

# North American Contact Dermatitis Group Patch Test Results: 2013–2014

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**Background:** Patch testing is the most important diagnostic tool for the assessment of allergic contact dermatitis.

**Objective:** This study documents the North American Contact Dermatitis Group (NACDG) patch testing results from January 1, 2013, to December 31, 2014.

**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  $\chi^2$  test.

**Results:** A total of 4871 patients were tested. There were 3255 patients (66.8%) who had at least 1 positive reaction and 2412 patients (49.5%) who were ultimately determined to have a primary diagnosis of allergic contact dermatitis. A total of 434 patients (8.9%) had occupationally related skin disease. There were 9726 positive allergic reactions. Compared with the previous reporting periods (2011–2012 and 2001–2012, including at least three 2-year cycles), positive reaction rates for the top 25 screening allergens statistically increased for 2 allergens: methylchloroisothiazolinone/methylisothiazolinone (6.4%; risk ratios, 1.26 [1.07–1.50] and 2.08 [1.84–2.37]) and hydroxyethyl methacrylate (2.6%; risk ratios, 1.34 [1.02–1.76] and 1.23 [1.00–1.51]). Methylisothiazolinone, which was added to the screening series for this 2013–2014 cycle, had the third highest positive reaction rate of allergens tested (10.9%). Four other newly added allergen preparations—formaldehyde 2% (7%), diphenylguanidine (3.8%), propylene glycol 100% (2.8%), and benzophenone-4 (2.1%)—all had reaction rates greater than 2%. Twenty-one percent of tested patients had at least 1 relevant allergic reaction to an allergen not on the NACDG series; 14.6% of these were occupationally related. The T.R.U.E. TEST (SmartPractice Denmark, Hillerød, Denmark) would have hypothetically missed one quarter to one third of reactions detected by the NACDG screening series.

**Conclusions:** These results confirm that the epidemic of sensitivity to methylisothiazolinone previously documented in Europe is also occurring in North America. Patch testing with allergens beyond a standard screening tray is necessary for the complete evaluation of occupational and nonoccupational allergic contact dermatitis.

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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. Periodically, these epidemiologic data are published.<sup>1–13</sup> This article summarizes results from 2013 to 2014.

## MATERIALS AND METHODS

Between January 1, 2013, and December 31, 2014, the NACDG consisted of 13 dermatologists in North America. Patients were patch tested with a screening series of 70 allergens (allergEAZE; SmartPractice, Calgary, Canada). Recent NACDG reports<sup>1–13</sup> described data collection methods in detail, which remain unchanged for this reporting cycle. Briefly, patch testing was performed with a standardized technique using Finn Chambers (SmartPractice, Phoenix, Ariz) on Scanpor tape (Norgesplaster

**TABLE 1. MOAHLFAP<sup>18</sup> Characteristics**

| Characteristic                          | n (%)       |
|-----------------------------------------|-------------|
| Male                                    | 1462 (30.0) |
| Occupational*                           | 434 (8.9)   |
| Atopic triad                            |             |
| Hay fever <sup>†</sup>                  | 1420 (29.2) |
| Eczema                                  | 1410 (28.9) |
| Asthma <sup>†</sup>                     | 829 (17.0)  |
| Hand <sup>‡</sup>                       | 982 (20.2%) |
| Leg <sup>‡</sup>                        | 224 (4.7)   |
| Face <sup>‡</sup>                       | 755 (15.5)  |
| Age > 40 years                          | 3289 (67.5) |
| Positivity rate (≥1 allergic reactions) | 3255 (66.8) |

\*Excludes uncertain.

<sup>†</sup>Not part of MOAHLFAP.

<sup>‡</sup>Primary site; when primary sites of the lips, nose, eyelids, and eyes are added to the face, the total for the face is 1489 (30.6%).

Alpharma 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 on the basis of the 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* (a 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 also coded using a 3-digit code.<sup>14</sup> Occupation and industry were coded by an occupational expert using the US 2000 Census Bureau Codes on the basis of answers to a series of 5 standardized questions collected for each patient.<sup>15</sup> 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 Corp, Redmond, Wash). All analyses were performed using SAS 9.2 (Statistical Analysis System; SAS Institute Inc, Cary, NC) according to recommended guidelines.<sup>16</sup> Pearson  $\chi^2$  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 Numbers (SPINs)<sup>17</sup> were calculated as in the previous data cycle reports.<sup>12,13</sup> Demographic data were displayed according to MOAHLFAP (male, occupational, atopic, hand, leg, foot, age >40, percent positive) guidelines.<sup>17</sup>

During this period, the NACDG screening series consisted of 70 allergens/allergen mixes. Compared with the previous period (2011–2012, 70 allergens), there were several changes: (1) the addition of a 2% aqueous (aq) concentration of formaldehyde and a 100% aq concentration of propylene glycol, supplementing formaldehyde 1% aq and propylene glycol 30% aq already on the screening series; (2) the addition of the following 5 allergens: methylisothiazolinone 0.2% aq, diphenylguanidine 1% in pet, benzophenone-4 10% in pet, parthenolide 0.1% in pet, and ethylhexylglycerin 5% in pet; and (3) the removal of benzyl alcohol, carmine, dibucaine, d-limonene, majantol, mercapto mix, and shellac.

## RESULTS

### Patient Characteristics

Demographics of patch-tested patients are summarized in Tables 1 to 3. Most were white (81.1%) and female (70.0%). The average age was 49 years (range, 2–97; median, 50). The most common primary sites of dermatitis were the following: hands, scattered/generalized pattern, and face. Of the 4871 patients tested, 66.8% (n = 3255) had at least 1 positive reaction, 30.5% (n = 1487) were polysensitized (≥3 allergic reactions,<sup>19</sup> Table 4), and 49.9% had a final primary diagnosis of ACD.

### Occupation

Among all tested patients, 8.9% (n = 434) had ACD that was determined to be related to their occupation (Table 1). Of the 867

**TABLE 2. Race and Occupation of Patch-Tested Patients**

| Characteristic                              | n (%)       |
|---------------------------------------------|-------------|
| Race (N = 4871)                             |             |
| White                                       | 3948 (81.1) |
| Asiatic                                     | 368 (7.6)   |
| Black                                       | 237 (4.9)   |
| Other/not specified                         | 200 (4.1)   |
| Hispanic                                    | 97 (2.0)    |
| Occupation (n = 4693*)                      |             |
| Not working <sup>†</sup>                    | 1890 (40.3) |
| Managerial or professional                  | 1305 (27.8) |
| Technical, sales, or administrative support | 632 (13.5)  |
| Service                                     | 386 (7.9)   |
| Operators, fabricators, and laborers        | 237 (5.1)   |
| Precision production, craft, and repair     | 217 (4.6)   |

\*Excludes 178 individuals missing industry/occupation codes.

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

**TABLE 3. Body Sites of Dermatitis and Final Diagnoses**

| Characteristic               | Primary, n (%)        | Total of up to 3 Listed*, n (%) <sup>†</sup> |
|------------------------------|-----------------------|----------------------------------------------|
| Dermatitis site <sup>‡</sup> | n = 4854*             | N = 4871                                     |
| Hand                         | 982 (20.2)            | 1180 (24.2)                                  |
| Scattered/generalized        | 808 (16.6)            | 1039 (21.3)                                  |
| Face                         | 755 (15.5)            | 1094 (22.5)                                  |
| Eyelids                      | 514 (10.5)            | 626 (12.9)                                   |
| Trunk                        | 319 (6.6)             | 704 (14.5)                                   |
| Arm                          | 251 (5.2)             | 781 (16.0)                                   |
| Leg                          | 224 (4.6)             | 589 (12.1)                                   |
| Scalp                        | 210 (4.3)             | 314 (6.5)                                    |
| Lips                         | 187 (3.9)             | 253 (5.2)                                    |
| Anal/genital                 | 147 (3.0)             | 198 (4.1)                                    |
| Foot                         | 126 (2.6)             | 273 (5.6)                                    |
| Other                        | 85 (1.8)              | 112 (2.3)                                    |
| Neck                         | 82 (1.7)              | 464 (9.5)                                    |
| Most exposed areas           | 56 (1.2)              | 66 (1.4)                                     |
| Ears                         | 54 (1.1)              | 122 (2.5)                                    |
| Eyes                         | 32 (0.7)              | 55 (1.1)                                     |
| Only under clothes           | 17 (0.4)              | 23 (0.5)                                     |
| Erythroderma                 | 4 (0.1)               | 7 (0.1)                                      |
| Nose                         | 1 (0.0)               | 5 (0.1)                                      |
| Final diagnoses              | n = 4832 <sup>§</sup> | N = 4871                                     |
| ACD                          | 2412 (49.9)           | 2809 (57.7)                                  |
| Other dermatitis             | 715 (14.8)            | 829 (17.0)                                   |
| Atopic dermatitis            | 622 (12.9)            | 836 (17.2)                                   |
| Irritant contact dermatitis  | 362 (7.5)             | 641 (13.2)                                   |
| Other dermatoses             | 361 (7.5)             | 494 (10.1)                                   |
| Psoriasis                    | 135 (2.8)             | 205 (4.2)                                    |
| Seborrheic dermatitis        | 63 (1.3)              | 84 (1.7)                                     |
| Nummular dermatitis          | 59 (1.2)              | 83 (1.7)                                     |
| Photo dermatitis             | 49 (1.0)              | 71 (1.5)                                     |
| Pompholyx                    | 24 (0.5)              | 30 (0.6)                                     |
| Stasis dermatitis            | 16 (0.3)              | 26 (0.5)                                     |
| Contact urticaria            | 14 (0.3)              | 33 (0.7)                                     |

\*Excludes 17 patients with no primary site listed.

<sup>†</sup>Total of percentages may exceed 100% because up to 3 sites/diagnoses per patient could be listed.

<sup>‡</sup>Total of any of up to 3 sites or up to 3 diagnoses listed.

<sup>§</sup>Excludes 39 patients with no primary final diagnosis.

patients with a relevant irritant identified (17.8% of the patch-tested population), 41.1% (n = 356) were deemed occupationally related. Of the 1030 patients who had relevant non-NACDG allergens identified, 14.6% (n = 150) were related to their occupation. Of those with occupational data (n = 4693), 40.3% (n = 1890) were not working (Table 2). Major occupational groups included professional specialties (n = 735, 15.7%), executive/administrative/managerial positions (n = 570, 12.1%), clerical support (n = 319, 6.8%), and sales (n = 192, 4.1%).

### Allergen Frequencies

Of the 9726 positive allergic reactions, the top 10 most frequent allergens (and respective prevalence rates) were nickel sulfate (20.1%),

fragrance mix I (11.9%), methylisothiazolinone (10.9%), neomycin (8.4%), bacitracin (7.4%), cobalt chloride (7.4%), *Myroxylon pereirae* (7.2%), *p*-phenylenediamine (7.0%), formaldehyde 2% (7.0%), and methylchloroisothiazolinone/methylisothiazolinone (MCI/MI, 6.4%). The performance of the new allergens/concentration changes/vehicle changes, in order of frequency, was MI (10.9%), formaldehyde 2.0% (7.0%), diphenylguanidine (3.8%), propylene glycol 100% (2.8%), benzophenone-4 (2.1%), parthenolide (0.8%), and ethylhexylglycerin (0.2%, Tables 5, 6).

### Comparison of Prevalence Rates for Allergens Between 2013–2014 and 2011–2012

As shown in Table 6, positive reaction rates significantly increased for 3 of the top 25 allergens (MCI/MI, oleamidopropyl dimethylamine [OPDMA], and hydroxyethyl methacrylate [HEMA]) and significantly decreased for 6 of the NACDG allergens (quaternium-15, diazolidinyl urea, dimethylol dimethyl [DMDM] hydantoin, glutaraldehyde, paraben mix, and hydrocortisone-17-butyrate).

### Comparison of Prevalence Rates for Allergens Between 2013–2014 and 2001–2012

When the positive reaction rates of each allergen in 2013–2014 were compared with the pooled prevalence rates for allergens that had been tested in each 2-year cycle for the previous 12 years (2001–2012), the following 5 allergens of the top 25 had statistically significantly higher rates in 2013–2014: nickel, fragrance mix I, *p*-phenylenediamine, MCI/MI, and lanolin. In addition, some of the top 25 allergens that had been added to the screening series at some point in the 2001–2012 period showed statistically higher rates in the 2013–2014 period: fragrance mix II, iodopropynyl butylcarbamate, cinnamic aldehyde, OPDMA, and HEMA. Twenty-two allergens had statistically lower rates in the 2013–2014 period as compared with those in the 2001–2012 period (neomycin, *M. pereirae*, formaldehyde 1% aq, quaternium-15, methyltribromo glutaronitrile/ phenoxyethanol, thiuram mix, potassium dichromate, propylene glycol 30% aq, colophony, propolis, diazolidinyl urea, imidazolidinyl

**TABLE 4. Number of Positive Patch Test Reactions per Patient**

| No. Positive Reactions to NACDG Screening Series | No. Patients | % (N = 4871) |
|--------------------------------------------------|--------------|--------------|
| 0                                                | 1616         | 33.2         |
| 1                                                | 946          | 20.8         |
| 2                                                | 822          | 16.2         |
| 3                                                | 527          | 10.5         |
| 4                                                | 348          | 6.3          |
| 5                                                | 228          | 3.6          |
| 6                                                | 140          | 2.3          |
| 7                                                | 95           | 1.6          |
| 8                                                | 49           | 0.9          |
| 9                                                | 30           | 0.7          |
| >10                                              | 70           | 1.0          |

**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                                 | 4850 | 975                | 258 (26.5)            | 344 (35.3) | 345 (35.4) | 27 (2.8)  |  | 10 (1.0)      | 197 (20.2) | 297 (30.5) | 338 (34.7) |
| Fragrance mix I, 8.0% pet                                            | 4858 | 576                | 80 (13.9)             | 153 (26.6) | 289 (50.2) | 50 (8.7)  |  | 10 (1.7)      | 183 (31.8) | 293 (50.9) | 25 (4.3)   |
| MI, 0.2% aq                                                          | 4857 | 527                | 152 (28.8)            | 159 (30.2) | 181 (34.3) | 31 (5.9)  |  | 38 (7.2)      | 240 (45.5) | 213 (40.4) | 9 (1.7)    |
| Neomycin sulfate, 20.0% pet                                          | 4857 | 409                | 59 (14.4)             | 91 (22.2)  | 213 (52.1) | 46 (11.2) |  | 15 (3.7)      | 49 (12.0)  | 37 (9.0)   | 217 (53.1) |
| Cobalt (II) chloride hexahydrate, 1.0% pet                           | 4859 | 361                | 78 (21.6)             | 117 (32.4) | 148 (41.0) | 18 (5.0)  |  | 0 (0.0)       | 30 (8.3)   | 122 (33.8) | 123 (34.1) |
| Bacitracin, 20.0% pet                                                | 4858 | 360                | 65 (18.1)             | 134 (37.2) | 130 (36.1) | 30 (8.3)  |  | 19 (5.3)      | 78 (21.7)  | 45 (12.5)  | 147 (40.8) |
| <i>Myroxylon pereirae</i> resin (balsam of Peru), 25.0% pet          | 4859 | 348                | 36 (10.3)             | 85 (24.4)  | 184 (52.9) | 41 (11.8) |  | 5 (1.4)       | 114 (32.8) | 187 (53.7) | 12 (3.4)   |
| 4-Phenylenediamine base, 1.0% pet                                    | 4853 | 342                | 105 (30.7)            | 81 (23.7)  | 138 (40.4) | 16 (4.7)  |  | 8 (2.3)       | 155 (45.3) | 73 (21.3)  | 57 (16.7)  |
| Formaldehyde, 2.0% aq                                                | 4858 | 339                | 48 (14.2)             | 129 (38.1) | 149 (44.0) | 13 (3.8)  |  | 1 (0.3)       | 75 (22.1)  | 208 (61.4) | 8 (2.4)    |
| MCI/MI, 0.01% aq                                                     | 4856 | 309                | 11 (3.6)              | 102 (33.0) | 177 (57.3) | 18 (5.8)  |  | 23 (7.4)      | 137 (44.3) | 125 (40.5) | 8 (2.6)    |
| Fragrance mix II, 14.0% pet                                          | 4859 | 277                | 23 (8.3)              | 56 (20.2)  | 165 (59.6) | 33 (11.9) |  | 7 (2.5)       | 102 (36.8) | 140 (50.5) | 7 (2.5)    |
| Formaldehyde, 1.0% aq                                                | 4858 | 274                | 26 (9.5)              | 75 (27.4)  | 145 (52.9) | 28 (10.2) |  | 0 (0.0)       | 50 (18.2)  | 175 (63.9) | 7 (2.6)    |
| Lanolin alcohol (Amerchol L 101), 50% pet                            | 4859 | 260                | 18 (6.9)              | 49 (18.8)  | 149 (57.3) | 43 (16.5) |  | 7 (2.7)       | 101 (38.8) | 118 (45.4) | 4 (1.5)    |
| Quaternium-15, 2.0% pet                                              | 4856 | 235                | 54 (23.0)             | 54 (23.0)  | 108 (46.0) | 19 (8.1)  |  | 1 (0.4)       | 46 (19.6)  | 159 (67.7) | 11 (4.7)   |
| Carba mix, 3.0% pet                                                  | 4859 | 234                | 16 (6.8)              | 52 (22.2)  | 139 (59.4) | 22 (9.4)  |  | 8 (3.4)       | 56 (23.9)  | 109 (46.6) | 23 (9.8)   |
| Iodopropynyl butylcarbamate, 0.5% pet                                | 4859 | 229                | 10 (4.4)              | 44 (19.2)  | 127 (55.5) | 47 (20.5) |  | 8 (3.5)       | 71 (31.0)  | 118 (51.5) | 6 (2.6)    |
| Cinnamal (cinnamic aldehyde), 1.0% pet                               | 4858 | 203                | 10 (4.9)              | 50 (24.6)  | 126 (62.1) | 15 (7.4)  |  | 2 (1.0)       | 74 (36.5)  | 95 (46.8)  | 10 (4.9)   |
| Diphenylguanidine, 1.0% pet                                          | 4859 | 185                | 4 (2.2)               | 41 (22.2)  | 114 (61.6) | 24 (13.0) |  | 7 (3.8)       | 31 (16.8)  | 88 (47.6)  | 6 (3.2)    |
| Methyldibromo glutaronitrile/phenoxxyethanol (Euxyl K 400), 2.0% pet | 4855 | 179                | 12 (6.7)              | 50 (27.9)  | 98 (54.7)  | 19 (10.6) |  | 1 (0.6)       | 41 (22.9)  | 96 (53.6)  | 4 (2.2)    |
| OPDMA, 0.1% aq                                                       | 4859 | 172                | 6 (3.5)               | 42 (24.4)  | 107 (62.2) | 17 (9.9)  |  | 1 (0.6)       | 29 (16.9)  | 114 (66.3) | 5 (2.9)    |
| Thiuram mix, 1.0% pet                                                | 4859 | 153                | 40 (26.1)             | 44 (28.8)  | 63 (41.2)  | 5 (3.3)   |  | 7 (4.6)       | 44 (28.8)  | 63 (41.2)  | 20 (13.1)  |
| Propylene glycol, 100.0% aq                                          | 4859 | 137                | 17 (12.4)             | 32 (23.4)  | 69 (50.4)  | 19 (13.9) |  | 11 (8.0)      | 59 (43.1)  | 49 (35.8)  | 2 (1.5)    |
| 2-HEMA, 2.0% pet                                                     | 4859 | 128                | 33 (25.8)             | 37 (28.9)  | 53 (41.4)  | 5 (3.9)   |  | 1 (0.8)       | 35 (27.3)  | 23 (18.0)  | 29 (22.7)  |
| Propylene glycol, 30.0% aq                                           | 4859 | 106                | 3 (2.8)               | 21 (19.8)  | 47 (44.3)  | 33 (31.1) |  | 9 (8.5)       | 47 (44.3)  | 42 (39.6)  | 0 (0.0)    |
| Potassium dichromate, 0.25% pet                                      | 4859 | 105                | 20 (19.0)             | 29 (27.6)  | 50 (47.6)  | 5 (4.8)   |  | 0 (0.0)       | 16 (15.2)  | 41 (39.0)  | 14 (13.3)  |
| Tixocortol-21-pivalate, 1.0% pet                                     | 4859 | 102                | 31 (30.4)             | 28 (27.5)  | 38 (37.3)  | 4 (3.9)   |  | 5 (4.9)       | 43 (42.2)  | 24 (23.5)  | 20 (19.6)  |
| 2-Bromo-2-nitropropane-1,3-diol (Bronopol), 0.5% pet                 | 4859 | 101                | 11 (10.9)             | 27 (26.7)  | 58 (57.4)  | 5 (5.0)   |  | 5 (5.0)       | 23 (22.8)  | 61 (60.4)  | 2 (2.0)    |
| Benzophenone-4, 10.0% pet                                            | 4857 | 100                | 2 (2.0)               | 10 (10.0)  | 75 (75.0)  | 13 (13.0) |  | 0 (0.0)       | 20 (20.0)  | 53 (53.0)  | 9 (9.0)    |
| Colophony (rosin), 20.0% pet                                         | 4858 | 92                 | 18 (19.6)             | 27 (29.3)  | 39 (42.4)  | 8 (8.7)   |  | 3 (3.3)       | 11 (12.0)  | 22 (23.9)  | 35 (38.0)  |
| Dimethylaminopropylamine, 1.0% aq                                    | 4858 | 89                 | 9 (10.1)              | 18 (20.2)  | 52 (58.4)  | 9 (10.1)  |  | 0 (0.0)       | 20 (22.5)  | 58 (65.2)  | 1 (1.1)    |
| Bisphenol A epoxy resin, 1.0% pet                                    | 4857 | 89                 | 23 (25.8)             | 30 (33.7)  | 32 (36.0)  | 4 (4.5)   |  | 2 (2.2)       | 28 (31.5)  | 15 (16.9)  | 22 (24.7)  |
| Decyl glucoside, 5.0% pet                                            | 4859 | 85                 | 8 (9.4)               | 15 (17.6)  | 46 (54.1)  | 15 (17.6) |  | 5 (5.9)       | 23 (27.1)  | 47 (55.3)  | 2 (2.4)    |
| Compositae mix, 6.0% pet                                             | 4859 | 83                 | 12 (14.5)             | 28 (33.7)  | 32 (38.6)  | 11 (13.3) |  | 4 (4.8)       | 12 (14.5)  | 46 (55.4)  | 2 (2.4)    |
| Propolis, 10.0% pet                                                  | 4859 | 82                 | 17 (20.7)             | 18 (22.0)  | 39 (47.6)  | 7 (8.5)   |  | 2 (2.4)       | 13 (15.9)  | 42 (51.2)  | 4 (4.9)    |
| Benzocaine, 5.0% pet                                                 | 4851 | 79                 | 12 (15.2)             | 23 (29.1)  | 38 (48.1)  | 6 (7.6)   |  | 5 (6.3)       | 10 (12.7)  | 7 (8.9)    | 28 (35.4)  |
| Cocamidopropyl betaine, 1.0% aq                                      | 4859 | 77                 | 1 (1.3)               | 12 (15.6)  | 41 (53.2)  | 21 (27.3) |  | 3 (3.9)       | 31 (40.3)  | 40 (51.9)  | 0 (0.0)    |
| Diazolidinyl urea (Germall II), 1.0% pet                             | 4858 | 76                 | 6 (7.9)               | 19 (25.0)  | 43 (56.6)  | 8 (10.5)  |  | 5 (6.6)       | 19 (25.0)  | 46 (60.5)  | 4 (5.3)    |
| Imidazolidinyl urea, 2.0% pet                                        | 4859 | 76                 | 9 (11.8)              | 16 (21.1)  | 42 (55.3)  | 9 (11.8)  |  | 0 (0.0)       | 21 (27.6)  | 45 (59.2)  | 4 (5.3)    |

(Continued on next page)

|                                            |    |           |           |           |           |          |           |           |           |
|--------------------------------------------|----|-----------|-----------|-----------|-----------|----------|-----------|-----------|-----------|
| 4859                                       | 64 | 8 (12.5)  | 22 (34.4) | 34 (53.1) | 0 (0.0)   | 0 (0.0)  | 23 (35.9) | 14 (21.9) | 11 (17.2) |
| 4859                                       | 59 | 12 (20.3) | 15 (25.4) | 26 (44.1) | 0 (0.0)   | 0 (0.0)  | 7 (11.9)  | 41 (69.5) | 1 (1.7)   |
| 4859                                       | 58 | 18 (31.0) | 23 (39.7) | 15 (25.9) | 2 (3.4)   | 0 (0.0)  | 11 (19.0) | 10 (17.2) | 17 (29.3) |
| 4859                                       | 58 | 3 (5.2)   | 9 (15.5)  | 25 (43.1) | 20 (34.5) | 1 (1.7)  | 13 (22.4) | 42 (72.4) | 0 (0.0)   |
| 4859                                       | 55 | 7 (12.7)  | 11 (20.0) | 35 (63.6) | 2 (3.6)   | 2 (3.6)  | 20 (36.4) | 12 (21.8) | 9 (16.4)  |
| 4859                                       | 51 | 12 (23.5) | 21 (41.2) | 17 (33.3) | 1 (2.0)   | 3 (5.9)  | 7 (13.7)  | 12 (23.5) | 10 (19.6) |
| 4859                                       | 50 | 10 (20.0) | 20 (40.0) | 19 (38.0) | 1 (2.0)   | 0 (0.0)  | 11 (22.0) | 15 (30.0) | 6 (12.0)  |
| 4859                                       | 49 | 0 (0.0)   | 10 (20.4) | 30 (61.2) | 9 (18.4)  | 6 (12.2) | 16 (32.7) | 22 (44.9) | 1 (2.0)   |
| 4859                                       | 49 | 10 (20.4) | 15 (30.6) | 21 (42.9) | 2 (4.1)   | 8 (16.3) | 13 (26.5) | 5 (10.2)  | 13 (26.5) |
| 4859                                       | 48 | 13 (27.1) | 17 (35.4) | 16 (33.3) | 2 (4.2)   | 3 (6.2)  | 6 (12.5)  | 14 (29.2) | 7 (14.6)  |
| 4859                                       | 48 | 7 (14.6)  | 6 (12.5)  | 21 (43.8) | 14 (29.2) | 0 (0.0)  | 23 (47.9) | 14 (29.2) | 1 (2.1)   |
| 4859                                       | 44 | 10 (22.7) | 14 (31.8) | 20 (45.5) | 0 (0.0)   | 5 (11.4) | 19 (43.2) | 8 (18.2)  | 6 (13.6)  |
| 4859                                       | 43 | 15 (34.9) | 16 (37.2) | 11 (25.6) | 1 (2.3)   | 1 (2.3)  | 11 (25.6) | 16 (37.2) | 0 (0.0)   |
| 4859                                       | 43 | 3 (7.0)   | 11 (25.6) | 27 (62.8) | 2 (4.7)   | 3 (7.0)  | 13 (30.2) | 8 (18.6)  | 3 (7.0)   |
| 4859                                       | 42 | 19 (45.2) | 13 (31.0) | 9 (21.4)  | 1 (2.4)   | 2 (4.8)  | 9 (21.4)  | 14 (33.3) | 13 (31.0) |
| 4859                                       | 42 | 3 (7.1)   | 8 (19.0)  | 23 (54.8) | 7 (16.7)  | 1 (2.4)  | 12 (28.6) | 24 (57.1) | 0 (0.0)   |
| 4859                                       | 41 | 9 (22.0)  | 14 (34.1) | 15 (36.6) | 3 (7.3)   | 1 (2.4)  | 11 (26.8) | 15 (36.6) | 0 (0.0)   |
| 4858                                       | 41 | 8 (19.5)  | 15 (36.6) | 18 (43.9) | 0 (0.0)   | 0 (0.0)  | 5 (12.2)  | 8 (19.5)  | 7 (17.1)  |
| 4859                                       | 34 | 4 (11.8)  | 7 (20.6)  | 18 (52.9) | 5 (14.7)  | 0 (0.0)  | 9 (26.5)  | 14 (41.2) | 3 (8.8)   |
| 4859                                       | 31 | 4 (12.9)  | 10 (32.3) | 14 (45.2) | 2 (6.5)   | 2 (6.5)  | 14 (45.2) | 14 (45.2) | 0 (0.0)   |
| 2-hydroxy-4-methoxy-benzophenone), 10% pet |    |           |           |           |           |          |           |           |           |
| 4859                                       | 30 | 1 (3.3)   | 11 (36.7) | 12 (40.0) | 6 (20.0)  | 0 (0.0)  | 12 (40.0) | 18 (60.0) | 0 (0.0)   |
| 4859                                       | 29 | 1 (3.4)   | 5 (17.2)  | 14 (48.3) | 9 (31.0)  | 3 (10.3) | 12 (41.4) | 14 (48.3) | 0 (0.0)   |
| 4859                                       | 27 | 2 (7.4)   | 9 (33.3)  | 15 (55.6) | 1 (3.7)   | 2 (7.4)  | 4 (14.8)  | 14 (51.9) | 0 (0.0)   |
| 4859                                       | 25 | 7 (28.0)  | 6 (24.0)  | 11 (44.0) | 1 (4.0)   | 2 (8.0)  | 4 (16.0)  | 12 (48.0) | 2 (8.0)   |
| 4859                                       | 25 | 4 (16.0)  | 7 (28.0)  | 9 (36.0)  | 4 (16.0)  | 0 (0.0)  | 6 (24.0)  | 16 (64.0) | 1 (4.0)   |
| 4859                                       | 22 | 1 (4.5)   | 7 (31.8)  | 12 (54.5) | 2 (9.1)   | 0 (0.0)  | 7 (31.8)  | 4 (18.2)  | 1 (4.5)   |
| 4859                                       | 18 | 2 (11.1)  | 7 (38.9)  | 8 (44.4)  | 1 (5.6)   | 2 (11.1) | 3 (16.7)  | 5 (27.8)  | 1 (5.6)   |
| 4859                                       | 17 | 1 (5.9)   | 5 (29.4)  | 6 (35.3)  | 5 (29.4)  | 2 (11.8) | 5 (29.4)  | 7 (41.2)  | 0 (0.0)   |
| 4859                                       | 12 | 3 (25.0)  | 3 (25.0)  | 4 (33.3)  | 2 (16.7)  | 0 (0.0)  | 5 (41.7)  | 6 (50.0)  | 1 (8.3)   |
| 4859                                       | 6  | 0 (0.0)   | 4 (66.7)  | 1 (16.7)  | 0 (0.0)   | 0 (0.0)  | 1 (16.7)  | 4 (66.7)  | 0 (0.0)   |
| 4859                                       | 6  | 1 (16.7)  | 1 (16.7)  | 3 (50.0)  | 1 (16.7)  | 0 (0.0)  | 2 (33.3)  | 2 (33.3)  | 2 (33.3)  |
| 4859                                       | 5  | 1 (20.0)  | 0 (0.0)   | 2 (40.0)  | 2 (40.0)  | 0 (0.0)  | 1 (20.0)  | 3 (60.0)  | 1 (20.0)  |

\*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                                | 2013-2014 |        | 2013-2014 vs                |      | 2001-2012 |        |        |        |        |                              |              |              | 2013-2014 vs |               |
|----------------------------------------------------|-----------|--------|-----------------------------|------|-----------|--------|--------|--------|--------|------------------------------|--------------|--------------|--------------|---------------|
|                                                    | n*        | Pos, % | RR (95% CI)                 |      | Pos, %    | Pos, % | Pos, % | Pos, % | Pos, % | Pos, %                       | Pos, %       | Pos, %       | RR (95% CI)  | 2001-2012; P, |
|                                                    |           |        |                             |      |           |        |        |        |        |                              |              |              |              |               |
| Nickel sulfate, 2.5% pet                           | 4850      | 20.1   | 0.0523, 1.09<br>(1.00-1.18) | 18.5 | 15.5      | 19.5   | 19.0   | 18.7   | 16.9   | 0.0008, 1.11<br>(1.05-1.18)  | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Fragrance mix I, 8% pet                            | 4858      | 11.9   | 0.7494, 0.98<br>(0.88-1.10) | 12.1 | 8.5       | 9.4    | 11.5   | 9.1    | 10.2   | 0.0002, 1.18<br>(1.08-1.28)  | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| MI, 0.2% aq                                        | 4857      | 10.9   | —                           | —    | —         | —      | —      | —      | —      | —                            | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Neomycin, 20% pet                                  | 4857      | 8.4    | 0.2667, 0.93<br>(0.81-1.06) | 9.1  | 8.7       | 10.1   | 10.0   | 10.6   | 11.4   | 0.0006, 0.84<br>(0.76-0.93)  | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Bacitracin, 20% pet                                | 4858      | 7.4    | 0.4909, 0.95<br>(0.82-1.10) | 7.8  | 8.3       | 7.9    | 9.2    | 7.9    | 7.7    | 0.0930, 0.91<br>(0.82-1.02)  | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Cobalt chloride, 1% pet                            | 4859      | 7.4    | 0.8519, 1.01<br>(0.88-1.17) | 7.3  | 6.2       | 8.2    | 8.4    | 8.4    | 7.5    | 0.4945, 0.96<br>(0.87-1.07)  | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| <i>Myroxylon perei</i> , 25% pet                   | 4859      | 7.2    | 0.2040, 0.91<br>(0.79-1.05) | 7.9  | 7.2       | 11.0   | 11.9   | 10.6   | 11.5   | <0.0001, 0.71<br>(0.64-0.79) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| p-Phenylenediamine, 1% pet                         | 4853      | 7.0    | 0.1687, 1.11<br>(0.95-1.30) | 6.3  | 5.5       | 5.3    | 5.0    | 4.7    | 4.8    | <0.0001, 1.34<br>(1.20-1.51) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Formaldehyde, 2% aq                                | 4859      | 7.0    | —                           | —    | —         | —      | —      | —      | —      | —                            | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| MCI/MI, 0.01% aq                                   | 4856      | 6.4    | 0.0068, 1.26<br>(1.07-1.50) | 5.0  | 2.5       | 3.6    | 2.8    | 2.2    | 2.3    | <0.0001, 2.08<br>(1.84-2.37) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Fragrance mix II, 14% pet                          | 4859      | 5.7    | 0.3256, 0.91<br>(0.76-1.09) | 5.2  | 4.7       | 3.6    | —      | —      | —      | 0.0004, 1.28<br>(1.12-1.48)  | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Formaldehyde, 1% aq                                | 4858      | 5.6    | 0.0665, 0.86<br>(0.73-1.01) | 6.6  | 5.8       | 7.7    | 9.0    | 8.7    | 8.5    | <0.0001, 0.73<br>(0.64-0.82) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Lanolin alcohol (Amerchol L 101), 50% pet†         | 4859      | 5.4    | 0.0926, 1.17<br>(0.97-1.40) | 4.6  | 2.5       | 2.1    | 1.8    | 2.2    | 2.3    | <0.0001, 2.10<br>(1.83-2.42) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Carba mix, 3% pet                                  | 4859      | 4.8    | 0.8747, 1.01<br>(0.84-1.22) | 4.7  | 4.6       | 4.5    | 3.9    | 4.0    | 4.5    | 0.1576, 1.10<br>(0.96-1.27)  | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Quaternium-15, 2% pet                              | 4856      | 4.8    | 0.0009, 0.75<br>(0.63-0.89) | 6.4  | 5.8       | 8.6    | 10.3   | 8.9    | 9.3    | <0.0001, 0.58<br>(0.51-0.67) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Iodopropynyl butylcarbamate, 0.5% pet              | 4859      | 4.7    | 0.2447, 1.12<br>(0.92-1.36) | 4.2  | 4.3       | 3.1    | 2.4    | —      | —      | <0.0001, 1.36<br>(1.17-1.57) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Cinnamic aldehyde, 1% pet                          | 4858      | 4.2    | 0.4649, 1.08<br>(0.88-1.32) | 3.9  | 2.3       | 2.4    | 3.1    | 2.4    | —      | <0.0001, 1.50<br>(1.29-1.75) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Diphenylguanidine, 1% pet                          | 4859      | 3.8    | —                           | —    | —         | —      | —      | —      | —      | —                            | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| Methyldibromo glutaronitrile/phenoxethanol, 2% pet | 4855      | 3.7    | 0.9522, 0.99<br>(0.81-1.23) | 3.7  | 3.8       | 5.5    | 5.8    | 6.1    | 5.5    | <0.0001, 0.72<br>(0.62-0.84) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |
| OPDMA, 0.1% aq                                     | 4859      | 3.5    | 0.0006, 1.53<br>(1.20-1.95) | 2.3  | 1.8       | —      | —      | —      | —      | <0.0001, 1.73<br>(1.40-2.12) | 201-2012; P, | 2013-2014 vs | 201-2012; P, | RR (95% CI)   |

|                                                        |      |     |                             |     |     |     |     |     |     |                              |
|--------------------------------------------------------|------|-----|-----------------------------|-----|-----|-----|-----|-----|-----|------------------------------|
| Thiuram mix, 1% pet                                    | 4859 | 3.1 | 0.4159, 1.10<br>(0.87–1.39) | 2.9 | 3.1 | 3.4 | 3.9 | 4.6 | 4.6 | 0.0350, 0.84<br>(0.71–0.99)  |
| Propylene glycol, 100% aq                              | 4859 | 2.8 | —                           | —   | —   | —   | —   | —   | —   | —                            |
| HEMA, 2% pet                                           | 4859 | 2.6 | 0.0338, 1.34<br>(1.02–1.76) | 2.0 | 2.0 | 2.4 | —   | —   | —   | 0.0473, 1.23<br>(1.00–1.51)  |
| Potassium dichromate, 0.25% pet                        | 4859 | 2.2 | 0.0532, 1.35<br>(0.99–1.82) | 1.6 | 2.3 | 4.1 | 4.8 | 4.3 | 4.1 | <0.0001, 0.60<br>(0.49–0.73) |
| Propylene glycol, 30% aq                               | 4859 | 2.2 | 0.1483, 0.82<br>(0.63–1.07) | 2.6 | 3.2 | 2.1 | 2.9 | 3.3 | 4.1 | 0.0011, 0.72<br>(0.59–0.88)  |
| 2-Bromo-2-nitro-1,3-propanediol,<br>0.5% pet           | 4859 | 2.1 | 0.0805, 1.31<br>(0.97–1.78) | 1.6 | 1.0 | 3.1 | 3.4 | 2.3 | 3.4 | 0.0851, 0.83<br>(0.68–1.03)  |
| Benzophenone-4, 10% pet                                | 4857 | 2.1 | —                           | —   | —   | —   | —   | —   | —   | —                            |
| Tixocortol-21-pivalate, 1% pet                         | 4859 | 2.1 | 0.4354, 0.90<br>(0.68–1.18) | 2.3 | 2.0 | 2.5 | 2.7 | 2.7 | 2.9 | 0.0721, 0.83<br>(0.67–1.02)  |
| Colophony, 20% pet                                     | 4858 | 1.9 | 0.2070, 0.83<br>(0.63–1.11) | 2.3 | 2.7 | 2.8 | 2.2 | 2.8 | 2.7 | 0.0041, 0.73<br>(0.59–0.91)  |
| Bisphenol A epoxy resin, 1% pet                        | 4857 | 1.8 | 0.1703, 1.25<br>(0.91–1.73) | 1.5 | 1.6 | 1.7 | 1.8 | 1.8 | 2.4 | 0.2906, 1.13<br>(0.90–1.41)  |
| Dimethylaminopropylamine, 1% aq                        | 4858 | 1.8 | 0.1716, 1.25<br>(0.91–1.73) | 1.5 | 2.0 | —   | —   | —   | —   | 0.6753, 1.06<br>(0.81–1.37)  |
| Compositae mix, 6% pet                                 | 4859 | 1.7 | 0.4611, 0.89<br>(0.66–1.21) | 1.9 | 1.9 | 1.4 | 1.2 | 1.3 | 1.0 | 0.1554, 1.19<br>(0.94–1.50)  |
| Decyl glucoside, 5% pet                                | 4859 | 1.7 | 0.4809, 1.12<br>(0.82–1.54) | 1.6 | 1.5 | —   | —   | —   | —   | 0.3443, 1.14<br>(0.87–1.49)  |
| Propolis, 10% pet                                      | 4859 | 1.7 | 0.6925, 0.94<br>(0.69–1.28) | 1.8 | 2.1 | 4.9 | —   | —   | —   | <0.0001, 0.55<br>(0.44–0.70) |
| Benzocaine, 5% pet                                     | 4851 | 1.6 | 0.4136, 1.15<br>(0.82–1.60) | 1.4 | 1.8 | 1.3 | 1.9 | 1.7 | 1.7 | 0.9950, 1.00<br>(0.79–1.27)  |
| Cocamidopropyl betaine, 1% aq                          | 4859 | 1.6 | 0.5773, 1.10<br>(0.79–1.53) | 1.4 | 1.4 | 1.1 | 1.8 | 1.8 | 2.9 | 0.4618, 0.91<br>(0.72–1.16)  |
| Diazolidinyl urea, 1% pet                              | 4858 | 1.6 | 0.0458, 0.74<br>(0.54–1.00) | 2.1 | 2.2 | 3.1 | 3.7 | 3.5 | 3.2 | <0.0001, 0.52<br>(0.41–0.66) |
| Imidazolidinyl urea, 2% pet                            | 4859 | 1.6 | 0.8012, 0.96<br>(0.69–1.32) | 1.6 | 2.2 | 2.4 | 2.9 | 2.9 | 3.1 | <0.0001, 0.62<br>(0.49–0.78) |
| Methyl methacrylate, 2% pet                            | 4859 | 1.3 | 0.0440, 1.51<br>(1.01–2.26) | 0.9 | 0.8 | 1.2 | 1.0 | 1.6 | 1.5 | 0.4069, 1.12<br>(0.86–1.46)  |
| Canaga odorata oil (ylang<br>ylang), 2% pet            | 4859 | 1.2 | 0.0147, 1.71<br>(1.11–2.65) | 0.7 | 1.3 | 1.4 | 1.5 | 1.2 | 1.2 | 0.9365, 0.99<br>(0.75–1.30)  |
| Ethylenediamine dihydrochloride,<br>1% pet             | 4859 | 1.2 | 0.5797, 0.90<br>(0.62–1.30) | 1.3 | 1.4 | 1.5 | 1.9 | 2.4 | 2.8 | 0.0007, 0.63<br>(0.48–0.82)  |
| Amidamine (stearamidopropyl<br>dimethylamine), 0.1% aq | 4859 | 1.2 | 0.9591, 0.99<br>(0.68–1.44) | 1.2 | 0.3 | 1.6 | 2.0 | 1.7 | 2.4 | 0.0600, 0.77<br>(0.59–1.01)  |
| Ethyl acrylate, 0.1% pet                               | 4859 | 1.1 | 0.3238, 1.23<br>(0.82–1.85) | 0.9 | 0.7 | 1.2 | 0.9 | 1.1 | 1.3 | 0.5320, 1.10<br>(0.82–1.46)  |

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TABLE 6. (Continued)

| Patch Test Allergen                                                     | 2013-2014 |        | 2013-2014 vs<br>2011-2012, P,<br>RR (95% CI) |        | 2001-2012            |                      |                      |                      |                      |                      |                                              |                                              | 2013-2014 vs<br>2011-2012, P,<br>RR (95% CI) |                                              |
|-------------------------------------------------------------------------|-----------|--------|----------------------------------------------|--------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|
|                                                                         | n*        | Pos, % | Pos, %                                       | Pos, % | 2011-2012,<br>Pos, % | 2009-2010,<br>Pos, % | 2007-2008,<br>Pos, % | 2005-2006,<br>Pos, % | 2003-2004,<br>Pos, % | 2001-2002,<br>Pos, % | 2013-2014 vs<br>2011-2012, P,<br>RR (95% CI) | 2013-2014 vs<br>2011-2012, P,<br>RR (95% CI) | 2013-2014 vs<br>2011-2012, P,<br>RR (95% CI) | 2013-2014 vs<br>2011-2012, P,<br>RR (95% CI) |
|                                                                         |           |        |                                              |        |                      |                      |                      |                      |                      |                      |                                              |                                              |                                              |                                              |
| Mixed dialkyl thioureas, 1.0% pet                                       | 4859      | 1.0    | 0.0637, 1.53<br>(0.97-2.41)                  | 0.7    | 1.0                  | 1.0                  | 0.9                  | 1.0                  | 1.0                  | 0.7                  | 0.2636, 1.19<br>(0.88-1.60)                  | 0.2636, 1.19<br>(0.88-1.60)                  | 0.2636, 1.19<br>(0.88-1.60)                  | 0.2636, 1.19<br>(0.88-1.60)                  |
| Black rubber mix, 0.6% pet                                              | 4859      | 1.0    | 0.3179, 0.82<br>(0.56-1.21)                  | 1.3    | 0.7                  | 0.7                  | 1.0                  | 1.0                  | 1.0                  | 1.0                  | 0.7910, 1.04<br>(0.77-1.41)                  | 0.7910, 1.04<br>(0.77-1.41)                  | 0.7910, 1.04<br>(0.77-1.41)                  | 0.7910, 1.04<br>(0.77-1.41)                  |
| DMDM hydantoin, 1% pet                                                  | 4859      | 1.0    | 0.0149, 0.64<br>(0.44-0.92)                  | 1.6    | 1.0                  | 1.0                  | 2.7                  | 2.6                  | 2.3                  | 2.8                  | <0.0001, 0.46<br>(0.35-0.62)                 | <0.0001, 0.46<br>(0.35-0.62)                 | <0.0001, 0.46<br>(0.35-0.62)                 | <0.0001, 0.46<br>(0.35-0.62)                 |
| Lidocaine, 15% pet                                                      | 4859      | 1.0    | 0.2509, 1.29<br>(0.83-2.01)                  | 0.8    | 0.7                  | 0.7                  | 0.9                  | 1.1                  | 0.6                  | 0.7                  | 0.1367, 1.26<br>(0.98-1.72)                  | 0.1367, 1.26<br>(0.98-1.72)                  | 0.1367, 1.26<br>(0.98-1.72)                  | 0.1367, 1.26<br>(0.98-1.72)                  |
| p-tert-Butylphenol formaldehyde resin, 1% pet                           | 4859      | 1.0    | 0.7239, 0.93<br>(0.62-1.39)                  | 1.1    | 1.5                  | 1.5                  | 1.2                  | 1.3                  | 1.8                  | 1.9                  | 0.0081, 0.67<br>(0.50-0.90)                  | 0.0081, 0.67<br>(0.50-0.90)                  | 0.0081, 0.67<br>(0.50-0.90)                  | 0.0081, 0.67<br>(0.50-0.90)                  |
| Disperse blue mix 106/124, 1% pet <sup>†</sup>                          | 4859      | 1.0    | 0.8019, 0.95<br>(0.63-1.43)                  | 1.0    | 1.0                  | 1.0                  | 0.9                  | 2.1                  | 1.9                  | 3.0                  | 0.0005, 0.60<br>(0.44-0.80)                  | 0.0005, 0.60<br>(0.44-0.80)                  | 0.0005, 0.60<br>(0.44-0.80)                  | 0.0005, 0.60<br>(0.44-0.80)                  |
| Tea tree oil, oxidized, 5% pet                                          | 4859      | 0.9    | 0.7807, 1.06<br>(0.69-1.65)                  | 0.9    | 1.0                  | 1.0                  | 1.4                  | 1.4                  | 0.9                  | —                    | 0.2027, 0.81<br>(0.59-1.12)                  | 0.2027, 0.81<br>(0.59-1.12)                  | 0.2027, 0.81<br>(0.59-1.12)                  | 0.2027, 0.81<br>(0.59-1.12)                  |
| Sesquiterpene lactone mix, 0.1% pet                                     | 4859      | 0.9    | 0.2848, 1.29<br>(0.81-2.06)                  | 0.7    | 0.6                  | 0.6                  | 0.6                  | 0.7                  | 0.6                  | 0.6                  | 0.0426, 1.41<br>(1.01-1.96)                  | 0.0426, 1.41<br>(1.01-1.96)                  | 0.0426, 1.41<br>(1.01-1.96)                  | 0.0426, 1.41<br>(1.01-1.96)                  |
| Tosylamide formaldehyde resin, 10% pet                                  | 4859      | 0.9    | 0.1079, 0.72<br>(0.48-1.08)                  | 1.2    | 0.9                  | 0.9                  | 1.0                  | 1.3                  | 1.7                  | 1.5                  | 0.0202, 0.69<br>(0.50-0.95)                  | 0.0202, 0.69<br>(0.50-0.95)                  | 0.0202, 0.69<br>(0.50-0.95)                  | 0.0202, 0.69<br>(0.50-0.95)                  |
| Budesonide, 0.1% pet                                                    | 4859      | 0.9    | 0.8463, 1.05<br>(0.67-1.63)                  | 0.8    | 0.8                  | 0.8                  | 0.9                  | 1.5                  | 1.8                  | 1.1                  | 0.0604, 0.74<br>(0.54-1.02)                  | 0.0604, 0.74<br>(0.54-1.02)                  | 0.0604, 0.74<br>(0.54-1.02)                  | 0.0604, 0.74<br>(0.54-1.02)                  |
| Cocamide DEA, 0.5% pet                                                  | 4859      | 0.9    | 0.9453, 1.02<br>(0.65-1.58)                  | 0.9    | 0.9                  | 0.9                  | 1.2                  | 1.0                  | 1.1                  | 1.2                  | 0.2333, 0.82<br>(0.60-1.14)                  | 0.2333, 0.82<br>(0.60-1.14)                  | 0.2333, 0.82<br>(0.60-1.14)                  | 0.2333, 0.82<br>(0.60-1.14)                  |
| Parthenolide, 0.1% pet                                                  | 4859      | 0.8    | —                                            | —      | —                    | —                    | —                    | —                    | —                    | —                    | —                                            | —                                            | —                                            | —                                            |
| Glutaral, 1% pet                                                        | 4858      | 0.8    | 0.0027, 0.56<br>(0.38-0.82)                  | 1.5    | 0.9                  | 0.9                  | 1.1                  | 1.3                  | 1.2                  | 1.3                  | 0.0253, 0.69<br>(0.50-0.96)                  | 0.0253, 0.69<br>(0.50-0.96)                  | 0.0253, 0.69<br>(0.50-0.96)                  | 0.0253, 0.69<br>(0.50-0.96)                  |
| Carvone, 5% pet                                                         | 4859      | 0.7    | 0.5192, 1.18<br>(0.71-1.98)                  | 0.6    | 1.1                  | 1.1                  | —                    | —                    | —                    | —                    | 0.3654, 0.83<br>(0.55-1.24)                  | 0.3654, 0.83<br>(0.55-1.24)                  | 0.3654, 0.83<br>(0.55-1.24)                  | 0.3654, 0.83<br>(0.55-1.24)                  |
| 2-Hydroxy-4-methoxy-benzophenone (benzophenone-3), 10% pet <sup>§</sup> | 4859      | 0.6    | 0.2891, 0.77<br>(0.48-1.25)                  | 0.8    | 0.9                  | 0.9                  | 0.9                  | 0.7                  | 0.7                  | 0.6                  | 0.3176, 0.83<br>(0.57-1.20)                  | 0.3176, 0.83<br>(0.57-1.20)                  | 0.3176, 0.83<br>(0.57-1.20)                  | 0.3176, 0.83<br>(0.57-1.20)                  |
| Paraben mix, 12% pet                                                    | 4859      | 0.6    | 0.0002, 0.44<br>(0.29-0.69)                  | 1.4    | 0.8                  | 0.8                  | 1.1                  | 1.2                  | 1.1                  | 0.6                  | 0.0065, 0.60<br>(0.41-0.87)                  | 0.0065, 0.60<br>(0.41-0.87)                  | 0.0065, 0.60<br>(0.41-0.87)                  | 0.0065, 0.60<br>(0.41-0.87)                  |
| Tocopherol (DL- $\alpha$ -tocopherol), 100.0%                           | 4859      | 0.6    | 0.5057, 0.84<br>(0.51-1.40)                  | 0.7    | 1.0                  | 1.0                  | 1.0                  | 0.7                  | 1.1                  | 1.1                  | 0.0179, 0.63<br>(0.43-0.93)                  | 0.0179, 0.63<br>(0.43-0.93)                  | 0.0179, 0.63<br>(0.43-0.93)                  | 0.0179, 0.63<br>(0.43-0.93)                  |
| <i>Mentha piperita</i> oil (peppermint oil), 2% pet                     | 4859      | 0.6    | 0.3779, 1.31<br>(0.72-2.37)                  | 0.4    | 0.6                  | 0.6                  | —                    | —                    | —                    | —                    | 0.7591, 1.08<br>(0.67-1.74)                  | 0.7591, 1.08<br>(0.67-1.74)                  | 0.7591, 1.08<br>(0.67-1.74)                  | 0.7591, 1.08<br>(0.67-1.74)                  |
| Mercaptobenzothiazole, 1% pet                                           | 4859      | 0.5    | 0.5197, 1.04<br>(0.58-1.85)                  | 0.5    | 0.7                  | 0.7                  | 1.0                  | 0.9                  | 1.3                  | 0.8                  | 0.0089, 0.58<br>(0.39-0.88)                  | 0.0089, 0.58<br>(0.39-0.88)                  | 0.0089, 0.58<br>(0.39-0.88)                  | 0.0089, 0.58<br>(0.39-0.88)                  |

|                                                                            |      |     |                             |     |     |     |     |     |                              |
|----------------------------------------------------------------------------|------|-----|-----------------------------|-----|-----|-----|-----|-----|------------------------------|
| <i>Jasminum officinale</i> oil<br>( <i>Jasminum grandiflorum</i> ), 2% pet | 4859 | 0.5 | 0.6544, 1.15<br>(0.63–2.08) | 0.4 | 1.0 | —   | —   | —   | 0.1417, 0.71<br>(0.45–1.12)  |
| 4-Chloro-3,5-xylene (PCMX,<br>chloroxylene), 1% pet                        | 4859 | 0.5 | 0.5377, 0.83<br>(0.46–1.49) | 0.5 | 0.5 | 0.4 | 0.5 | 0.7 | 0.4318, 0.84<br>(0.54–1.31)  |
| Ethyl-2-cyanoacrylate, 10.0% pet                                           | 4859 | 0.4 | 0.7513, 1.12<br>(0.56–2.25) | 0.3 | —   | —   | —   | —   | —                            |
| <i>Lavandula angustifolia</i> oil<br>(lavender oil), 2% pet                | 4859 | 0.3 | 0.8219, 0.92<br>(0.47–1.83) | 0.4 | 0.2 | —   | —   | —   | 0.5718, 1.19<br>(0.65–2.21)  |
| Ethylhexylglycerin, 5% pet                                                 | 4859 | 0.2 | —                           | —   | —   | —   | —   | —   | —                            |
| Desoximetasone, 1% pet                                                     | 4859 | 0.1 | 0.2002, 0.52<br>(0.19–1.44) | 0.2 | 0.2 | 0.2 | —   | —   | 0.2173, 0.58<br>(0.24–1.39)  |
| Clobetasol-17-propionate, 1% pet                                           | 4859 | 0.1 | 0.1328, 0.47<br>(0.18–1.28) | 0.3 | 0.3 | 0.6 | 0.8 | 0.7 | 0.0001, 0.23<br>(0.10–0.52)  |
| Hydrocortisone-17-butyrate, 1% pet                                         | 4859 | 0.1 | 0.0176, 0.31<br>(0.11–0.86) | 0.3 | 0.7 | 0.5 | 0.6 | 0.5 | <0.0001, 0.20<br>(0.08–0.49) |

\*Number tested to specific allergen.

†2009–2010 cycle lanolin alcohol tested at 30% concentration.

‡2007–2008 cycle tested disperse blue T06 (not the 124/106 mix).

§2007–2008 cycle tested 3% benzophenone (not 10%).

CI indicates confidence interval; NC, not calculated; NT, not tested; pet, petrolatum; Pos, positive; PCMX, para chloro meta xylene.

urea, ethylenediamine hydrochloride, DMDM hydantoin, *p*-tert-butylphenol formaldehyde resin, tosylamide formaldehyde resin, glutaraldehyde, paraben mix, tocopherol, mercaptobenzothiazole, clobetasol-17-propionate, and hydrocortisone-17-butyrate).

### Detection Rate of the NACDG Screening Series

Of the 4871 patients, 1030 (21.1%) had a relevant allergen not on the NACDG screening series. Of these non-NACDG allergens, 14.6% were occupationally related ( $n = 150$ ). Specific names of non-NACDG allergens were 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 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, an NACDG antigen 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 35 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 75.9% (7381/9726). 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 66.0% (6416/9726). Importantly, these calculations do not include the 21.7% of patients who had clinically relevant reactions to allergens not present on the NACDG standard series.

### Significance-Prevalence Index Numbers for NACDG Allergens

The SPIN calculations<sup>17</sup> and order ranking for this reporting period are listed in Table 8. This calculation allows for the identification of “hot allergens,” incorporating a composite measure of clinical relevance combined with prevalence.

### 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. Allergens

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

| Source                                                        | No. Patients | % (n = 1030) |
|---------------------------------------------------------------|--------------|--------------|
| Cosmetics, beauty preparations, skin and health care products | 406          | 39.4         |
| Drugs, medications, alcoholic beverages                       | 242          | 23.5         |
| Clothing, wearing apparel, protective equipment, textiles     | 171          | 16.6         |
| Animals, infectious agents, plants, minerals, persons         | 67           | 6.5          |
| Chemicals and chemical products                               | 66           | 6.4          |

with positive reactions having a greater than 30% proportion of past relevance are noted in Table 9.

### Common Sources of Irritants

Relevant irritants were observed in 867 patients (17.8%). Among the 867 with relevant irritants, 356 (41.1%) were occupationally related. The most common sources of identified irritants were cosmetic/personal care products (Table 10).

### DISCUSSION

Many of the current findings are consistent with previous NACDG reports. As compared with the last reporting cycle, the individual components of MOAHLFAP<sup>18</sup> varied by less than 5%. The polysensitization rate in the last cycle was 26.9% as compared with 31.0% in this cycle. Sites of dermatitis and final diagnoses (Table 3) were relatively similar.<sup>13</sup>

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*), 5 preservatives (MI, MCI/MI, formaldehyde [1% and 2%], quaternium-15, and iodopropynyl butylcarbamate), *p*-phenylenediamine, lanolin alcohol, and carba mix. As compared with the 2011–2012 cycle, only 1 allergen, MI, broke into the top 15 group debuting in third place, whereas cinnamic aldehyde moved down 1 place and out of the top 15.

Methylchloroisothiazolinone/methylisothiazolinone was the only allergen that was tested in each cycle from 2001 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 12 years (2001–2012; risk ratios [RRs], 1.26 and 2.08, respectively). The doubling of positive reactions to MCI/MI is consistent with the epidemic of allergy to this preservative that has been seen in Europe.<sup>20–26</sup> Its continued rise in the 2013–2014 cycle as compared with the 2011–2012 cycle 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 the increased use of MI in personal care products during this recent period. The 2013–2014 NACDG screening series was notable for

**TABLE 8. Significance-Prevalence Index Number\***

| Rank | Patch Test Allergen                                  | SPIN |
|------|------------------------------------------------------|------|
| 1    | MI, 0.2% aq                                          | 551  |
| 2    | Nickel sulfate, 2.5% pet                             | 490  |
| 3    | Fragrance mix I, 8% pet                              | 470  |
| 4    | MCI/MI, 0.01% aq                                     | 320  |
| 5    | <i>Myroxylon pereirae</i> , 25% pet                  | 294  |
| 6    | <i>p</i> -Phenylenediamine, 1% pet                   | 275  |
| 7    | Fragrance mix II, 14% pet                            | 248  |
| 8    | Formaldehyde, 2% aq                                  | 246  |
| 9    | Lanolin alcohol, 50% pet                             | 234  |
| 10   | Iodopropynyl butylcarbamate, 0.5% pet                | 192  |
| 11   | Formaldehyde, 1% aq                                  | 185  |
| 12   | Bacitracin, 20% pet                                  | 175  |
| 13   | Quaternium-15, 2% pet                                | 171  |
| 14   | Cinnamic aldehyde, 1% pet                            | 170  |
| 15   | Carba mix, 3% pet                                    | 165  |
| 16   | Propylene glycol, 100% aq                            | 135  |
| 17   | Methyldibromo glutaronitrile/phenoxethanol, 2.0% pet | 124  |
| 18   | Cobalt chloride, 1% pet                              | 123  |
| 19   | Neomycin, 20% pet                                    | 123  |
| 20   | OPDMA, 0.1% aq                                       | 118  |
| 21   | Diphenylguanidine, 1% pet                            | 116  |
| 22   | Thiuram mix, 1% pet                                  | 115  |
| 23   | Propylene glycol, 30% aq                             | 112  |
| 24   | Tixocortol-21-pivalate, 1% pet                       | 85   |
| 25   | 2-Bromo-2-nitro-1,3-propanediol, 0.5% pet            | 84   |
| 26   | Cocamidopropyl betaine, 1% aq                        | 76   |
| 27   | Decyl glucoside, 5% pet                              | 71   |
| 28   | Diazolidinyl urea, 1% pet                            | 69   |
| 29   | Dimethylaminopropylamine, 1% aq                      | 65   |
| 30   | Benzophenone-4, 10% pet                              | 64   |
| 31   | HEMA, 2% pet                                         | 64   |
| 32   | Imidazolidinyl urea, 2% pet                          | 60   |
| 33   | Compositae mix, 6% pet                               | 56   |
| 34   | Bisphenol A epoxy resin, 1% pet                      | 51   |
| 35   | Propolis, 10% pet                                    | 51   |
| 36   | Potassium dichromate, 0.25% pet                      | 50   |
| 37   | DMDM hydantoin, 1% pet                               | 49   |
| 38   | Amidoamine, 0.1% aq                                  | 48   |
| 39   | <i>Melaleuca alternifolia</i> (tea tree oil), 5% pet | 41   |
| 40   | Disperse blue 124/106 mix, 1% pet                    | 41   |
| 41   | Methyl methacrylate, 2% pet                          | 40   |
| 42   | Ethyl acrylate, 0.1% pet                             | 38   |
| 43   | Lidocaine, 15% pet                                   | 37   |
| 44   | Ylang ylang, 2% pet                                  | 37   |
| 45   | Colophony, 20% pet                                   | 36   |
| 46   | Cocamide DEA, 0.5% pet                               | 36   |
| 47   | DL- $\alpha$ -Tocopherol, 100%                       | 32   |
| 48   | Benzophenone-3, 10% pet                              | 31   |
| 49   | Tosylamide formaldehyde resin, 10% pet               | 30   |
| 50   | Sesquiterpene lactone mix, 0.1% pet                  | 28   |
| 51   | Benzocaine, 5% pet.                                  | 28   |
| 52   | Paraben mix, 12% pet                                 | 28   |
| 53   | Budesonide, 0.01% pet                                | 27   |
| 54   | Parthenolide, 0.1% pet                               | 26   |

TABLE 8. (Continued)

| Rank | Patch Test Allergen                                                     | SPIN |
|------|-------------------------------------------------------------------------|------|
| 55   | Black rubber mix, 0.6% pet                                              | 24   |
| 56   | <i>p</i> -tert-Butylphenol formaldehyde resin, 1% pet                   | 24   |
| 57   | Mixed dialkyl thioureas, 1% pet                                         | 23   |
| 58   | Ethylenediamine, 1% pet                                                 | 22   |
| 59   | Carvone, 5% pet                                                         | 22   |
| 60   | <i>Mentha piperita</i> oil (peppermint oil), 2% pet                     | 21   |
| 61   | <i>Jasminum officinale</i> oil ( <i>jasminum grandiflorum</i> ), 2% pet | 18   |
| 62   | Mercaptobenzothiazole, 1% pet                                           | 17   |
| 63   | Chloroxyleneol (PCMX), 1% pet                                           | 13   |
| 64   | <i>Lavandula angustifolia</i> oil (lavender oil), 2% pet                | 13   |
| 65   | Ethyl-2-cyanoacrylate, 10.0% pet                                        | 13   |
| 66   | Glutaral, 1% pet                                                        | 12   |
| 67   | Ethylhexylglycerin, 5% pet                                              | 9    |
| 68   | Desoximetasone, 1% pet                                                  | 3    |
| 69   | Hydrocortisone-17-butyrate, 1% pet                                      | 3    |
| 70   | Clobetasol-17-propionate, 1% pet                                        | 3    |

\*SPIN is a weighted calculation depending on degree of certainty ascribed to relevance.<sup>17</sup> A corrected version is used here:

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

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

its inclusion of MI at a concentration of 2000 ppm (0.2% aq), yielding a 10.9 % positivity rate. In its first cycle, MI has impressively debuted at number 1 in the SPIN calculations, a positivity score weighted by relevance, indicating the current importance of including it in any standard screening series. Recent prospective and retrospective patch-test prevalence studies have underlined MI's high sensitization rate across various populations.<sup>27,28</sup> The NACDG will provide a more in-depth analysis of its MCI/MI and MI data in a future article.

Nickel sulfate retained its position as the most commonly positive allergen in the screening series, reaching a prevalence of 20.1%, its highest level since the NACDG systematically began reporting patch test data. This strongly suggests that, like the European Union, North American countries should institute regulations limiting the levels of leachable nickel in items that are likely to have direct skin contact.

Aside from MI, 4 of the 7 allergen preparations added in the 2013–2014 cycle—formaldehyde 2% (7.0%), diphenylguanidine (3.8%), propylene glycol 100% (2.8%), and benzophenone-4 (2.1%)—all had reaction rates greater than 2%, whereas parthenolide (0.8%) and ethylhexylglycerin (0.2%) had low rates.

TABLE 9. Past Clinical Relevance

| Allergen   | Past Clinical Relevance, % | Prevalence, % |
|------------|----------------------------|---------------|
| Neomycin   | 53.1                       | 8.4           |
| Bacitracin | 40.8                       | 7.4           |
| Colophony  | 38.0                       | 1.9           |
| Benzocaine | 35.4                       | 1.6           |
| Nickel     | 34.7                       | 20.1          |
| Cobalt     | 34.1                       | 7.4           |

Formaldehyde 2% aq was added to the NACDG standard series for the 2013–2014 cycle on the basis of data obtained from the favorable comparison of rates of patch test positivity between 2% and 1% aq in a pilot study in Malmö, Sweden.<sup>29</sup> This was subsequently confirmed in a multicenter study performed in 12 dermatology clinics (11 in Europe and 1 in the United States).<sup>30</sup> This contributed to formaldehyde being named as the Allergen of the Year 2015 by the *American Contact Dermatitis Society*.<sup>31</sup> The NACDG data for the 2013–2014 cycle showed a 7% positivity rate for formaldehyde 2% compared with 5.7% for formaldehyde 1%, with a favorable SPIN of 246 versus 185. It is possible that the 1% concentration tested on its own may have shown a rate less than 5.7% if the 2% concentration had not been tested as well—as with MCI/MI and MI, a more liberal interpretation of a positive reaction to 1% may occur if a clear positive reaction to formaldehyde 2% has been noted. Interestingly, the ratios between cases found in the international multicenter study when patch testing with 2.0% compared with 1.0% ranged from 5 to 1.

Irritancy rate with formaldehyde 2% aq was 3.1% (vs 0.7% for the 1% aq concentration), the highest of any NACDG standard allergen, illustrating the well-acknowledged trade-off between higher test sensitivity versus irritancy. Propylene glycol 100% aq, on the other hand, had a relatively low irritancy rate of 1.4% as compared with 0.7% with the 30% aq concentration, whereas it was clearly more effective at discerning positive and relevant positive reactions (2.8% vs 2.2%; SPIN, 135 vs 112). Propylene glycol 100% aq was added to the standard series on the basis of the collective experience of some NACDG members who had found a higher rate of bonafide positive reactions without a significant increase in irritancy.

There were statistically significant decreases in rates from both the previous reporting cycle (2011–2012) and the pooled rates from the previous 12 years (2001–2012) for the following 3 formaldehyde-releasing preservatives: quaternium-15 (RRs, 0.75 and 0.58), diazolidinyl urea (RRs, 0.74 and 0.52), and DMDM hydantoin (RRs, 0.64 and 0.46). Compared with the previous 12 years, formaldehyde 1% and all formaldehyde-releasing preservatives except for 2-bromo-2-nitro-1,3-propanediol (bronopol) significantly decreased by 27% to 54% (formaldehyde 1% RR, 0.73;

TABLE 10. Five Most Common Sources of Irritants

| Source                                                              | No. Patients (n = 867) | %    |
|---------------------------------------------------------------------|------------------------|------|
| Cosmetics, beauty preparations, skin and health care products       | 251                    | 29.0 |
| Animals, infectious agents, plants, minerals, persons               | 133                    | 15.3 |
| Soaps, detergents, cleansers, disinfectants, laundry aids (nonskin) | 119                    | 13.7 |
| Chemicals and chemical products                                     | 107                    | 12.3 |
| Drugs, medications, alcoholic beverages                             | 64                     | 7.4  |
| Clothing, wearing apparel, protective equipment, textiles           | 64                     | 7.4  |

quaternium-15 RR, 0.58; diazolidinyl urea RR, 0.52; imidazolidinyl urea RR, 0.62; and DMDM hydantoin RR, 0.46). The prevalence of positive reactions to formaldehyde 2% in the current cycle is less than the peak prevalence for formaldehyde 1% of 8.4% that occurred within the 2001–2012 reporting period.<sup>8</sup>

The US Department of Health and Human Services classified formaldehyde as a carcinogen in 2011,<sup>32</sup> and although it did not implicate formaldehyde-releasing preservatives, several large manufacturers have recently eliminated this group of preservatives from products.<sup>33</sup>

Parabens also showed a statistically significant decrease in rates in the 2013–2014 cycle as compared with our 2 comparison periods (RRs, 0.44 and 0.60). Parabens are some of the most commonly used preservatives in personal care products. They continue to show the lowest prevalence of positivity of any major preservative on the North American market and, from a contact allergy perspective, are one of the safest groups of preservatives. The replacement of formaldehyde-releasing preservatives and parabens by other preservatives, especially MI, will impact sensitivity rates as documented by our data.

Current trends suggest that HEMA may be an allergen that bears watching in the future. There was a statistically significant increase in prevalence rates from both the previous reporting cycle (2011–2012; 2.6%; RR, 1.34) and the pooled rate from the previous 6 years (2007–2012; RR, 1.23). Methacrylates are mainstay in materials used in modern dental restorations. In addition, they have assumed an important role in the burgeoning nail aesthetic industry. In 2012, annual industry statistics indicate that US \$7.47 billion were spent in nail salons in the United States with more than 53,000 nail salons in operation. Thirty-six percent of this revenue was derived from gel (traditional), gel (brush-on), and acrylic nails.<sup>34</sup> The latest industry figures for 2015 show total revenue at 8.51 billion dollars spread over 129,000 salons nationwide.<sup>35</sup> Methacrylates can be the key components in both “gel” and “shellac” nails, including some home-applied preparations.

Five allergens continued to show low positive prevalence rates for at least three 2-year cycles and are now considered poor candidates for inclusion in a screening series: 3 topical corticosteroids (desoximetasone, hydrocortisone-17-butyrate, and clobetasol-17-propionate) and 2 fragrances (lavender and jasmine). These will be replaced by other allergens in the 2017–2018 cycle.

Mild and doubtful reactions are often nonreproducible,<sup>36,37</sup> 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.<sup>38</sup> Herein, we only report the reaction strength of positive reactions; nonetheless, using a crude cutoff of greater than 50% of positive reactions as doubtful or mild, the following allergens fall into this category: fragrances and flavorings (fragrance mix I and II, balsam of Peru

[*M. pereirae*], cinnamic aldehyde, colophony, peppermint oil, jasmine, lavender oil, ylang ylang oil, and carvone), preservatives (MCI/MI, formaldehyde 1%, quaternium-15, diazolidinyl urea, imidazolidinyl urea, DMDM hydantoin, bronopol, iodopropynyl butylcarbamate, methyldibromo glutaronitrile/phenoxyethanol, propylene glycol 30% and 100% aq, and chloroxylenol), surfactants (OPDMA, decyl glucoside, cocamidopropyl betaine, dimethylaminopropylamine, amidoamine, and cocamide diethanolamine [DEA]), corticosteroids (budesonide, clobetasol-17-propionate, and hydrocortisone-17-butyrate), other topical agents (lanolin benzophenone-3, benzophenone-4, benzocaine, tocopherol, propolis, neomycin, and tosylamide formaldehyde resin), methacrylates/acrylates (methyl methacrylate, ethyl acrylate, and ethylcyanoacrylate), selected rubber accelerators (carba mix and diphenylguanidine), and miscellaneous compounds (compositae mix, potassium dichromate, and disperse blue mix 124/106). 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.

Hypothetically, T.R.U.E. Test would have detected 66.0% to 75.9% of reactions found by the NACDG screening series during this data period. Of the top 40 NACDG allergens, the following antigens are not on the T.R.U.E. TEST: MI, fragrance mix II, iodopropynyl butylcarbamate, OPDMA, propylene glycol, HEMA, benzophenone-4, dimethylaminopropylamine, bisphenol A epoxy resin, decyl glucoside, propolis, cocamidopropyl betaine, methyl methacrylate, and amidoamine. Although not represented in the top 40, other important non-T.R.U.E. TEST allergens include tosylamide formaldehyde resin, tea tree oil, benzophenone-3, lidocaine, ylang ylang oil, and the mixed dialkyl thioureas. A customizable standard series such as the NACDG 70 allows for the flexibility of adding or subtracting allergens on an ongoing basis after 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. More than 20% 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, personal products, and workplace materials. The American Contact Dermatitis Society recommends a core antigen panel of 80 allergens.<sup>39</sup>

Limitations of this study include the following:

- The NACDG data represent a 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, source codes, and other collected variables are standardized wherever possible.
- The NACDG does not collect data on non-NACDG allergens other than presence and source.

- A change in the supplier of NACDG standard series allergen occurred after the 2009–2010 data cycle. This could possibly have impacted the comparison of prevalence rates of positivity between the 2013–2014 and the 2001–2012 periods.
- The composition of the group underwent a few changes from the previous cycle: a longstanding member from the southeastern United States, who had contributed 64 patients to the 2011–2012 data set, retired from data collection, and 2 new members practicing in the northeastern part of the United States and Canada contributed 898 patients to this 2013–2014 database. Therefore, comparisons of previous cycles could, in part, reflect these changes but 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 care for patients with dermatitis. Patch testing remains a critical diagnostic tool. This latest NACDG data summary for 2013–2014 adds to the references available on emerging trends and patterns in the field.

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