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A unique water optional health care personnel handwash provides antimicrobial persistence and residual effects while decreasing the need for additional products

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Background: The Centers for Disease Control and Prevention (CDC) has published guidelines for hand hygiene practices, recommending a handwash regimen that alternates between waterless alcohol products and antimicrobial or nonantimicrobial soap and water. The advent of an alcohol-based product that can be used with or without water (ie, water optional) to decontaminate the hands while providing immediacy of kill and antimicrobial persistence could reduce the confusion associated with handwash guidelines. Such a product has been developed, is alcohol-based (61 %), and zinc pyrithione (ZPT) preserved (61 % alcohol-ZPT) and has proven to be fully compliant with the Food and Drug Administration (FDA) and CDC guidelines.

Methods: FDA-required testing of the 61 % alcohol-ZPT product for the health care personnel handwash indication was performed as outlined in the Tentative Final Monograph (TFM) for Health-Care Antiseptic Drug Products, employing waterless and water-aided product applications. It was next assessed for antimicrobial persistence and residual effects by comparing it, in separate waterless and water-aided applications, with commonly available handwashes containing various antimicrobials in a 5-day study employing 49 subjects, in which samples were collected immediately and at 4 hours and 8 hours postapplication. The skin conditioning properties of this formulation were investigated via appropriate methods.

Results: The 61 % alcohol-ZPT product easily produced >3.0 log10 reduction in the indicator strain (Serratia marcescens) following the first wash, exceeding the 2.0 log10 FDA requirement. This level of performance was maintained through the tenth wash, surpassing the 3.0 log10 FDA requirement for the handwash indication. For the assessment of persistence and residual effect in the waterless mode, the water-optional, 61 % alcohol-ZPT product consistently produced log10 reductions of nearly 3.5 or greater at every point over the entire study period. In the water-aided configuration, similar results were obtained as log10 reductions of 2.5 were observed. The formulation is nonirritating, actually contributing to hand skin condition.

Conclusions: The 61 % alcohol-ZPT product exceeds all FDA criteria for the health care personnel handwash indication and is a significant advancement in the concept of skin antisepsis. It represents a single product suitable for use in all hand hygiene settings, demonstrating improved antimicrobial persistence and residual effects. The 61 % alcohol-ZPT formulation contributes positively to overall hand conditioning, and a previously reported study has documented it to be virucidal for several DNA and RNA viruses. (Am J Infect Control 2005;33:207-16.)
the alcohol hand sanitizers. Moreover, the alcohol-only products provide no appreciable antimicrobial persistence.

According to Hilburn et al., in the United States, there are 2.0 million nosocomial infections each year. These account for 5% to 10% of hospitalized patients, result in 88,000 deaths (eighth leading cause), and cost the US economy over $4.5 billion annually. Again, compliance with established handwashing policies was considered a key factor in breaking the chain of infection. Often, compliance is low, in the range of only 20% to 50%. Proper hand hygiene is a very important tool in reducing nosocomial infections; one that could realize potential annual savings in the range of $1.5 billion. Recent studies with alcohol-based hand sanitizers have shown that these products can reduce the incidence of nosocomial infections by 30.0% to 36.1%. The Centers for Disease Control and Prevention (CDC) has published hand hygiene practices for health care personnel, recommending that alcohol-based hand sanitizers be used routinely, interspersed frequently with thorough handwashes throughout the workday. Therefore, hand hygiene as envisioned by the CDC could be accomplished by the routine use of a combination of waterless hand sanitizers and water-aided handwashes. Compliance with CDC handwash guidelines may be enhanced by an alcohol-based product that could be used with or without water—because this one, single product would prove beneficial for those incidents in which the hands are soiled and a water-aided wash is needed, as well as for the more routine waterless hand hygiene episodes. Therefore, the number of products required for hand sanitization would be reduced and, thus, some of the confusion surrounding the hand hygiene experience and compliance eliminated.

For example, a new water-optional health care personnel handwash, 61% ethyl alcohol preserved with zinc pyrithione (61% alcohol-ZPT), has been designed to fulfill this need. It was tested in vitro and then in vivo in both waterless and water-aided applications and has been found compliant with the FDA criteria for this indication, as set forth in the Tentative Final Monograph (TFM) for “Effectiveness Testing of an Antiseptic Handwash or Healthcare Personnel Handwash.” The in vivo testing was performed per the TFM in the waterless as well as the water-aided modes to ensure that the product was FDA compliant regardless of application method.

This FDA test procedure assesses reductions in numbers of a bacterial contaminant (Serratia marcescens) on the hands of human volunteer subjects immediately following use of a hand cleanser. Persistent and
residual antimicrobial effects are not evaluated in this TFM-based study design. Even so, persistent effects (continued antimicrobial activity for an extended period—e.g., 6 hours—following product use to prevent microbial recolonization) and residual effects (the progressive increase or cumulative antimicrobial activity with repeated use of a product over time) would be properties highly desirable in a health care handwash product.6,7 Neither of these characteristics are inherent with alcohol-only hand gels. As stated above, ZPT was incorporated as the preservative system for this product. This was done in accordance with the TFM authorization allowing for the addition of preservatives to alcohol-based products.5 The FDA’s rationale is that alcohol-based products of skin antisepsis do not provide the antimicrobial persistence necessary to prevent microbial recolonization beyond 2 to 3 hours. A properly selected preservative added to alcohol-based products can extend the antimicrobial effects for hours longer.

Therefore, a second comparative study was designed, in which 4 products were tested—a novel, water-optional 61% alcohol-ZPT (Trisepin Water-optional; HEALTHPOINT, Ltd., Fort Worth, TX), a no-rinse 61% ethanol hand sanitizer without a preservative system (Avagard D; 3M Health Care, St. Paul, MN), a 0.5% triclosan water-aided handwash (CV Medicated Lotion Soap; STERIS Corporation, Mentor, OH), a 2% chlorhexidine gluconate (CHG) water-aided handwash (BactoShield; STERIS Corporation)—and a 4% CHG handwash was employed as a reference product (HIBICLENS; Regent Medical, Norcross, GA). The thrust of this 5-day study was to characterize and compare the immediate, persistent, and residual antimicrobial effects of these products on the resident and transient microflora present on the hands of human volunteers. In addition, the skin-conditioning benefits of the 61% alcohol-ZPT formulation were measured via an exaggerated handwash study8,9; the virucidal effectiveness while assessed was reported elsewhere previously.10,11

All data reported here were obtained by tests performed at contract laboratory facilities. The supporting institutional review board for each test facility approved the in vivo protocol(s).

MATERIALS AND METHODS

TFM testing

Prior to product testing, a neutralization study was performed, following the guidelines set forth in the American Society for Testing Materials (ASTM) Method E 1054-02, Standard Test Methods for Evaluation of Inactivators of Antimicrobial Agents.12 Because the postneutralization test population mean log_{10} values were within 0.25 log_{10} of the initial population mean log_{10} values, the neutralization was considered successful. Both in vitro and in vivo testing are mandated by the FDA's TFM,5 and these studies were conducted...
for the 61% alcohol-ZPT product. Only the in vivo data are discussed here because they relate to criteria that are health care personnel handwash indication specific. In vitro data are on file and available. The in vitro tests included the minimum inhibitory test employing approximately 1100 organisms (bacteria and yeast) of various genera and species, many of which are known human pathogens. Similarly, log10 time kill studies were performed on species of bacteria and yeasts to verify the prompt, efficient microbial kill of the product.

Subjects recruited for these studies were male and female paid volunteers (33 total) between the ages of 17 and 70 years. Seven days prior to the testing, subjects were instructed to avoid using medicated soaps, lotions, deodorants, and shampoos, as well as to avoid skin contact with solvents, detergents, acids, and bases or any other products known to affect the normal microbial populations of the skin. Subjects were supplied with a personal hygiene kit and instructed to use the enclosed items exclusively for the duration of the studies. In both the waterless and water-aided TFM required in vivo studies, testing entailed 11 consecutive hand contaminations with a marker organism, Serratia marcescens (ATCC 14756). The first followed by sampling for baseline, and each of the remaining 10 by a hand-cleansing procedure using one of the test or comparator formulations, without water in one study group (18 subjects) or water-aided in the other (15 subjects).

Using aseptic techniques, a 5.0-mL aliquot of the microbial inoculum, containing not less that 10^8 organisms/mL, was evenly distributed over both hands, but not above the wrists, through gentle continuous massage for 45 seconds. After a timed 2-minute air-dry, the subjects applied the assigned product with or without water (water temperature regulated at 40°C ± 2°C), as per product label use instructions. This contamination/product application procedure was performed a total of 10 times, allowing 5 to 15 minutes between cycles. Glove-juice samples were taken following contamination/product application cycles 1, 3, 7, and 10. The estimated log10 number of viable microorganisms recovered from each hand was designated the “R-value;” the adjusted average log10 colony count measurement for each subject at the sampling time. A log10 transformation was performed on the collected data to prepare them for statistical analysis. Comparator products for these studies included marketed health care handwash products containing 2.0% chlorhexidine gluconate (CHG; BactoShield) or 0.5% Triclosan (STERIS Corporation) for the water-aided application and 61% ethyl alcohol without preservative (Avagard D; 3M Health Care) for the waterless application. The water-aided product application times were 30 seconds for the CHG and Triclosan comparator products but only 15 seconds for the test formulation–61% alcohol-ZPT.

Assessment of persistence and residual effects

Subjects recruited for these non-TFM, additional studies of antimicrobial persistence and residual effects were male and female paid volunteers (49 total) between the ages of 17 and 70 years. Prior to product testing, a neutralization study was performed, following the guidelines set forth in the American Society for Testing Materials (ASTM) Method E 1054-02, Standard Test Methods for Evaluation of Inactivators of Antimicrobial Agents. Because the postneutralization test
population mean log\textsubscript{10} values were within 0.25 log\textsubscript{10} of the initial population mean log\textsubscript{10} values, the neutralization was considered successful. A 7-day pretest period preceding the baseline portion of the study, during which the personal hygiene kit was used, allowed for stabilization of the normal microbial populations residing on the hands. The following week, subjects’ hands were sampled for microorganisms on days 1 and 5 to establish a mean baseline population count for each subject’s hands. Subjects clipped their fingernails to 1-mm free edge and removed all jewelry from hands and forearms. For each baseline determination, subjects rinsed their hands and the lower two thirds of their arms in tap water regulated at 40°C and cleaned their fingernails using a nail cleaner. Under supervision of a technician, subjects then washed their hands and forearms with 5 mL of a liquid, nonmedicated, baseline soap, working up a lather. Throughout this procedure, subjects maintained their hands in a position above their elbows. Following a 30-second rinse in 40°C tap water, the glove-juice sampling procedure was performed by laboratory personnel as follows. Powder-free, loose-fitting, sterile latex gloves were placed on subjects’ hands, and laboratory personnel instilled 75.0 mL sterile stripping fluid without product neutralizers into each of the gloves. The wrists were then secured, and laboratory technicians massaged the hands through the gloves in a standardized manner for 60 seconds. A 5-mL aliquot of the glove juice was removed from each of the gloves, and each aliquot was diluted in 5 mL Butterfield’s phosphate buffer solution with product neutralizers (dilution 10\textsuperscript{6}). The 10\textsuperscript{6} dilution was then serially diluted in Butterfield’s phosphate buffer solution with product neutralizers. Duplicate spread and/or spiral plates were prepared from each of the glove-juice dilutions using Tryptic soy agar with 0.07% lecithin (wt/vol) and 0.5% Tween 80 (wt/vol) and were incubated at 30°C for approximately 72 hours. Following incubation, the colonies on the plates were counted and the data recorded using the computerized Q-count plate-counting system.

The following week (test week), each subject applied a single, randomly assigned product 4 times each day for 5 consecutive days, with a minimum of 15 minutes between applications. The water-optional handwash product (61% alcohol-ZPT) was tested in both a waterless and a water-aided configuration. Hence, a total of 5 test configurations, 2 employing waterless products and 3 employing water-aided products, were evaluated. Nine volunteer subjects were assigned randomly to each of the 5 test configurations, and glove-juice sampling was performed immediately, 4 hours, and 8 hours following completion of the fourth product application on test days 1, 3, and 5. Sampling times–immediate, 4 hours, or 8 hours–were assigned randomly to the 2 hands of each of the 9 subjects for each of the test configurations, thereby providing 6 hand samples at each of the 3 time points. Four additional subjects were assigned randomly to use the water-aided 4% CHG reference product, as an internal

### Table 1. Summary comparison of log\textsubscript{10} reductions produced immediately and 8 hours following application

| Product                      | Day 1 log\textsubscript{10} reductions | Day 3 log\textsubscript{10} reductions | Day 5 log\textsubscript{10} reductions |
|------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
|                              | Immediate | 8 Hour | Immediate | 8 Hour | Immediate | 8-Hour |
| Waterless                    | 3.50      | 3.30    | 3.83      | 3.61    | 3.75      | 3.77   |
| Test product: 61% alcohol-ZPT*| 3.50      | 3.30    | 3.83      | 3.61    | 3.75      | 3.77   |
| Comparator: 61% Ethanol       | 2.22      | 0.00 (P < .05) | 2.42 | 0.82 (P < .05) | 2.19 (P < .05) | 0.42 (P < .05) |
| Water aided                  | 3.25      | 3.05    | 3.57      | 3.37    | 3.51      | 3.44   |
| Test product: 61% alcohol-ZPT*| 3.25      | 3.05    | 3.57      | 3.37    | 3.51      | 3.44   |
| Comparator: 2% CHG            | 3.25      | 3.05    | 3.57      | 3.37    | 3.51      | 3.44   |
| Comparator: 0.5% Triclosan§   | 0.00 (P < .05) | 0.00 (P < .05) | 0.21 (P < .05) | 0.00 (P < .05) | 0.21 (P < .05) | 0.00 (P < .05) |
| Reference: 4% CHG             | 0.86      | 0.89    | 2.26      | 1.88    | 2.36      | 1.60   |
|                              | 6.02 log\textsubscript{10}, n = 9     | 6.02 log\textsubscript{10}, n = 9     | 6.02 log\textsubscript{10}, n = 9     |

*Trisep Water-Optional Healthcare Personnel Handwash (HEALTHPOINT, Ltd., Fort Worth, TX).
†Avagard D Instant Hand Antiseptic with Moisturizers (3M Health Care, St. Paul, MN).
‡BactoShield CHG 2% Surgical Scrub (STERIS Corporation, Mentor, OH).
§CV Medicated Lotion Soap (STERIS Corporation).
∥HIBICLENS Antiseptic/Antimicrobial Skin Cleanser (Regent Medical, Norcross, GA).
control, 4 times on each of the 5 test days, with glove-juice samples taken immediately and 8 hours following the fourth wash on test days 1, 3, and 5.

For the 2 test products used in waterless applications—the 61% alcohol-ZPT product and the 61% ethyl alcohol hand sanitizer—quantities sufficient to wet all hand surfaces thoroughly were dispensed into subjects’ hands. Next, paying particular attention to interdigital spaces, fingernails, and cuticles, subjects applied the product uniformly until air-dry (a minimum of 5 minutes of air-drying prior to sampling on test days 1, 3, and 5). The 61% alcohol-ZPT product was applied in this same way when tested as a water-aided product, except that the application time was 15 seconds, followed by a handrinse in tap water. For this, and all other handwash procedures, the temperature of the tap water was regulated at 40°C ± 2°C. For the remaining water-aided products—the 0.5% Triclosan and 2% CHG test products and the 4% CHG reference product—5 mL- aliquots were applied to subjects’ wet hands. Subjects then spread their product over all surfaces of the hands and fingers, washed their hands thoroughly for 30 seconds, and rinsed their hands for 30 seconds.

The estimated log_{10} numbers of viable microorganisms recovered from the baseline and postproduct-use glove-juice samples were designated the “R-values,” the adjusted average log_{10} colony count measurement for each subject at baseline and at each sampling time postproduct use. Each R-value was determined using the formula, \( R = \log_{10}[F \times C_i \times 10^{-2}] \times 2 \), in which F = the amount of sterile sampling solution instilled into a glove (in this study, F = 75 mL), \( C_i \) = the arithmetic average colony count from the 2 plates for each hand at a particular dilution level, D = the dilution factor, and 2 = the neutralization dilution. A log_{10} transformation was performed on the collected data to prepare them for statistical analysis.

Skin-friendliness testing

This was a controlled clinical trial enrolling a total of 58 female paid volunteers ranging in age from 17 to 70 years. It was designed to evaluate the irritation potential of the water-optional health care personnel handwash formulation applied in the waterless mode under exaggerated hand skin exposure conditions.8,9 This method was chosen because it may be considered “worse case” when compared with a water-aided application or to other types of skin-friendliness testing. During a 1-week conditioning phase prior to baseline, subjects used Dove (Unilever PLC) soap for general body cleansing, including the hands and face, Suave (Unilever PLC) shampoo and conditioner for hair care, and vinyl gloves when using household cleansers or other potentially harsh agents. At baseline, subjects’ hands were qualified according to protocol eligibility criteria and underwent multidimensional assessments9 that included clinical grading, self-assessment questionnaires, and noninvasive bioengineering measurements (TEWL [DermaLab; Cortex Technology], and skin hydration measured as a function of capacitance [Corneometer CM 820; Courage+Khazaka electronic GmbH] and as a function of impedance [NOVA DPM 9003; NOVA Technology Corporation]). Qualified subjects washed both hands with Dove liquid soap. After completion of the wash, subjects participated in 5 cycles of product application. Subjects returned to the clinic on days 2, 3, 4, and 5 for a controlled series of product applications, as were performed at baseline. Prior to beginning each cycle of applications, subjects’
hands were examined clinically. Subjects were disqualified if they presented with an inappropriate skin condition or a score of 3 or greater for any of the clinically graded parameters. Subjects disqualified because of clinical scores of 3 or greater participated in end point procedures described below. At day 3, subjects’ hands were graded clinically, and noninvasive bioengineering measurements were performed approximately 2 hours after completion of the last repeated exposure cycle. The end point procedures were completed for all subjects 2 hours after the completion of the last repeated exposure cycle on day 5 or when a subject was disqualified, as indicated earlier. End point procedures included clinical grading, self-assessment questionnaires, and noninvasive bioengineering measurements.

RESULTS

In vivo TFM antimicrobial efficacy testing

The critical indices specified by the FDA TFM5 for health care personnel handwash products are ≥2 log_{10} reduction from baseline populations immediately following product application 1 and ≥5 log_{10} reduction from baseline populations immediately following product application 10. A series of 2-sample Student’s t tests, comparing baseline populations of Serratia marcescens to postproduct-use populations, showed that the 61% alcohol-ZPT product, both in the waterless and the water-aided mode of application, produced significant population reductions (P < .05) from baseline at all sample points.

Water-aided applications. When used in a water-aided wash, the 61% alcohol-ZPT product produced mean reductions in the Serratia marcescens population of 3.36 log_{10} following wash 1 and 3.23 log_{10} following wash 10 (Fig 1). At wash 1, the 61% alcohol-ZPT product was significantly more efficacious (P < .05) than either the 2.0% CHG product or the 0.5% Triclosan product, as measured by log_{10} reduction parameters. By wash 10, both the 61% alcohol-ZPT product and the CHG-based handwash product were significantly (P < .05) better than the Triclosan-based handwash. The higher reduction from baseline observed at wash 10 with the CHG product may be related to the application times because the 61% alcohol-ZPT product was applied for 15 seconds per wash, compared with the 30-second time for the 10 CHG-based product applications.

Waterless applications. The 61% alcohol-ZPT product in a waterless application produced mean reductions in the Serratia marcescens population of 3.43 log_{10} following application 1 and 3.10 log_{10} following application 10 (Fig 2). At wash 10, the 61% alcohol-ZPT product was significantly (P < .05) more efficacious than the 61% ethyl alcohol handrub without preservative (log_{10} reduction = 1.22). Hence, whether used with or without water, the 61% alcohol-ZPT product satisfied the requirements specified by the FDA: a ≥2 log_{10} reduction in population following wash 1 and a ≥3 log_{10} reduction in population following wash 10.

Persistence and residual effects

Waterless applications. Use of the 61% alcohol-ZPT product resulted in a reduction from the baseline population of more than 3.0 log_{10} on test days 1, 3, and 5. The product also demonstrated significant (P < .05) persistent antimicrobial properties, preventing regrowth of microbial populations to baseline levels (Fig 3). Determining the residual properties of the 61% alcohol-ZPT product proved difficult because it demonstrated greater than a 3.0 log_{10} reduction from baseline on all 3 sample days, a level of antimicrobial activity better than observed for the other product tested. The unpreserved 61% ethyl alcohol hand sanitizer demonstrated statistically significant (P < .05) log_{10} microbial reductions from baseline but failed to achieve a 3 log_{10} reduction on test day 5. Additionally, microbial regrowth 8 hours postproduct-application showed antimicrobial persistence to be relatively poor, and no appreciable residual activity was apparent over the 5-day course of study (P > .05). By test day 5, the 61% alcohol-ZPT product was significantly (P < .05) more efficacious than the unpreserved 61% ethyl alcohol product at every time point as measured by log_{10} reduction parameters (see Table 1).
Skin-friendliness testing

Fifty-eight female subjects fulfilling all inclusion and exclusion criteria were enrolled for study participation, and 21 subjects completed the study. Twenty subjects voluntarily withdrew during the washout phase prior to testing, and 17 were disqualified for failing to meet clinical grading criteria at baseline. The 61% alcohol-ZPT product was shown to be very well tolerated under exaggerated conditions of exposure. Only mild, clinically insignificant changes were observed, which included small increases in dryness and hand skin erythema prior to washes performed on days 4 and 5 and following washes on day 5. Results of the self-assessment questionnaires at day 5 end point revealed no significant perceived changes in hand skin moisture, skin condition, feeling of healthy skin, skin cracking, or redness. Noninvasive bioengineering measurements confirmed that hand skin condition was not compromised during the exaggerated use of the cleanser (data not shown).

DISCUSSION

In vivo TFM antimicrobial efficacy testing

The 61% alcohol-ZPT product formulation exceeds all in vivo criteria established by the FDA in the TFM for the waterless and water-aided applications and, hence, is a water-optional health care personnel handwash. Comparable data were obtained as well for the required in vitro studies (data on file but not shown). The nature and characteristics of the ZPT preservative system has been discussed elsewhere.11

The increased efficacy observed with the 2.0% CHG (3.81 log10 reduction) versus the 61% ethyl alcohol product (3.23 log10 reduction) at wash 10 in the water-aided mode (Fig 1) is likely to be related to product application times (30 seconds for the 2.0% CHG product vs 15 seconds for the 61% alcohol-ZPT product) coupled with the nature of the health care personnel handwash in vivo test. This test requires the contamination of the hands with 5.0 ml of a solution containing not less than 10⁸ organisms/ml of the indicator strain (Serratia marcescens) at baseline determination and prior to each of the required 10 washes. Therefore, >10⁹ cfu of Serratia marcescens are applied to the hands during the course of the test. Differences in efficacy that are in the range of ~0.5 log10 under the conditions of unequal wash times should be viewed cautiously. For these reasons, the authors are more likely to consider the data generated in the corresponding persistence and residual effects study (Fig 4) as reflective of actual product performance because a total of 20 washes are used over a 5-day period for each product, thus minimizing to some degree the lack of parity associated with wash times.

Persistence and residual effects

Waterless applications. Although 61% ethyl alcohol alone does provide antimicrobial action immediately postapplication (>2.0 log10 reduction on all 3 test days), this product was unable to compete with the 61% alcohol-ZPT product in terms of persistent effect at the 8-hour postapplication time point (see Fig 3). The unpreserved ethyl alcohol product did not achieve the immediacy of kill or the residual/persistent effects observed with the 61% alcohol-ZPT product used in a waterless application. In the waterless mode of application, the 61% alcohol-ZPT product exhibits significantly greater (P < .05) antimicrobial properties (see Table 1).

Water-aided applications. The 2.0% CHG, 4.0% CHG, and the 61% alcohol-ZPT products performed generally in an acceptable manner, with some noteworthy differences in efficacy among the products. The 61% alcohol-ZPT product, in general, demonstrated better persistence (especially at the 8-hour time point) than did the other water-aided products. It is interesting to note that, for the 2% CHG, multiple 30-second applications were required over 2 to 3 days to achieve marginal antimicrobial persistence at the 8-hour test point (see Fig 4 data for test days 3 and 5). A surprising outcome of this study was the failure of the 0.5% Triclosan product to produce any significant antimicrobial effects, despite 20 applications of 30 seconds each over the 5-day period.

The data in Table 1 compare log10 reduction values from the immediate and 8-hour sample collection times and, therefore, may provide the best opportunity to assess overall antimicrobial persistence and residual effects. As noted previously, the 61% alcohol-ZPT product when applied waterless produced log10 reductions from baseline that average at least 3.5, thus it is difficult to assess the residual effects. The antimicrobial persistence, however, is unsurpassed by any other product or application technique waterless or water-aided. For the water-aided applications, only the 0.5% Triclosan product failed to demonstrate persistence or residual effects. The difference among the other products was not statistically significant, despite the shorter water-aided wash time for the 61% alcohol-ZPT product.

In vivo skin-friendliness testing

Overall, the results show that the 61% alcohol-ZPT product was tolerated exceptionally well under exaggerated exposure conditions, as shown by the parallelism in results observed among the clinical assessment parameters, the subjective self-assessment responses, and the noninvasive bioengineering measurements. These results uniformly indicate that real
skin-conditioning benefits are realized when the 61% alcohol-ZPT product is used in a setting such as that exemplified by health care, in which hand sanitation is practiced repeatedly and often.

The virucidal efficacy of this formulation has been documented previously. The data confirmed the virucidal action of the 61% alcohol-ZPT product against a wide variety of viral agents to include coronavirus (HCoV, ATCC VR-740, both HCoV and SARS-HCoV belong to the virus family Coronaviridae), the human immunodeficiency virus type 1 (HIV-1, from Zepto Metrix Corp. of Buffalo, NY), hepatitis A virus (HAV, from CREM, University of Ottawa), herpes simplex type 1 (HSV-1, ATCC VR-260), and human rotavirus (strain Wa, ATCC VR-2018). These agents represent both RNA and DNA viruses, some with envelopes and others without, which are known to be responsible for a significant amount of human morbidity and some mortality. Furthermore, HAV and the human rotavirus are known to be resistant to several of the antimicrobials commonly used for hand antisepsis. For these in vitro studies, the viral agents were cultured using standards methods in cell lines appropriate for propagation to levels at or above the required titer of $10^6$ infectious units/mL. The viruses were harvested, baseline numbers determined, and exposed for 3 minutes (30 seconds for the human coronavirus) to the test formulation diluted by virus inoculum to a 90% concentration. Following exposure to the test product, the surviving population was determined for each virus, employing techniques appropriate for that virus. To be considered virucidal, the baseline populations must be reduced by not less than 3 log$_{10}$ beyond observed cytotoxicity. All testing was performed per American Society for Testing and Materials (ASTM) method E 1052-96, a Standard Test Method for Efficacy of Antimicrobial Agents Against Viruses in Suspension.

Routine use of the 61% alcohol-ZPT product would not only greatly reduce the transient and resident bacterial and yeast flora but also might decrease significantly the likelihood of transmitting viral agents of disease to others by contaminated hands. This improvement in hand hygiene could also yield significant economic savings because viruses are a leading cause of morbidity and mortality in humans, and even mild infections can be a significant burden on the health care system and the general economy. Data obtained in the United States for over 2 decades incriminate viruses in 5% of all nosocomial infections. This number climbs to as high as 32% in the pediatric setting. More recent developments in the medical community suggest that the impact of viruses as agents of nosocomial disease may be greater now. Viruses can survive on human hands for hours, and experiments with human volunteers have demonstrated the potential for hands to spread viral agents, including those of the common cold and enteric diseases. As one might expect, caregivers and food handlers are most often implicated in this type of disease transmission. In summary, the 61% alcohol-ZPT product formulation meets or exceeds all requirements of the ASTM method to be considered as a virucidal agent. Properly formulated alcohol-based products can have potent virucidal action against even some of the most resistant viral agents. This important aspect of skin antisepsis should not be overlooked when selecting a surgical scrub or health care personnel handwash.

CONCLUSION

The 61% alcohol-ZPT water-optional product meets or exceeds requirements for the health care personnel handwash indication and is therefore FDA and CDC compliant. It is formulated with surfactants and therefore is appropriate for use as either a water-aided or a waterless health care handwash. It may be used waterless for hands that are not visibly soiled or with water for hands that are contaminated with blood, other body fluids, or other types of organic material or to assist in the removal of bacterial spores such as those of Clostridium difficile. The product provides antimicrobial persistence, and residual effects and repeated use contributes positively to overall skin conditioning. It is cidal for many viral agents of human disease that are readily transmitted via contact with contaminated hands. Finally, it is nontoxic and not subject to inactivation by anions or changes in pH as has been observed with CHG. A product with these attributes fulfills a previously unmet need and could favorably impact compliance with handwashing protocols.

The authors wish to direct your attention to another recently published AJIC manuscript—Sickert-Bennett EE, Weber DJ, Gergen-Teague MF, Sobsey MD, Samsa GP, Rutala WA. Comparative efficacy of hand hygiene agents in the reduction of bacteria and viruses. Am J Infect Control 2005;33:67-77. We believe that the data presented in our paper offer an alternate point of view and evidence that properly formulated alcohol-based products of hand antisepsis will provide excellent immediate kill, as well as persistent and residual antimicrobial effects. In addition, these results are achievable against hand flora with product use for as brief as 15 seconds.

References

1. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. MMWR 2002;51(RR16):1-44.
2. Pittet D. Improving adherence to hand hygiene practice: a multidisciplinary approach [Special Issue]. Emerging Infect Dis 2001;7:234-40.
3. Centers for Disease Control and Prevention. Guideline for prevention of surgical site infection 1999. Infect Control Hosp Epidemiol 1999;20: 267.
4. Hilburn J, Hammond BS, Fendler EJ, Groziak PA. Use of alcohol sanitizer as an infection control strategy in an acute care facility. Am J Infect Control 2003;31:109-16.
5. Food and Drug Administration. Topical antimicrobial drug products for over the counter human use: tentative final monograph for healthcare antiseptic drug products. Federal Register 1994;59(116):31402-52.

6. Paulson DS. A broad-based approach to evaluating topical antimicrobial products. In: Joseph M. Ascenzi, editor. Handbook of disinfectants and antiseptics. New York: Marcel Dekker; 1996. p. 18-9.

7. Paulson DS. Current topical antimicrobials. In: Paulson DS, editor. Measurement of antimicrobial action of topical antimicrobials. New York: Marcel Dekker; 1999. p. 61.

8. Ertel KD, Keswick BH, Bryant PB. A forearm controlled application technique for estimating the relative mildness of personal cleansing products. J Soc Cosmet Chem 1995;46:67-76.

9. Rizer RL, Sigler ML, Miller DL. Evaluating performance benefits of conditioning formulations on human skin. In: Schueller R, Romanowski P, editors. Conditioning agents for hair and skin. New York/Basel: Marcel Dekker; 1999. p. 337-67.

10. Sattar SA, Springthorpe VS, Tetro J, Vashon R, Keswick B. Hygienic hand antiseptics: should they not have activity and label claims against viruses. Am J Infect Control 2002;30:355-72.

11. Guthrey E, Seal LA, Anderson EL. Zinc pyrithione as a preservative system for products of skin antisepsis. Am J Infect Control 2005;33:15-22.

12. American Society for Test Materials (ASTM). Method E 1052-96, a standard test method for efficacy of antimicrobial agents against viruses in suspension. West Conshohocken (PA): The Society.

13. Rosenberg A, Alatary SD, Peterson AF. Safety and efficacy of the antiseptic chlorhexidine gluconate. Surg Gynecol Obstet 1976;143:789-92.

14. Paulson DS. Current topical antimicrobials. In: Paulson DS, editor. Topical antimicrobial testing and evaluation. New York: Marcel Dekker; 1999. p. 53-9.