropyl dimethylamine, shellac, decyl glucoside, cocamidopropyl betaine, majantol, DMDM hydantoin, and glutaral. While not represented in the top 40, other important non-T.R.U.E. TEST allergens include tosylamide formaldehyde resin, amidoamine, acrylates/methylacrylates, tea tree oil, benzophenone-3, and the mixed dialkyl thioureas. The American Contact Dermatitis Society recommends a core antigen panel of 80 allergens.⁴⁸

The NACDG antigens are added and deleted periodically based on new data in the literature and member experience testing with additional allergens. It is likely that many of the patients had previous patch testing to T.R.U.E. TEST prior to referral to an NACDG clinic; the impact of prior testing on changing prevalence rates is unclear. Long-term trends⁴⁹ are not reported herein. One-quarter of 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 as well as personal products and workplace materials.

Limitations of this data include the following: (1) NACDG data represent a referral patient group and thus do not reflect the general population or general dermatology patients. (2) Patch testing is both science and learned art. Distinctions between positive and irritant reactions, occupational relevance, source codes, and other collected variables are standardized whenever possible. (3) The NACDG does not collect data on non-NACDG allergens other than presence and source. (4) While 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 benefit in the diagnosis and management of patients with dermatitis. Patch testing remains a critical diagnostic tool. This latest NACDG data summary for 2011–2012 adds to the references available on emerging trends and patterns in the field.

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