Dermal safety assessment of Arm & Hammer laundry products formulated for sensitive skin

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Abstract

Context: The prevalence of sensitive skin among the general population in industrialized countries is reported to be over 50%. Sensitive skin subjects often report significant reactions to contact with cosmetics, soaps and other consumer products.

Objective: This paper describes the overall skin compatibility and mildness program for a newly developed, lightly fragranced, colorant free laundry product (i.e. Arm & Hammer™ Sensitive Skin plus Skin-Friendly Fresh Scent), specially formulated for individuals with sensitive skin. The skin mildness of the product was compared to Arm & Hammer™ Free & Clear liquid laundry detergent with no fragrance or colorant, and an established history of safe use by sensitive skin consumers.

Materials and methods: The test material was a liquid laundry product with a light scent formulated for sensitive skin consumers (Arm & Hammer™ Sensitive Skin plus Skin-Friendly Fresh Scent). The product was compared to commercially marketed products for sensitive skin with a history of skin safety in the marketplace, including: a very similar product formulation (Arm & Hammer™ Free & Clear with no fragrance), and several selected competitors’ products. Studies were conducted among individuals with self-assessed sensitive skin (based on a questionnaire) using standard protocols for the Human Repeat Insult Patch Test (HRIPT), 10-Day Cumulative Irritation, the Wrist Band Wear test, and the Safety In-Use testing. Responses in all protocols were evaluated by visual scoring of potential dermatologic reactions, and recording any sensory effects at the time of the examination. In addition, sensory effects collected from panelists’ daily diaries were also evaluated.

Results: The HRIPT confirmed that neither the fragrance alone, nor the product formulation with fragrance, induced contact sensitization in sensitive skin subjects. The 10-Day cumulative irritation study conducted using sensitive skin subjects showed highly favorable skin compatibility, and the test product was comparable to the control product (Arm & Hammer Free & Clear) and other nonirritant controls. In the Wrist Band Wear test, exposure to laundered fabrics under exaggerated conditions gave similar results for the test and control products, with no objective signs of skin irritation, and no self-reported persistent adverse sensory effects. Very mild, transient and isolated sensory effects were noted in daily diaries by a small proportion of subjects, and were similar for the test and control products. The Safety In-Use tests evaluated 4-week exposure to product and laundered fabrics under realistic use conditions. There were no clinically objective signs of skin irritation, and reports of transitory, mild sensory effects were minimal and similar for the test and controls.

Discussion and conclusion: A comprehensive skin safety program on a lightly scented sensitive skin laundry formulation (i.e. Arm & Hammer™ Sensitive Skin plus Skin-Friendly Fresh Scent) conducted among panels of self-assessed sensitive skin subjects demonstrated that the presence of a light fragrance did not adversely impact skin compatibility in any of the testing protocols when the product was compared to a similar product with no fragrance. The lightly fragranced product demonstrated overall skin compatibility and mildness when tested in a self-assessed sensitive skin population, and compared favorably to currently marketed sensitive skin products.

Introduction

Sensitive skin is identified as a hypersensitivity to stimuli

and is defined clinically by a set of unpleasant and subjective sensory perceptions including tightness, stinging, burning, tingling, pain and itching

. Often, objective signs of any skin irritation are absent

. Sensitive skin was initially referred to in 1947

, and for many years it was thought to be an unusual condition confined to a few individuals. More recently it has become evident that a large portion of the population experiences this phenomenon

. Sensitive skin subjects experiencing this condition report exaggerated...
reactions when their skin is in contact with cosmetics, soaps and other consumer products, and often report worsening condition after exposure to dry and cold climate\textsuperscript{2}.  

In a recent review Richters, et al., summarized physiologic factors that may lead to sensitive skin as:\textsuperscript{1} sensory hyper-reactivity,\textsuperscript{2} impaired barrier function,\textsuperscript{3} inflammatory or vascular responsiveness, and\textsuperscript{4} atopic predisposition.\textsuperscript{10} However, host factors (e.g. life style choices, gender, age and anatomic site), and environmental factors (e.g. climate) are also known contributors\textsuperscript{4,4,11,12}. Several investigators are evaluating the role of a specific sensory receptor; the transient receptor potential vanilloid-1 (TRPV1). TRPV1 is a non-selective, thermo-sensitive cation channel that responds to heat and low pH, and is related to nociception, neurogenic inflammation, and pruritus\textsuperscript{13,14}. The expression of this channel has been found to be upregulated in subjects with sensitive skin, and correlates with the intensity of the symptoms\textsuperscript{15,16}. Topical application of the TRPV1 antagonist 4-t-butylcyclohexanol has been demonstrated to have an anti-stinging/anti-burning effect in a capsaicin-induced sting test\textsuperscript{14}.  

The unpleasant sensory reactions that are associated with sensitive skin, and the absence of objective signs and symptoms in most individuals, mean that the condition is largely self-reported. As a result, surveys have been a popular approach to evaluating the prevalence of this condition among the general population. A review of the literature published in 2012 identified over 15 surveys on the prevalence of self-assessed sensitive skin conducted in over 20 geographic regions in Europe, North American and Latin America\textsuperscript{17}. Since that time, the scientific community has continued to evaluate this condition in other countries, including China\textsuperscript{18}, Mexico\textsuperscript{19}, Japan\textsuperscript{20}, Brazil and Russia\textsuperscript{21}. Estimates of the overall prevalence of this condition vary as a result of differences in the approaches to conducting the surveys and in the wording of specific questions. However, the general consensus is the prevalence of sensitive skin among the general population is over 50\%\textsuperscript{2,7}. There is some variation depending on the specific geographic region\textsuperscript{6}, which could be related to differing weather patterns. Higher rates may be reported in some geographies due to a higher percentage of the population having a fair skin phenotype that is more closely associated with sensitive skin\textsuperscript{22}. Cultural factors may also play a role\textsuperscript{5}. Aggressive advertising of products targeted for sensitive skin may lead to a higher level of understanding and acceptance of this condition\textsuperscript{17}. In addition, cultures with a greater emphasis on appearance and fashion may have a higher level of exposure to potential irritants that trigger adverse sensory responses\textsuperscript{23}.  

Manufacturers of consumer products have long conducted programs on products and ingredients to confirm skin compatibility and mildness\textsuperscript{24,25}. However, with the recent realization of the high prevalence of sensitive skin in industrialized societies, manufacturers are developing products especially formulated for this large subgroup of consumers. The overall approach is similar to that previously described for other consumer products\textsuperscript{24–26} and involves a stepwise evaluation of skin mildness and compatibility, with a comparative approach to confirmatory testing in which newly developed products are compared to reference, commercially marketed products with an established history of safe use. However, when products are specifically formulated for the sensitive skin consumer, additional testing is warranted to ensure mildness for this population.  

The objective of this program was to evaluate the skin compatibility of a laundry product developed for the sensitive skin consumer. Further, we wanted to determine if the addition of a light scent to a sensitive skin laundry product would adversely affect the skin compatibility and mildness of the product. A testing program was developed to compare the scented, dye-free formula (Arm & Hammer\textsuperscript{TM} Sensitive Skin plus Skin-Friendly Fresh Scent, or A&H Sensitive Skin+Scent), to the safely marketed, fragrance- and dye-free formula (Arm & Hammer\textsuperscript{TM} 2X Laundry Detergent, Sensitive Skin). The overall approach to the program is outlined in Figure 1. Initial development of the laundry detergent test formulations used carefully selected ingredients with excellent overall skin compatibility, a demonstrated mildness to skin, and a long history of safe use in consumer products developed for similar uses. Product versions containing a light scent were developed to appeal to those sensitive skin consumers who prefer a dermatologically safe, scented product. The fragrance was specially formulated to: (1) contain a minimal number of ingredients, (2) ensure that all ingredients comply with the International Fragrance Association (IFRA) usage standards and guidelines (accessible at: http://www.ifraorg.org), (3) contain none of the 26 fragrance allergens recognized by the European Union (EU) as having the potential to cause allergy\textsuperscript{27}, and (4) contain no fragrance ingredients included on the American Contact Dermatitis Society (ACDS) Core Allergen Series Group\textsuperscript{28}. We conducted a confirmatory testing program on the Arm & Hammer\textsuperscript{TM} Sensitive Skin plus Skin-Friendly Fresh Scent (A&H Sensitive Skin+Scent) formulation to evaluate skin compatibility and mildness among the target consumer population, i.e. individuals with sensitive skin. Standard test protocols were used to assess gentleness and mildness among sensitive skin consumers under expected use conditions and exaggerated exposure conditions. Endpoints measured in these studies included objective signs of irritation, and a recording of sensory effects.  

**Methods**

**Materials tested**

Information on the formulations and other materials used in the skin mildness program are shown in Table 1. The composition of the formulations is proprietary, but a concentration range of key components is provided in Table 1(a). The test product (T: Arm & Hammer\textsuperscript{TM} Sensitive Skin plus Skin-Friendly Fresh Scent) contained a proprietary, mild fragrance blend (W). Other materials in the test product were the same as the control product (C: Arm & Hammer\textsuperscript{TM} Free & Clear (fragrance-free, dye-free)).  

The skin compatibility and mildness studies conducted with the test product are shown in Table 1(b). The dilutions used in the HRIPT and cumulative irritation studies are provided. For the wrist band and safety in use tests, exposure was to laundered fabric, as detailed in the protocol.
Approach to developing products for sensitive skin individuals. Formulations are developed by selecting ingredients and fragrances with extensive safety data and a long history of safe use and mildness in similar consumer products. Resulting formulations are subjected to confirmatory testing using volunteer panels of self-assessed sensitive skin individuals. Tests should include evaluations for contact sensitization (HRIPT), and test protocols designed to evaluate skin compatibility and mildness of the product and laundered fabrics under exaggerated exposure conditions (Cumulative Irritation test for the product and Wrist-Band Wear test for laundered fabric) and expected use conditions (In-Home Safety In-Use test).

### Table 1. Liquid laundry detergent formulations used in safety program.

|                | Test product (T) | Control product (C) |
|----------------|------------------|---------------------|
| Fragrance oil (W) | 0.8%            | None                |
| Total builder    | 3.0–6.0%        | 3.0–6.0%            |
| Total anionic surfactant | 2.5–6.0%    | 2.5–6.0%            |
| Total nonionic surfactant | 3.5–6.5%    | 3.5–6.5%            |
| Fluorescent whitening agent | <1%            | <1%                 |
| Suds control agent | <0.5%           | <0.5%               |

### a. Basic formulation comparison (range of concentration of key components)

|                | Test product (T) | Control product (C) |
|----------------|------------------|---------------------|
| Fragrance oil (W) | 0.8%            | None                |
| Total builder    | 3.0–6.0%        | 3.0–6.0%            |
| Total anionic surfactant | 2.5–6.0%    | 2.5–6.0%            |
| Total nonionic surfactant | 3.5–6.5%    | 3.5–6.5%            |
| Fluorescent whitening agent | <1%            | <1%                 |
| Suds control agent | <0.5%           | <0.5%               |

### b. Test articles included in skin compatibility testing program conducted among sensitive skin subjects.

|                | HRIPT<sup>a</sup> | Cumulative irritation<sup>b</sup> | Wrist band study | Safety in Use Test 1 | Safety in Use Test 2 |
|----------------|-------------------|----------------------------------|------------------|---------------------|---------------------|
| Test articles  |                   |                                  |                  |                     |                     |
| W Test product fragrance oil | ST-7359         | ST-7360                          | ST-7362          | ST-7357             | ST-7358             |
| T Arm & Hammer<sup>TM</sup> Sensitive Skin plus Skin-Friendly Fresh Scent | 0.22             | 0.066                            |                  |                     |                     |
| Control product |                   |                                  |                  |                     |                     |
| C A&H Free & Clear (fragrance-free, dye-free) | 0.22             | 0.066                            |                  |                     |                     |
| Competitors’ control products |                   |                                  |                  |                     |                     |
| E Tide<sup>TM</sup> Free And Gentle Liquid Laundry Detergent | 0.22             | 0.066                            |                  |                     |                     |
| F All<sup>TM</sup> Free Clear Liquid Detergent (2X) | 0.14             | 0.066                            |                  |                     |                     |
| H Purex<sup>TM</sup> Free and Clear Laundry Detergent | 0.13             | 0.067                            |                  |                     |                     |
| Other control materials |                   |                                  |                  |                     |                     |
| I 0.9% Saline | Neat              |                                  |                  |                     |                     |
| J Baby oil (J&J) | Neat              |                                  |                  |                     |                     |

<sup>a</sup>Fragrance tested at 0.8% in mineral oil. Test and control product concentrations were chosen to be minimally irritating based on previous experience.

<sup>b</sup>Test and control products tested at the recommended use concentrations.

<sup>c</sup>Test samples were fabric swatches laundered three times in detergent at either recommended use concentration (1X samples) or 3-fold higher than recommended use concentration (3X samples).

<sup>d</sup>Panelists provided with detergent to use for all home laundry.
irritation test: 0.9% sodium chloride, and undiluted baby oil (Johnson & Johnson™, New Brunswick, NJ).

Subjects

All the studies were conducted among healthy adult volunteers with self-declared sensitive skin. Subjects were classified as sensitive skin based on a self-assessed history of short-term skin intolerance or skin reactivity following contact with cleaning products (e.g. laundry detergents, fabric softeners, or dishwashing and household cleaning products), or personal care products (e.g. cosmetics, lotions, shaving products and hair products). The participants were specifically asked to identify specific laundry and fabric softener products that they perceived caused adverse reactions in the past. Volunteers were excluded from participation for reasons including: any systemic or dermatologic disease or disorder which could interfere with the conduct of the study or increase the subject’s risk of adverse reactions, pregnancy or nursing, taking anti-inflammatory, corticosteroids or other medications that may interfere with test results, or participation in a patch test study within the previous 28 days. Selected participants signed an informed consent document, and could withdraw from the studies at any time. All study protocols were reviewed and pre-approved by board-certified dermatologists and the test facilities’ Institutional Review Board (IRB), and were conducted in accordance with Good Clinical Practice (GCP) Regulations (21 CFR 50: Protection of Human Subjects-Informed Consent and ICH-GCP Consolidated Guidelines, May 9, 1997 Federal Register). A summary of the number and mean age of participants for each study is provided in Table 2.

Human repeat insult patch test (HRIPT)

The test was conducted at a contract facility (Reliance Clinical Testing Services, Inc., Irving TX 75062) using a standard HRIPT protocol (similar to 29,30). Study participants were 95 self-declared sensitive subjects age 20–60. Test products were diluted in deionized distilled water to result in solutions equivalent to the recommended use concentrations on the package labels. This concentration has been demonstrated in previous tests conducted by the Company on liquid detergent formulations to be minimally irritating under occlusive patch conditions. In addition to test and control products, the fragrance itself was diluted in mineral oil to the concentration intended for the final formulation (0.8%). Test solutions were prepared fresh each day. For application, 0.2 ml of each test article solution was applied to the back between the left scapula and the spinal mid-line using occlusive patches of nonwoven cotton (2 cm × 2 cm Parke-Davis Readi Bandages). Test and control skin test sites were randomized. The induction phase consisted of nine 24-h patches at a single site on the back with a 24-h rest between (48 h on weekends). The patch sites were graded for skin responses prior to each application and at the removal of the test patches. Approximately, 14 days after the last induction application, 24-h challenge patches were applied to previously unpatched sites on the back. Reactions were scored daily for 4 days (i.e. at 24, 48, and 72 and 96 h) after removal of the challenge patch. Visual assessment was conducted by an expert grader (at 24, 48 and 96 h) and a board certified dermatologist (at 72 h) under a 100 watt incandescent bulb using a scale where “0” indicated no visible reaction, “0.5” was a barely perceptible reaction, “1” was mild, “2” was moderate, “3” was marked, and “4” was severe. The presence of edema and/or papules, spreading or vesicles was also noted.

Cumulative irritation study

Study participants were 26 self-declared sensitive subjects age 18–65. The study was conducted at a contract testing facility (Hill Top Research, St. Petersburg, FL) using the facility’s standard Cumulative Irritation protocol. Test articles were diluted in deionized distilled water to the recommended use concentrations. Patches were applied on the back, and sites

Table 2. Summary of number and mean age of sensitive skin participants completing each study.

| Sensitization | Exaggerated exposure to product | Exaggerated exposure to laundered fabric |
|---------------|---------------------------------|----------------------------------------|
| HRIPT         | Cumulative Irritation           | Wrist Band Study                        |
| Test sample (s) | ST-7359 6 test and control samples<sup>a</sup> | ST-7360 7 test and control samples<sup>a</sup> | ST-7362 1X Test product T and Control C 3X Test product T and Control C |
| Total         | 95                              | 26                                     | 17                                               | 16 |
| Male          | 36 (38%)                        | 5 (19%)                                | 3 (18%)                                          | 2 (12%) |
| Female        | 59 (62%)                        | 21 (81%)                               | 14 (82%)                                         | 14 (88%) |
| Mean Age (SD) | 39 (11.5)                       | 27 (12.8)                              | 48 (12.6)                                        | 45 (11.6) |

| Standard use conditions | Safety In-Use Test 1 ST-7357 | Safety In-Use Test 2 ST-7358 |
|-------------------------|-------------------------------|-------------------------------|
| Test sample (s)         | Test product T | Control C | Test product T | Control C |
| Total                   | 32                        | 32                  | 52              | 53 |
| Male                    | 6 (19%)                   | 5 (16%)             | 1 (2%)          | 5 (9%) |
| Female                  | 26 (81%)                  | 27 (84%)            | 51 (98%)        | 48 (91%) |
| Mean Age (SD)           | 47 (11.3)                 | 48 (10.4)           | 43 (11.0)       | 47 (9.9) |

<sup>a</sup>See Table 1 for a list of samples tested.
were randomized for the test and control articles. For application, 0.2 ml of each test article solution was applied using occlusive patches of nonwoven cotton (Webril®) covered by and secured on all sides by hypoallergenic tape (Blenderm™). Approximately, 23 h after application test materials were removed, test sites were evaluated, and fresh test patches were re-applied to the same test site. Panelists were exposed to test substances for 10 consecutive days. Skin reactions were evaluated by visual assessment prior to any treatment (Day 1), and after removal of each of the test material application (Day 2–10).

Visual assessment was conducted using a standardized grading scale for erythema of ‘‘0–7’’ where ‘‘0’’ is no apparent cutaneous involvement and ‘‘7’’ is a strong reaction spreading beyond test site31. Glazing, fissuring and erosions were scored on a separate scale of ‘‘0–3’’, and the numerical equivalent added to the erythema score to produce a transformed daily numerical score. This resulted in a maximum transformed numerical score of ‘‘10’’ for a test site (erythema of ‘‘7’’ and erosions of ‘‘3’’). The same grader was used throughout an experiment, and the grader was not aware of treatment assignments. If a test site exhibited a strong reaction at any site (i.e. a daily numerical score of ‘‘3’’ or greater), the test material was not reapplied at that site. It is noteworthy that none of the test or control articles produced individual scores approaching ‘‘3’’ throughout the course of the study.

The study was conducted under the supervision of a board certified dermatologist. Scoring was conducted daily. Cumulative transformed irritation scores were determined for the panel for each test material. Using this evaluation method and panel size, a cumulative irritation score of 0–24 indicates a mild article with no irritation; 25–95 indicates probably mild in normal use; 96–213 indicates possibly mild in normal use; 214–276 indicates a cumulative irritant; and 277–300 indicates a primary irritant.

Statistical analyses were conducted by the test facility to compare the cumulative irritation scores for days 1, 7, and 10. Initially, a Friedman rank sum test was performed. If significant differences were found using this approach, a Fishers Least Significant Difference test was performed.

Wrist band wear

Study participants were 33 self-declared sensitive subjects aged 18–65. The parallel-group, double-blind, randomized study was conducted at a contract facility (Harrison Research Labs, Union, NJ 07083). The protocol was similar to one published for evaluating the skin compatibility to laundry detergents32. Four different sets of swatches were prepared by pre-laundering; two sets were prepared by laundering fabric three times in the recommended use concentration of each of the products (referred to as 1X samples), and two sets were prepared by laundering three times in solutions that were triple the recommended use concentration (referred to as 3X samples).

Laundered fabric swatches were applied to each wrist (randomly determined), and held in place using tape and an elastic terry-cloth wristband. Subgroup 1 consisted of 17 subjects who received 1X samples of the test product T on one wrist and 1X samples of the control product C on the other. Subgroup 2 consisted of 16 subjects and received the 3X test and control samples. Subjects were instructed to wear the test samples for 8 h before removing them. Samples were applied daily for 4 total days. A trained grader conducted dermatologic evaluations of the test sites prior to each sample application (including a baseline evaluation prior to the first sample application), and on the morning of day 5 after 4 full days of exposure.

Safety in-use

Two independent parallel-group, double-blind, randomized studies were conducted at contract facilities (Harrison Research Labs, Union, NJ 07083 and Clinical Research Laboratories, Piscataway, NJ, 08854). The two studies used the identical protocol, and test and control products. The participants were healthy volunteers with self-declared sensitive skin aged 18–63. Sixty-four subjects completed the first study (32 for test product T, and 32 for control product C). The second was completed by 105 subjects (53 for T, and 52 for C).

In each of the two studies, participating subjects received an examination by a board certified dermatologist prior to any exposure to the test or control products to establish baseline scores for erythema, edema and dryness. The examination included an evaluation of the hands, legs, arms, chest and back. A total of 23 sites per subject were rated for these three parameters. After the dermatological examination, subjects were provided test or control product and instructed to use it as the only laundry detergent for a 4-week period, including a minimum of 2 laundry loads per week, and a minimum of 2–3 min twice per week of hand laundry and/or stain pretreatment using the assigned detergent. The subjects kept a daily diary to record the date and time of the laundry, including hand laundry and pretreatment, the amount of detergent used, and any adverse sensory reactions related to product use. After 2 and 4 weeks of test product use, dermatologic evaluations were conducted, and subjects were asked to rate the intensity of any sensory reactions, such as, itching, dryness and stinging/burning.

All the dermatologic evaluations (erythema, edema and dryness) and the sensory reactions (itching, dryness, stinging/burning) were rated on a scale of ‘‘0–3’’, where ‘‘0’’ indicated none, ‘‘0.5’’ was barely perceptible, ‘‘1’’ was mild, ‘‘2’’ was moderate, ‘‘3’’ was severe. Statistical analyses were conducted by the test facility using the Chi-Square test to compare responses of the test groups for baseline, week 2 and week 4 evaluations.

Results

HRIPT for contact sensitization

The HRIPT was conducted to confirm the fragranced formulation did not cause contact sensitization in self-declared sensitive skin subjects. Test and control products were evaluated at the recommended use concentrations under occlusive patch. None of the test or control samples produced responses indicating sensitization. Figure 2 illustrates the low level of responses at challenge (48-h after removal of the
challenge patch). There were a small percentage of scores of ‘‘0.5’’, indicative of barely perceptible reactions, and no scores of ‘‘1’’ after challenge with the fragrance oil alone (W), the test product (T), or the key control product (C). All of the competitors’ sensitive skin products were also negative for sensitization (test samples E, F and H).

Cumulative irritation

Results of the 10-day cumulative irritation study are shown in Figure 3(a). The test product (T) produced no evidence of irritation, even with the exaggerated exposure conditions of occlusive patches repeated daily. Results were not significantly different from the key control product (C: A&H Free & Clear), or from the nonirritant controls (I: 0.9% saline, and J: baby oil). The cumulative irritation score of ≤5 for the test formulation resulted in a classification of ‘‘mild, with no irritation’’ (classification is detailed in the methods section).

Each of the competitors’ products formulated for sensitive skin produced scores that indicated they were mild to the skin in this sensitive skin population. However, control products E, and F produced cumulative irritation scores that were significantly different (p ≤ 0.05) from the A&H Sensitive Skin + Scent product (T). Two of the control products (E and F) produced cumulative irritation scores of 25, placing them just barely in the category of ‘‘probably mild in normal use’’ (i.e. cumulative score of 25–95).

The mean cumulative irritation score is plotted in Figure 3(b). On the scoring scale that was used in this study, a ‘‘1’’ indicates minimal, barely perceptible erythema31. All the test and control materials produced a mean score that was at or below ‘‘1’’.

Wrist band wear

In the wrist band wear test sensitive skin subjects were exposed to fabrics laundered in either the test (T: A&H Sensitive Skin + Scent) or control (C: A&H Free & Clear) product using 1X or 3X the recommended use concentrations. Fabrics were worn on the wrist in close proximity to the skin for prolonged periods (8 h per day for 4 days), thus providing an exaggerated exposure compared to the exposures expected under normal consumer use conditions.

Results of the wrist band wear test are summarized in Table 3. The dermatologic evaluations showed that none of the subjects exhibited any erythema, dryness, or edema during the dermatologic examinations as a result of exaggerated exposure to the fabric swatches laundered with either the test product (T) or the control product (C) at 1X or 3X recommended use concentration, i.e. all scores were ‘‘0’’.

Further, none of the study subjects reported any sensory responses (burning, stinging, itching, dryness, other) at the time of the evaluation visits.

Daily diaries were reviewed for evidence of transient adverse sensory reactions that may not have been present at the evaluation visits. Reported effects appeared to be isolated incidents that were very mild in nature and short in duration. Even among this sensitive skin population, the incidence of reported sensory effects was very low. Two subjects out of the 17 who participated (i.e. 12%) reported slight to moderate itching to the 1X samples of the test product (T) compared to three subjects reporting slight itching to 1X samples of the control product (C) (17%). As a result of wearing the 3X samples, three subjects reported mild itching to test product T (19%) and four subjects to control C (25%).

Safety in-use

Results of the Safety In-Use testing are summarized in Figure 4. After 2- and 4-weeks of home product usage, dermatologic evaluations were conducted on 23 sites per subject, including sites on the hands, legs, arms, chest and back. Evidence of dermatologic reactions was very low for both the products (test and control) in both the studies. At the 2- and 4-week evaluation, mean ratings for erythema (Figure 4(a)) were consistently below 0.2, and mean ratings for dryness (Figure 4(b)) were consistently below 0.4. There was no evidence of edema at any time in either study (data not shown). There were no significant differences between the test and control products in either of the two studies for any of the dermatologic parameters.

Reports of sensory effects at the skin evaluation time points were low, with a small number of subjects in both groups (test and control) reporting mild dryness (Table 4). There were no reports of itching or burning. When daily diary
reports were reviewed for sensory comments, a small number of subjects reported transient, mild itching, redness or dryness. Statistical analysis indicated no differences between test groups.

Discussion

Consumers with sensitive skin can have intolerance to products that other consumers can use with no adverse consequences.
As early as 1977, Frosch and Kligman described unexpected, adverse sensory reactions among consumers to products that had been thoroughly evaluated for irritation and sensitization. In an unpublished research study conducted by the Church & Dwight Co., Inc., we found that 17% of the laundry detergent users self-reported that they had previously had reactions to laundry detergents. Among individuals with sensitive skin the percentage is higher. Farage reported that over 50% of the individuals with self-declared sensitive skin have experienced adverse skin reactions to laundry products at some time compared to approximately 20% of individuals not claiming sensitive skin. This program was designed to evaluate a lightly scented laundry product for mildness and skin compatibility among sensitive skin consumers.

Results in the HRIPT demonstrated an absence of contact sensitization to the product formulation and the fragrance. This result was expected based on the selection of only those ingredients with extensive safety data, including evaluations of contact sensitization potential, and a long history of safe use and mildness in similar consumer products. The exaggerated exposure to product solution in the 10-day cumulative irritation study among sensitive skin subjects resulted in classification of the test products as ‘mild, causing no irritation’. Importantly, the lightly fragranced test product (T, with 0.8% fragrance) was very similar to the fragrance-free control (C), demonstrating that the inclusion of fragrance in the formulation did not alter the skin mildness or compatibility of the product. Although all of the tested materials were mild in this study, the test product produced significantly lower cumulative irritation scores than two of the competitors’ commercially marketed sensitive skin products.

Table 4. Safety in-use studies on self-assessed sensitive skin subjects: reports of subjective effects.

| Products                              | Total number of subjects (both studies) | Reported at skin evaluations | Daily diary reports |
|---------------------------------------|----------------------------------------|-----------------------------|---------------------|
|                                       |                                       | Itching Dryness Burning     | Itching Dryness Redness |
| T: A&H Sens Skin + Scent              | 85                                     | 0 4 0                        | 0 2 1               |
| C: A&H Free and Clear (no fragrance)  | 84                                     | 0 2 0                        | 3 1 2               |

*Number of subjects at any time point.
All reported sensory effects were mild (score 0.5–1) in intensity and transient in nature.

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Results in the HRIPT demonstrated an absence of contact sensitization to the product formulation and the fragrance. This result was expected based on the selection of only those ingredients with extensive safety data, including evaluations of contact sensitization potential, and a long history of safe use and mildness in similar consumer products. The exaggerated exposure to product solution in the 10-day cumulative irritation study among sensitive skin subjects resulted in classification of the test products as ‘mild, causing no irritation’ (Figure 3). Importantly, the lightly fragranced test product (T, with 0.8% fragrance) was very similar to the fragrance-free control (C), demonstrating that the inclusion of fragrance in the formulation did not alter the skin mildness or compatibility of the product. Although all of the tested materials were mild in this study, the test product produced significantly lower cumulative irritation scores than two of the competitors’ commercially marketed sensitive skin products.

During the laundering process, materials from laundry product have the potential to deposit on fabric. With modern fabrics and laundering methods, residues on laundered fabric represent a major source exposure to
The only symptom experienced by these individuals is dryness and edema, that are the typical endpoints for these types of studies are likely not sufficient for sensitive skin consumers. However, the objective signs of irritation, such as, erythema, dryness and edema, that are the typical endpoints for these types of studies are likely not sufficient for sensitive skin consumers. In fact, subjective sensory perceptions are often the only symptom experienced by these individuals. A careful review of sensory responses is essential in evaluating products for sensitive skin consumers.

In the Wrist Band Wear test fabric is laundered under extreme conditions to maximize deposition of formulation components, i.e. use of a three-fold concentrated wash solution. Exposure conditions are also extreme, with exposure via elastic wrist bands worn continuously 8 h per day for 4 days. In the wrist band test conducted among sensitive skin subjects there was no evidence of either skin irritation or persistent adverse sensory effects as a result of exposure to fabrics laundered in the test product (T, with 0.8% fragrance). The small number of mild, transient sensory effects recorded in the participants’ daily diaries was similar to those recorded for the control product (C with no fragrance) (Table 3). The in-home Safety In-Use test among sensitive skin subjects provided a 4-week duration of exposure under actual expected product use conditions. Subjects were exposed to the product (during hand laundry and pre-treating), and to clothing and bedding fabrics laundered in the product. There was no evidence of erythema or dryness among sensitive skin panelists using either the test (T) or control (C) product (Figure 4). During the safety in-use studies, very few adverse sensory reactions were reported at either the skin evaluation intervals or in the daily diary entries (Table 4).

In the Safety In-Use Study 1 (Figure 4), the mean scores for erythema and dryness appear to decrease after 2 and 4 weeks of product use. This apparent decrease is very marginal and, likely insignificant. Scores throughout both in-use tests were very low. At the baseline dermatological evaluations (prior to product exposure), mean scores for erythema and dryness were less than 0.5, which is defined as “barely perceptible”.

Table 5. Summary of skin compatibility program performed among sensitive skin subjects.

| Study                                      | Formulations/ Materials Tested                                                                 | No. of subjects | Results                                                                                     |
|--------------------------------------------|---------------------------------------------------------------------------------------------|----------------|---------------------------------------------------------------------------------------------|
| **Sensitization**                          |                                                                                             |                |                                                                                             |
| Human Repeat Insult Patch Test (HRIPT)     | A&H Sens Skin + Scent (0.8% fragrance) (T) A&H Free & Clear (no fragrance) (C)                | 95 sensitive skin subjects | No indications of contact sensitization as a result of exposure to the fragrance alone, or any of the test or control products. |
| **Exaggerated exposure to product**        |                                                                                             |                |                                                                                             |
| Cumulative Irritation Test                 | A&H Sens Skin + Scent (0.8% fragrance) (T) A&H Free & Clear (no fragrance) (C)                | 26 sensitive skin subjects | Addition of fragrance had no adverse effect on skin mildness or compatibility among self-assessed sensitive skin subjects as a result of exaggerated exposure to product. |
| **Exaggerated exposure to laundered fabric**|                                                                                             |                |                                                                                             |
| Wristband Wear Test                        | Fabrics laundered in 1X and 3X wash solution concentrations of: A&H Sens Skin + Scent (0.8% fragrance) (T) A&H Free & Clear (no fragrance) (C) | 33 sensitive skin subjects (17 in the 1X group and 16 in the 3X group) | Addition of fragrance had no adverse effect on skin mildness or compatibility among self-assessed sensitive skin subjects as a result of exaggerated exposure to laundered fabric. |
| **Standard use conditions**                |                                                                                             |                |                                                                                             |
| Independent Safety-in-Use Test (Studies 1 and 2 combined) | A&H Sens Skin + Scent (0.8% fragrance) (T) A&H Free & Clear (no fragrance) (C) | 169 sensitive skin subjects (both studies combined) (84 in group T and 85 in group C) | Addition of fragrance had no adverse effect on skin mildness or compatibility among self-assessed sensitive skin subjects as a result of exposure to product under actual use conditions. |

detergent components. Therefore, evaluating laundered fabric is an important part of any overall skin compatibility program. However, the objective signs of irritation, such as, erythema, dryness and edema, that are the typical endpoints for these types of studies are likely not sufficient for sensitive skin consumers. In fact, subjective sensory perceptions are often the only symptom experienced by these individuals. A careful review of sensory responses is essential in evaluating products for sensitive skin consumers. Individuals with sensitive skin are known to react to cosmetic, personal care and other household products. With increasing evidence of the high prevalence of sensitive skin among the general population, manufacturers of consumer products are focusing more and more on developing products that were not specifically formulated for sensitive skin consumers. Such efforts will allow the sensitive skin consumer to comfortably enjoy the performance benefits of modern formulation technology.

**Conclusions**

We conducted a comprehensive skin compatibility and mildness program using volunteer test panels consisting of individuals with self-declared sensitive skin in order
determine if the addition of a light scent to a sensitive skin laundry product would adversely affect the skin compatibility and mildness of the product. The program included confirmatory testing for the absence of contact sensitization (HRPIPT), and evaluations of skin effects from exaggerated exposures to product solutions (Cumulative Irritation test) and laundered fabrics (Wrist Band Wear test). Skin compatibility under expected use and exposure conditions was also evaluated in 4-week Safety In-Use testing. In all test protocols, the lightly scented sensitive skin laundry product was mild to skin and comparable to marketed sensitive skin products with a history of safety and skin compatibility in the marketplace. The addition of the light scent chosen for the product (i.e. Arm & Hammer™ Sensitive Skin plus Skin-Friendly Fresh Scent) had no adverse effects on skin compatibility or mildness.

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Declaration of interest

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