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Two randomized studies to evaluate the cooling sensation, consumer liking, and tolerability of a skin disinfectant spray

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Synopsis

The aim of these two clinical studies was to evaluate the sensory characteristics and irritation potential of a prototype disinfectant spray (containing 0.13% w/v benzalkonium chloride and a cooling agent) in subjects with experimental wounds. The pilot study was a single center, "replicated latinClinicalTrials. ClinicalTrials. square design," randomized and double-blinded study. The pivotal study was a single center, randomized, controlled, crossover, double-blinded study, following a direct comparison test design of the study products. The experimental wounds were generated using sequential tape strippings of the forearm skin before product application. The test product was compared with the currently marketed BACTROBAN® disinfectant spray, negative control (0.9% w/v saline), and positive control (70% w/v isopropyl alcohol, pilot study only). The pilot study was intended to inform the study design and sample size for the pivotal study. The pilot study demonstrated that the positive control product delivered significantly more irritancy (stinging /burning sensory) than the negative control product on the experimental wound, which verified the integrity of the wound model. The results of the pivotal study suggested that the prototype formulation delivered significantly more cooling sensation than both BACTROBAN® disinfectant spray and negative control at 3 and 5 min after product application, and overall for a 15-min period after application. No statistically significant differences in product liking were observed between the prototype disinfectant spray and the BACTROBAN® disinfectant spray or negative control. The prototype disinfectant spray, BACTROBAN® disinfectant spray, and control products were well-tolerated in these studies.

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® BACTROBAN® is a registered trademark owned by GSK group of companies.

INTRODUCTION

The skin is one of the most important parts of the body because it interfaces with the environment and is the first line of defense from external factors. The skin plays a key role in protecting the body against pathogens (1) and excessive water loss (2).

Skin wounds are susceptible to infection because of the loss of sterility of the innate barrier function of the skin and dermal appendages, facilitating the development of microbial communities within the wound environment (3,4). A wound infection can cause delayed healing and if infection is not controlled it may lead to cellulitis, bacteraemia, and septicaemia (5). It is reported that antiseptic solutions can reduce infection in traumatic lacerations (6) and are commonly recommended in current clinical practices (7). Benzalkonium chloride has been used safely and effectively as an antiseptic for wound management for several decades. Marple *et al*. reviewed 18 studies on the safety of benzalkonium chloride in nasal solutions and concluded that benzalkonium chloride appeared "safe and well-tolerated for both long- and short-term clinical use" (8). The Food and Drug Administration has found benzalkonium chloride to be generally recognized as safe and effective/Category I for products to clean skin wounds (short duration use) under first-aid antiseptic and consumer antiseptic monographs at concentrations between 0.1 and 0.13% (9). It is a Category III ingredient under health care antiseptic monograph for most other uses because of the lack of enough data to determine safety or efficacy (10). In China, there are several products including 0.1% benzalkonium chloride approved by the health authorities as wound antiseptics in the market.

BACTROBAN® disinfectant spray (GlaxoSmithKline, Nanjing, China), marketed in China since July 2011, is a skin wound disinfectant containing 0.13% benzalkonium chloride in an aqueous solution. Consumer insight into market research identified that delivering a cooling sensory benefit together with the existing attributes of the current formulation could provide an enhanced product experience for consumers. A prototype wound wash product formulation using a cooling technology was developed to include a cooling agent (menthol derivatives) and a solubilizer into the currently marketed formulation.

Menthol and related cooling compounds are widely used in food and pharmaceutical industries (11). It is widely used in dermatologic practice in topical antipruritic, antiseptic, analgesic, and cooling formulations (12). Menthol has been demonstrated to activate the transient receptor potential melastatin type 8, a recognized thermo-receptor expressed in sensory nerves and/or skin cells, the physiological role of which as a transducer of gentle cooling is widely accepted (13–15). The sensory impact of menthol when applied to skin depends on the concentration of menthol. Low concentrations give a cool sensation whereas high concentrations of 2–5% menthol cause irritation. Menthol has also been reported to be associated with allergic contact dermatitis (11,12); therefore, the level of menthol in the formulation was selected to provide optimum cooling versus minimal irritation.

A sensory evaluation in an expert panel with healthy skin successfully demonstrated that the prototype disinfectant spray formulation could deliver more cooling sensation than the currently marketed product (a sensory study conducted by MMR Research Worldwide, China; data on file). The sensory study was performed on healthy skin rather than the product's indication of wounded skin; therefore, it is not necessarily indicative of the prototype product's performance in real use because the penetration of the topically applied product will be faster on wounded skin. Therefore, to understand the sensory

impact of the prototype formulation in its intended use, it was considered necessary to evaluate the prototype formulation on wounded skin. Since there are multiple issues associated with conducting clinical studies on subjects with wounded skin (recruitment, evaluation, and timing), the use of an experimental wound methodology offered a convenient and clinically relevant approach to evaluate product-use experience, irritation potential, and sensory factors.

This article describes two clinical studies (the pilot and the pivotal study) to evaluate the sensory characteristics and irritation potential of a prototype disinfectant spray in subjects with experimental wounds compared with reference and control products. The experimental wounds were generated using sequential tape strippings of the forearm skin before product application. The wound model used was a modification of the method reported by Pagnoni (16) (adapted from the method of Bashir (17)). Pagnoni reported that they were able to use 40 strippings of the Transpore® tape (3M Health Care, St. Paul, MN) to disrupt the stratum corneum barrier to successfully demonstrate the sensory responses from a first-aid formulation applied to experimental wounds. In recent years, the Corneofix® (Courage & Khazaka Electronic GmbH, Cologne, Germany) tape (2×1.95 cm) is much more frequently used than the Transpore® tape in clinical practice in China.

Informed by the pilot study results and the MMR sensory research outcomes, the pivotal study was conducted to further explore the sensory performance as well as the tolerability of prototype formulations. Some modifications to the study design were made for the pivotal study based on learning's from the pilot and additional sensory studies conducted on healthy skin.

MATERIALS AND METHODS

The pilot study was a single center, "replicated latin square design", randomized, and double-blinded. The pivotal study was a single center, randomized, controlled, crossover, and double-blinded study, following a direct comparison test design of the study products.

For both studies, the screening and treatment took place at the first visit and follow-up visits occurred on Day 4 and Day 8, where the test sites were assessed visually. In the pilot study, the transepidermal water loss (TEWL) values were measured before and after wounding on Day 1 to ensure disruption of skin barrier and again on Day 4 and 8 to evaluate skin integrity restoration. The TEWL after wounding will be measured three times, and the arithmetic mean value will be taken as the TEWL value.

Both studies were conducted at the Guangzhou Landproof Testing Technology Co., Ltd. (**Guangzhou, China**). The pilot study was conducted between August 12 and 19, 2013, and the pivotal study between May 16 and June 10, 2014. The study protocols and consent forms were reviewed and approved by the Guangdong Cosmetics Institutional Review Board.

SUBJECT SELECTION

In the pilot study, ~15 subjects were planned to be screened to randomize a maximum of 12 subjects with the intention that 10 subjects complete the study. There were no statistical considerations taken into account in the selection of the sample size as this was a

pilot study so it was not formally powered to detect differences between the test product and other treatments. There were 12 subjects screened and randomized to treatment; 11 completed all four treatment periods, and one subject completed only three treatment periods (discontinued before receiving BACTROBAN® disinfectant spray because of withdrawal of consent, the subject did not want to wait for the last treatment). All subjects were included in the analysis.

In the pivotal study, ~60 subjects were planned to be screened to randomize a maximum of 50 subjects with the intention that 45 subjects should complete the study. The study had 85% power to detect a difference of 12 mm [in visual analogue scale (VAS)] between products assuming a standard deviation (SD) of the difference to be 26.1 with 45 completers (within-subject SD = 18.46 based on the review and analysis of the data from the pilot study). There were 50 subjects screened and randomized to treatment; 49 subjects completed the study. All subjects were included in the analysis.

The main inclusion criteria for both studies were subjects aged 18–60 year old with generally good health and healthy skin condition, who provided written informed consent and were willing and capable to comply with all study procedures.

TEST SITES AND WOUNDING PROCEDURE

Figure 1 shows a total of four test areas: I, II, III, and IV, two on each volar forearm that were identified. The center of test site I was vertically 5 cm away from the middle of transverse cubital crease and the center of test site II, respectively, in the left volar forearm. The positions of test sites III and IV were identical with those of site I and II, respectively, in the right volar forearm. For the pivotal study site, only three test areas were selected—site IV was omitted. In addition, sites II and III exchanged positions to avoid

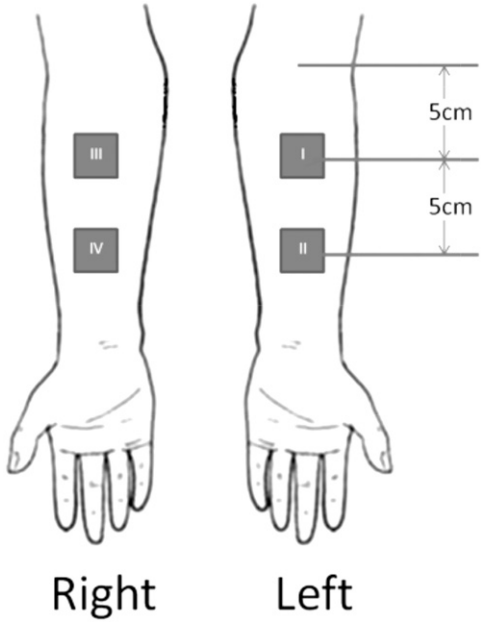

Figure 1. Pilot study - test areas. Test area IV was not included for pivotal study.

the application of two products, and the subsequent sensory assessment occurring consecutively on the same forearm, therefore, reduces interference between products.

Each superficial wound was created by a sequential removal of the stratum corneum layers using the Corneofix® tape (2 × 1.95 cm) until a clear glistening layer was visualized (at least 40 times). The TEWL measurements were taken after wound creation and before test product application. The procedure was conducted in all four test areas for the pilot study and three test areas for the pivotal study except the TEWL measurements.

The sequence of wounding was I, II, III (and IV, pilot study only), and the sequence of allocation of product to each test site was randomized.

FORMULATIONS AND BLINDING

For both studies, the test product was a prototype disinfectant spray containing 0.13% benzalkonium chloride and 1% menthol derivatives (menthone glycerin acetal). The reference product was the BACTROBAN® disinfectant spray (0.13% benzalkonium chloride) sourced from a market place in China. The negative control was 0.9% w/v sodium chloride solution (saline) (China Otsuka Pharmaceuticals Co., Ltd., **Foshan, China**). The pilot study also included a positive control (70% v/v isopropyl alcohol); this was not included in the pivotal study. The active ingredient, batch number, and expiration date of the test products are provided in Table I.

The sequence of product applications on wound sites (I, II, II, and IV for the pilot study and I, II, and III for the pivotal study) was randomly assigned to each subject. There were eight different sequences in the pilot study and six different sequences in the pivotal study. The randomization schedule was generated using a computerized randomization generator and provided to the site by the GSK Biostatistics Department.

In the pilot study, a square filter paper (1.8 × 1.8 cm) (Courage + Khazaka electronic GmbH, Köln, Germany) saturated with each product was applied and left on each test

Table I
The Active Ingredient, Batch Number, and Expiration Date of Test Products

Product	Ingredients	Batch No.	Use By
Prototype disinfectant spray	0.13% Benzalkonium chloride (active) Menthone glycerin acetal (active) Polysorbate 20 Edetate disodium dihydrate Propylene glycol Sodium bicarbonate Purified water	RDMF0024B01	May 6, 2014
BACTROBAN® disinfectant spray	0.13% benzalkonium chloride (active) Polysorbate 20 Edetate disodium dihydrate Propylene glycol Sodium bicarbonate Purified water	BDB130104	January 24, 2015
0.9% w/v sodium chloride solution	0.9% w/v sodium chloride Aqua	1H73G1	July 1, 2016
70% v/v isopropyl alcohol	70% v/v isopropyl alcohol Aqua	1BI0808	August 31, 2014

site for 15 s, and there was at least 10 min interval between the study product applications. In the pivotal study, the product was applied by spraying twice onto the experimental wound from a distance of ~10 cm within 2 min of wound creation. There was at least a 30 min interval between the product applications. The product application in the pivotal study used spray instead of filter paper to more accurately reflect real-life use.

The examiner conducting the skin assessments had no involvement in product application and remained blinded to the identity of the investigational product. All the products were identical in appearance and packaging to maintain blinding. The subjects were also blinded to the treatment identity.

ASSESSMENT

TEWL MEASUREMENT (PILOT STUDY ONLY)

The TEWL was measured ($g/m^2/h$) by means of a Tewameter TM300® (Courage & Khazaka Electronic GmbH) under standard conditions, and the probe of the Tewameter TM300® was warmed up to 30.0° ± 1.0°C. Subjects were in a temperature- and humidity-controlled room (19°–21°C and 45–55% relative humidity) for 15 min before each TEWL measurement.

SUBJECT PERCEPTION

In the pilot study, subjects rated their response to the perceived product performance (cooling/fresh and pleasant feeling intensities), tolerability (stinging/burning and itching intensities), and overall rating of the product liking using a questionnaire containing five-point categorical scales. For the pivotal study, subjects were asked to rate their perceived cooling intensity using a 100 mm VAS at four time points (immediately 3, 5, and 15 min after product application) and to rate their overall sensory liking of the product using a nine-point categorical scale. The VAS rating in millimeter (mm) was measured and recorded by one member of the site staff.

SAFETY

Safety was assessed through adverse events spontaneously reported by subjects or observed by the investigator and the TEWL measurements (pilot study only). Changes in performance and tolerance variables, e.g., cooling, burning, and itching intensities, were not classified as adverse events.

STATISTICAL METHODS

PILOT STUDY

The proportions of subjects within a treatment experiencing cooling/fresh sensation, pleasant feeling, stinging/burning, and itching sensation during 15 s of test product

application were presented, and the corresponding 95% confidence intervals were calculated using one-sample exact binomial test.

The intensity of each reported cooling/fresh sensation, pleasant feeling, stinging/burning, and itching sensation was summarized using suitable summary statistics and compared using the Wilcoxon signed-rank test.

The statistical significance level for all statistical tests was 0.05 as this was an exploratory study with a very small sample size; no adjustment for multiplicity was used. All *p*-values should be considered as an indicator of a trend but not a confirmation of a difference between products or a confirmation of a trend.

PIVOTAL STUDY

Cooling sensation VAS at each assessment time (immediately 3, 5, and 15 min after each study product application) and overall product liking score were analyzed using the mixed effect analysis of variance (ANOVA) with product use and assessment site as fixed effects and subject as random effect. Product differences together with *p*-values and 95% Confidence Intervals (CIs) were provided. The assumption of residual normality was investigated and considered as satisfied.

Cooling sensation area under effect-time curve (AUEC) over 15 min was calculated for each subject on each test. An average AUEC (AUEC/15) was analyzed using the same mixed effect ANOVA model as used in the primary analysis.

RESULTS

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

In the pilot study, a total of 12 Asian subjects were included in the randomized population consisting of six females (50%) and six males (50%). The mean age was 39.3 ranging from 21 to 53 year.

In the pivotal study, a total of 50 Asian subjects were included in the randomized population consisting of 25 females (50%) females and 25 (50%) males. The mean age was 40.0 ranging from 21 to 59 year.

EFFICACY RESULTS

PILOT STUDY

Table II summarizes the frequency of responses to the questionnaire containing five-point categorical scales (1, 2, 3, 4, and 5), where subjects rated their responses to the treatments in terms of perceived performance (cooling/fresh and pleasant feeling intensities), tolerability (stinging/burning and itching intensities), and overall rating of the product liking from the pilot study.

For overall rating, the proportion of subjects indicating they liked the product was 58% for the prototype disinfectant spray, 64% for the BACTROBAN® disinfectant spray, 33% for 70% v/v isopropyl alcohol, and 42% for 0.9% w/v sodium chloride solution (saline).

Table II
Pilot Study Subject Sensory Questionnaire Responses

	Prototype disinfectant spray (*N* = 12)	BACTROBAN® disinfectant spray (*N* = 11)	70% isopropyl alcohol (*N* = 12)	0.9% sodium chloride solution (*N* = 12)
	N (%)	*N* (%)	*N* (%)	*N* (%)
Cooling/Fresh sensation				
None	0	0	0	0
Weak	2 (16.7)	1 (8.3)	4 (33.3)	2 (16.7)
Moderate	5 (41.7)	4 (33.3)	3 (25.0)	2 (16.7)
Strong	4 (33.3)	7 (58.3)	4 (33.3)	4 (33.3)
Extremely strong	1 (8.3)	0	1 (8.3)	4 (33.3)
Pleasant feeling				
Disagree strongly	0	0	1 (8.3)	0
Disagree moderately	1 (8.3)	0	2 (16.7)	0
Neither agree nor disagree	4 (33.3)	1 (9.1)	0	5 (41.7)
Agree	7 (58.3)	10 (90.9)	8 (66.7)	7 (58.3)
Strongly agree	0	0	1 (8.3)	0
Stinging/Burning sensation				
None	4 (33.3)	5 (45.5)	4 (33.3)	7 (58.3)
Weak	5 (41.7)	3 (27.3)	3 (25.0)	4 (33.3)
Moderate	3 (25.0)	3 (27.3)	2 (16.7)	1 (8.3)
Strong	0	0	3 (25.0)	0
Unbearable	0	0	0	0
Itching sensation				
None	9 (75.0)	10 (90.9)	10 (83.3)	9 (75.0)
Weak	3 (25.0)	1 (9.1)	2 (16.7)	3 (25.0)
Moderate	0	0	0	0
Strong	0	0	0	0
Unbearable	0	0	0	0
Overall product rating				
Dislike very much	0	0	0	0
Dislike moderately	0	0	3 (25.0)	0
Neither like nor dislike	5 (41.7)	4 (36.4)	5 (41.7)	7 (58.3)
Like moderately	6 (50.0)	6 (54.5)	3 (25.0)	5 (41.7)
Like very much	1 (8.3)	1 (9.1)	1 (8.3)	0

The Wilcoxon signed-rank test results showed the difference in rating between products for all attributes (Table III). This was a pilot study and not powered to show statistically significant differences between treatments. The only statistically significant difference observed was between the negative (sodium chloride solution) and positive control (70% isopropyl alcohol) in relation to the "stinging/burning sensation" in favor of the negative control. No itching sensation was recorded by subjects after applying any of the four products.

PIVOTAL STUDY

The cooling sensation VAS score raw means are plotted in Figure 2 by treatment and assessment time for all treatments. Treatment comparisons are provided in Table IV.

Statistically significant product differences were observed between the prototype formulation and the BACTROBAN® disinfectant spray at 3 and 5 min after application

Table III
Pilot Study Comparison of Treatments using Wilcoxon Signed-Rank Test

	Prototype disinfectant spray (N = 12)	BACTROBAN® disinfectant spray (N = 11)	70% isopropyl alcohol (N = 12)
Cooling/Fresh sensation			
BACTROBAN® disinfectant spray	0.7500		
70% isopropyl alcohol	0.6875	0.5625	
0.9% sodium chloride solution (N = 12)	0.1825	0.1758	0.4375
Pleasant feeling			
BACTROBAN® disinfectant spray	0.1250		
70% isopropyl alcohol	1.0000	0.5625	
0.9% sodium chloride solution (N = 12)	1.0000	0.2500	1.0000
Stinging/Burning sensation			
BACTROBAN® disinfectant spray	1.0000		
70% isopropyl alcohol	0.4082	0.5313	
0.9% sodium chloride solution (N = 12)	0.1875	0.3594	0.0313
Itching sensation			
BACTROBAN® disinfectant spray	1.0000		
70% isopropyl alcohol	1.0000	1.0000	
0.9% sodium chloride solution (N = 12)	1.0000	1.0000	1.0000
Overall product liking			
BACTROBAN® disinfectant spray	1.0000		
70% isopropyl alcohol	0.0625	0.1250	
0.9% sodium chloride solution (N = 12)	0.3750	0.3750	0.5625

and in average AUEC in favor of the prototype formulation. Statistically significant product differences were also observed in favor of the prototype formulation compared with the negative control (saline) at 3, 5, and 15 min after application and in average AUEC.

For overall liking score, the raw means of the three treatments are plotted in Figure 3, and treatment comparisons are provided in Table V. There were no statistically significant differences observed. The comparison between prototype formulation and negative control (saline) approached significance (difference 0.4 and p-value 0.0561).

SAFETY RESULTS

PILOT STUDY

No adverse event was recorded. At the Day 4 and Day 8 follow-up visits, mild erythema was observed in 50% of subjects localized at one or more of the wound sites. The findings were observed across all treatment groups. The examining clinician and Principal Investigator diagnosed these signs as being part of the normal wound healing, inflammatory response with no causal relationship to test products. These observations were not recorded as Adverse Event (AEs) per the protocol definition of an AE as an untoward/unintended medical occurrence. The four treatment groups had similar TEWL means

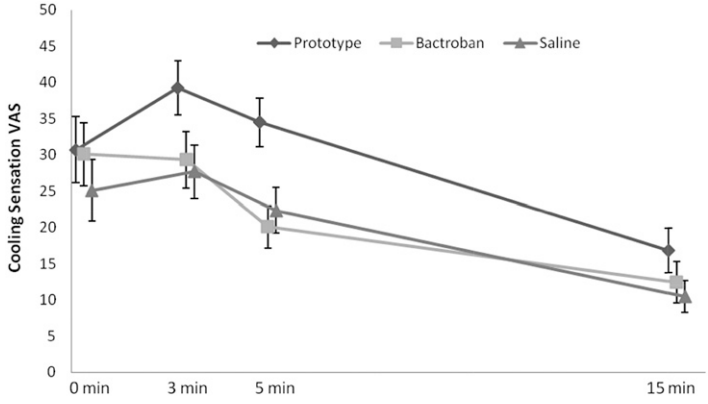

Figure 2. Pivotal study cooling VAS by treatment and time (mean ± SE).

before wounding and after wounding. The TEWL means were higher after wounding as compared with before wounding in all treatments and all sites.

PIVOTAL STUDY

One subject reported three AEs. The adverse events occurred after the application of each of the three products. They were reported as "itch in all three wounds," and the severity was mild. The itching sensation was reported to start the day after product application and resolved 2 d later without requiring treatment intervention. These adverse events were not considered related to the test products.

Table IV
Pivotal Study Treatment Comparison on Cooling VAS Score

	Treatment comparison	Difference[a] (95% CI[a])	*p*-value[a]
Immediate	Prototype vs. BACTROBAN®	0.5 (–5.4, 6.3)	0.8711
	Prototype vs. saline	5.5 (–0.4, 11.3)	0.0659
	BACTROBAN® vs. saline	5.0 (–0.8, 10.8)	0.0928
3 min	Prototype vs. BACTROBAN®	9.7 (2.7, 16.7)	0.0069
	Prototype vs. saline	1s1.4 (4.4, 18.4)	0.0016
	BACTROBAN® vs. saline	1.7 (–5.3, 8.7)	0.6323
5 min	Prototype vs. BACTROBAN®	14.3 (8.4, 20.2)	<0.0001
	Prototype vs. saline	12.1 (6.2, 18.0)	<0.0001
	BACTROBAN® vs. saline	–2.2 (–8.1, 3.7)	0.4645
15 min	Prototype vs. BACTROBAN®	4.4 (–1.6, 10.4)	0.1482
	Prototype vs. saline	6.4 (0.4, 12.4)	0.0357
	BACTROBAN® vs. saline	2.0 (–4.0, 8.0)	0.5030
Average AUEC (AUEC/15)	Prototype vs. BACTROBAN®	8.9 (4.3, 13.4)	0.0002
	Prototype vs. saline	9.4 (4.9, 14.0)	<0.0001
	BACTROBAN® vs. saline	0.6 (–4.0, 5.1)	0.8006

[a]From mixed effect ANOVA analysis with treatment and site as fixed effects and subject as random effect. Difference is the first named treatment minus second named treatment such that a positive difference favors the first named treatment.

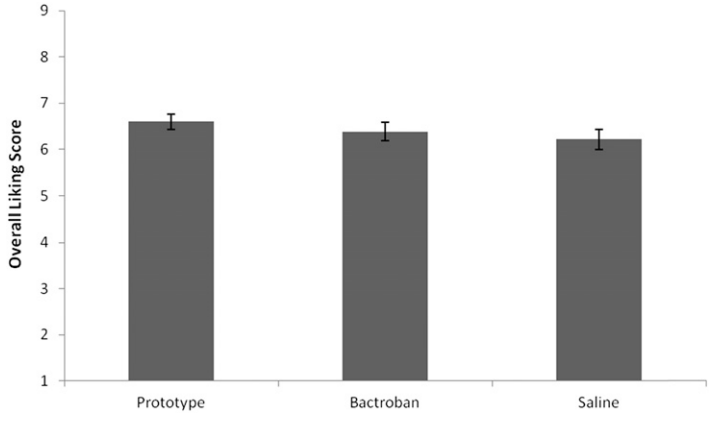

Figure 3. Pivotal study overall liking score by treatment (mean ± SE).

DISCUSSION

The pilot study results demonstrated a significantly more stinging/burning sensation from the positive control than the negative control providing confidence in the reliability of this model to differentiate on this variable. The skin barrier disruption was also verified by the TEWL after wounding which increased compared with the TEWL before wounding. The results of the pilot study also showed that numerically a higher proportion of subjects preferred the prototype disinfectant spray formulation to both controls, although the liking was comparable with the currently marketed formulation. A higher proportion of subjects reported cooling sensation relative to positive and negative control products. Although the sensory endpoints did not achieve statistical significance, the observed effect size was used to help to design and calculate the sample size for the pivotal study.

Following the pilot study and additional inhouse sensory research on healthy skin, it was decided to use a more sensitive and well-validated scale to detect potential differences in product sensory performance for the pivotal study. Three different rating scales such as the VAS, numerical rating scale (NRS), and verbal rating scale (VRS) are commonly used to measure pain, itching, and other subjective sensory responses. All these scales have been proven to have a high reliability and concurrent validity, and NRS-11, VRS-7, and VAS all worked well for pain intensity evaluation (18,19). To maintain consistency between clinical and sensory studies, a 100 mm VAS was selected for the pivotal study.

Table V
Pivotal Study Treatment Comparison on Overall Liking Score

Time	Treatment comparison	Difference[a] (95% CI[a])	*p*-value[a]
After 15 min	Prototype vs. BACTROBAN®	0.22 (–0.17, 0.62)	0.2663
	Prototype vs. Saline	0.38 (–0.01, 0.78)	0.0561
	BACTROBAN® vs. Saline	0.16 (–0.23, 0.56)	0.4169

[a]From mixed effect ANOVA analysis with treatment and site as fixed effects and subject as random effect. Difference is the first named treatment minus second named treatment such that a positive difference favors the first named treatment.

Earlier market research had indicated that the addition of cooling attributes to the existing BACTROBAN® disinfectant spray was desirable by consumers. In the pivotal study, although there was a significant increase in consumer perceived cooling from the prototype formulation, this did not correspond to a significant increase in overall product liking for the prototype compared with the existing marketed product in this study.

CONCLUSIONS

Experimental wound models are an effective means of evaluating sensory characteristics of disinfectant sprays.

The prototype formulation containing a cooling agent delivered significantly more cooling sensation than both BACTROBAN® disinfectant spray and the negative control product on experimental wounds at 3 and 5 min after product application, and overall for a 15-min period after application.

No statistically significant differences in product liking were observed between the prototype disinfectant spray compared with BACTROBAN® disinfectant spray formulations or negative control product.

The prototype disinfectant spray, BACTROBAN® disinfectant Spray, and control products were well-tolerated in these studies.

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