

## Hand hygiene strategies to fight pathogenic bacteria in an outpatient surgery clinic

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A prospective, randomized controlled trial was performed comparing the efficacy of multiple use soap-and-water or alcohol versus a single use benzalkonium chloride- based lotion hand sanitizer. Subjects were followed through a 3-hour clinic session with hourly hand bacterial counts taken to identify the presence of *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. A total 68 subjects met the study criteria having less than 50 colony forming units (CFU). No statistical differences were found between hand bacterial counts using the three different hand hygiene methods at four hourly time points ( $p > 0.05$ ). Hand bacterial counts increased significantly over the 3-hour clinic session. The single-use long-lasting BC lotion performed as well as the multiple-use hand sanitizers.

**Keywords:** antibacterial; benzalkonium chloride; hand sanitizers

### 1. Introduction

Drastic measures have been taken by hospital systems to improve compliance and control hospital-acquired infections. Measures include implementation of complex technological systems,(1-3) or direct monitoring of hand hygiene.(4). It is unrealistic, however, to implement these hand hygiene systems in a broad-based manner considering the necessary costs and manpower. There are various reasons for the lack of compliance with hand hygiene measures, including skin irritation, inaccessibility to hand washing supplies, inconvenient placement of sinks, neglect, high workloads, and lack of time (5-8). Therefore, it is not surprising that the selection of a particular hand hygiene agent by healthcare workers is determined by its antiseptic efficacy, cost, smell, consistency, color, tendency to cause skin irritation, and time needed for drying.(9)

Commercial antimicrobial agents include those based on alcohol, chlorhexidine, chlorine, hexachlorophene, iodine, chloroxylenol (PCMX), quaternary ammonium compounds, and triclosan.(10). While alcohol-based hand antiseptics have been found to rapidly reduce hand bacteria counts more so than soaps or detergents containing hexachlorophene, povidone-iodine, 4% chlorhexidine, or triclosan,(11, 12) they perform poorly against bacterial spores, irritate the skin, provide no barrier protection, and have little long-lasting activity.(9) *Soft&Shield*<sup>TM</sup> (Bioderm Technologies, Inc., Trenton, NJ) is an alcohol-free, hypoallergenic hand sanitizer and moisturizer. The active agent in the sanitizer is 0.13% benzalkonium chloride. The sanitizer works via dual methods, by forming a protective barrier on the skin and via long-lasting anti-microbial activity for up to four hours with only one application (13). This study specifically compares the *in vivo* efficacy of 3 different hand hygiene methods in their ability to remove resident flora from the hands of medical personnel. The products used in our trial were *Avagard D*<sup>TM</sup> (3M Health Care, St. Paul, MN), an alcohol-based (61% ethanol) sanitizer that is used throughout the University Hospital in Newark, New Jersey, *Soft&Shield*<sup>®</sup> and soap-and-water hand-washing.

### 2. Methods

*Clinical study:* a prospective, randomized equivalence trial comparing the antiseptic efficacy of *Avagard D*<sup>TM</sup>, *Soft&Shield*<sup>®</sup>, and soap-and-water hand washing in their ability to remove resident flora from the hands of medical personnel was conducted. Eligible subjects included full-time employees (>30 hours per week) in the Division of Plastic and Reconstructive Surgery of Rutgers-New Jersey Medical School aged 18-65. Exclusion criteria included those with allergy to study products or latex as were those receiving topical or systematic steroids or antibiotics, and those with diagnosed dermatologic conditions such as psoriasis. The study protocol was approved by the Institutional Review Board representing Rutgers-New Jersey Medical School. Subjects who met criteria were randomly assigned to one of the three hand hygiene regimens. At the beginning of each trial, which was a 3-hour session in the outpatient plastic surgery clinic, all subjects washed their hands with non-antimicrobial liquid soap (see hand washing protocol below) before being given an antiseptic product: *Soft&Shield*<sup>®</sup> or *Avagard D*<sup>TM</sup>. Subjects in the soap-and-water hand washing group were not provided any additional antiseptic product. Subjects subsequently treated patients (except those with confirmed *Clostridium difficile* or multi-drug resistant infections) during our outpatient clinic for a 3-hour period. Subjects were instructed to wear gloves whenever contacting patients. For those in the *Soft&Shield*<sup>®</sup> group, 0.5 mL of product was dispensed into the subject's non-dominant palm, and then rubbed into the fingers and palm until well-

dispersed. Hands were rinsed with cold water during the trial only if visibly soiled. The product was not reapplied throughout the course of the clinic. For those in the *Avagard D<sup>TM</sup>* group, 2-3 mL of product was dispensed into the subject's non-dominant palm, and then rubbed into the fingers and palm until well-dispersed. The product was reapplied prior to each new patient contact. Subjects in the soap-and-water hand-washing group were instructed to rinse their hands before each patient encounter. For each washing, subjects were instructed to rinse two-thirds of their forearms with tap water for 30 seconds, scrub hands with soap for 30 seconds, and then rinse hands with tap water for 30 seconds. For *Soft&Shield<sup>®</sup>* and *Avagard D<sup>TM</sup>* groups, subjects were instructed to refrain from washing hands with soap.

**Microbiology:** Hand cultures were obtained 4 times during each clinic session (1 minute following antiseptic application, 1 hour later, 2 hours later, and 3 hours later). Samples were collected from subjects at these intervals immediately after each leaving a patient's room, prior to any additional hand hygiene regimens. Samples were collected by taking a 5-second imprint of the middle and index fingers of the dominant hand of each subject on commercial contact bacterial agar plates. Plates were incubated at 35°C under aerobic conditions. The total bacterial contamination of hands was recorded as the number of CFU (colony forming units) per plate after 72 hours of incubation. Counts were made to a maximum of 50 CFU due to confluent growth of colonies beyond this point. No anaerobic cultures were performed. The trained microbiologist examining the culture plates was blinded to the hand hygiene method used. All microbiological testing was performed by an independent laboratory, Water-Jel Technologies, LLC (Carlstadt, NJ).

**Hand assessment protocol:** The number of patients contacted and the number of hand hygiene regimens was recorded over the 3-hour time period. Each subject completed a Hand Skin Assessment (HSA) questionnaire, a self-rating scale used to measure skin condition, prior to the trial. Subjects give their dominant hand a score from 1 to 7 in 4 dimensions: appearance, intactness, moisture content, and sensation. The resulting score ranges from 4 to 28, with 28 indicating completely healthy skin. HSA scores correlate significantly with physiologic measures of skin damage (14). To address potentially confounding effects, the frequency of gloving was recorded as well.

**Data Analysis:** To normalize the data, microbial counts were converted to log<sub>10</sub>. Statistical analysis was performed using analysis of variance to compare microbial counts between the 3 intervention groups at each time point, and to compare microbial counts of each intervention group between time points. Changes in HAS scores were determined for each subject in the trial. Nonparametric analysis was performed using Mann-Whitney *U* tests and Kruskal-Wallis tests as indicated. All statistical analysis was performed using Stata/MP 13.0 (StataCorp LP, College Station, TX). Threshold for significance was set at  $p < 0.05$  with use of the Bonferroni correction method.

### 3. Results

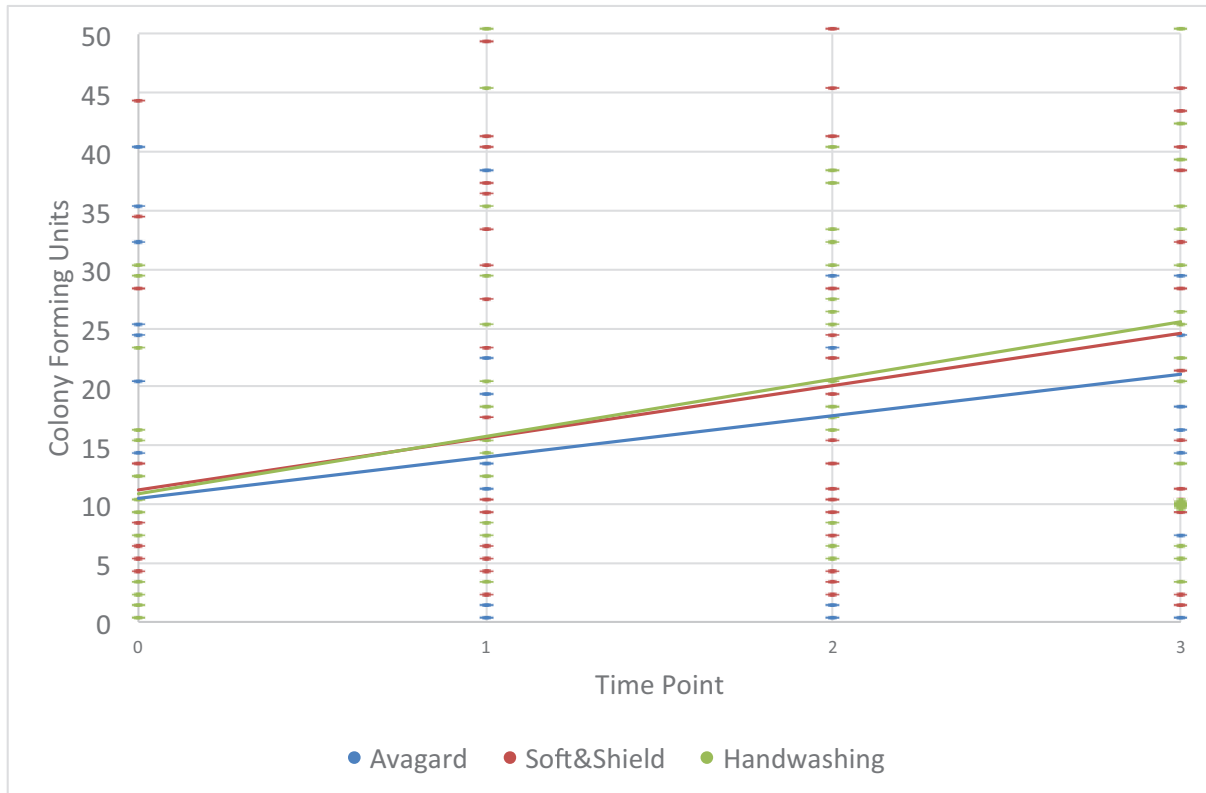
Ninety-five subjects participated in the trial, with 36 subjects randomized to the *Avagard D<sup>TM</sup>* group (37.9%), 38 subjects to the *Soft&Shield<sup>®</sup>* group (40%), and 21 subjects to the soap-and-water hand washing group (22.1%). Seventy-five subjects were male (78.9%) and 20 subjects were female (21.0%). The average age of the study population was 28.6 years (median 29, range 22-38). Sixty-four subjects were Caucasian (67.4%), 26 were Asian (27.4%), and 5 were Hispanic (5.3%). Prior to the trial, 34 subjects reported having redness, itching, cracking or dryness of the hands that was mild and infrequent.

To ensure exclusion of doubtful high CFU trials, a more restrictive criterion was applied to plates with >50 CFU or too numerous to count, which were eliminated: 9 plates in the *Avagard D<sup>TM</sup>* group, 11 plates in the *Soft&Shield<sup>®</sup>*, and 10 plates in the soap-and-water handwashing group. See Table 2 for complete results.

**Table 1** Frequency of plates with >50 CFU by hand hygiene method and time points.

	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>
<i>Avagard D<sup>TM</sup></i>	2	1	2	5
<i>Soft&amp;Shield<sup>®</sup></i>	2	2	3	4
Hand-washing	0	2	3	5

Implementing the previous restrictions, hand bacterial counts increased significantly over the 3-hour clinic session with *Avagard D<sup>TM</sup>* (9.24 to 21.90 CFU,  $p=0.0021$ ), *Soft&Shield<sup>®</sup>* (6.69 to 21.59 CFU,  $p<0.00001$ ), and soap-and-water hand-washing (8.43 to 22.75 CFU,  $p=0.0009$ ) based on analysis of variance testing. Post-hoc subgroup analysis between time points indicated that there was a significant difference in CFU between T<sub>0</sub> and T<sub>3</sub> with all hand hygiene methods (see Figure 1). With *Soft&Shield<sup>®</sup>* there was also a significant difference between T<sub>0</sub> and T<sub>1</sub> as well as between T<sub>0</sub> and T<sub>2</sub>. See Table 2 for complete results. Interestingly, the distribution of hand bacterial counts appeared bimodal for all hand hygiene methods. The percentage of subject trials with less than or equal to 20 CFU decreased over the course of the study period for all hand hygiene methods. Conversely, the percentage of subject trials with greater than 20 CFU increased during the study for all hand hygiene methods. The percentage of conversion from low to high colony count trials was lowest for *Soft&Shield<sup>®</sup>* (29%), compared with *Avagard D<sup>TM</sup>* (48%) and soap-and-water hand-washing (57%).



**Fig. 1** Scatter plot with line-of-best-fit showing bacterial CFU from cultured hand samples by hand hygiene method and time point.

**Table 2** Mean bacterial CFU from cultured hand samples by hand hygiene method and time point.

	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	P value
<i>Avagard D<sup>TM</sup></i>	9.24 ± 11.74 (n = 34)	17.23 ± 13.52 (n = 35)	14.76 ± 12.66 (n = 34)	21.90 ± 15.14 (n = 31)	0.0021* T <sub>0</sub> vs. T <sub>3</sub> 0.001
<i>Soft&amp;Shield<sup>TM</sup></i>	6.69 ± 10.25 (n = 36)	21.94 ± 15.91 (n = 36)	21.23 ± 15.43 (n = 35)	21.59 ± 16.27 (n = 34)	<0.00001* T <sub>0</sub> vs. T <sub>1</sub> <0.0001 T <sub>0</sub> vs. T <sub>2</sub> <0.0001 T <sub>0</sub> vs. T <sub>3</sub> <0.0001
Hand-washing	8.43 ± 9.51 (n = 21)	18.95 ± 12.83 (n = 19)	22.72 ± 11.42 (n = 18)	22.75 ± 14.76 (n = 16)	0.0009* T <sub>0</sub> vs. T <sub>1</sub> 0.046 T <sub>0</sub> vs. T <sub>2</sub> 0.003 T <sub>0</sub> vs. T <sub>3</sub> 0.004
P value	0.6008	0.3840	0.0677	0.9700	

Significance determined by analysis of variance.

\*Statistically significant.

Significant results from post-hoc analysis between time points listed.

The change in HAS score for *Avagard D<sup>TM</sup>* was 0.25 ± 1.02 (n=36, median 0, range -3 to 3), for *Soft&Shield<sup>®</sup>* was 0.29 ± 0.93 (n=38, median 0, range -2 to 2), and for hand-washing was -0.95 ± 1.43 (n=21, median 0, range -5 to 0). Nonparametric analysis between the 3 experimental groups indicated a significant difference between the groups (p=0.0010). Post-hoc subgroup analysis revealed that both *Avagard D<sup>TM</sup>* (p=0.0009) and *Soft&Shield<sup>®</sup>* (p=0.0007) resulted in better hand condition than soap-and-water hand-washing based on change in HAS score before and after a 3-hour clinic session using a single hand hygiene regimen. Multivariate regression analysis was performed with change in HAS score as the dependent variable and number of hand washings, number of hand dryings, number of patients contacted, and total number of hand hygiene regimens during a 3-hour clinic session as independent variables. None of the independent variables were found to be predictors of change in hand condition (p=0.1844).

#### 4. Discussion

An important consideration is the difference between transient flora and resident flora. Transient floras are acquired from patient contact and contaminated surfaces, and are more frequently associated with health-care associated infections. They are more amenable to removal with routine hand-washing. Resident floras, on the other hand, are less likely to be associated with infection and are more resistant to removal. The number of both types of flora varies between people, but stays relatively constant for each individual. No transient floras were found on the treated hands of

subjects in our study. In this monitored study, when subjects are forced to utilize hand hygiene measures, pathogenic bacteria can be minimized in outpatient clinical settings. It was noticed that certain subjects who participated in the study more than once were found to consistently have high resident flora counts. This is consistent with the idea that some people will naturally have higher bacterial counts than others and that this is not an indication of lack of efficacy of the hand hygiene regimens in this population.

Previously, it has been shown that duration of clinical activity with patient contact is associated with intensity of hand bacterial contamination (15). Our study findings are consistent with the above, as hand bacterial counts increased from the beginning of the trial to the end regardless of the hand hygiene method. However, despite receiving only one application, subjects in the *Soft&Shield*<sup>TM</sup> group did not have an increased accumulation of bacteria compared to the other two groups that were utilizing hand hygiene regimens between each patient encounter.

An important conclusion from the study is that *Soft&Shield*<sup>®</sup> has *persistent* activity, which inhibits the proliferation and survival of organisms hours after application, confirming our earlier published in vitro efficacy studies (13). Alkyl benzalkonium chloride, a quaternary ammonium compound, is the active ingredient in *Soft&Shield*<sup>®</sup>. There is a relative dearth of data regarding quaternary ammonium compounds in hand hygiene because of its infrequent use in the US. It has, however, been shown to outperform alcohol-based sanitizers in one study (16). Clearly, additional studies will be helpful in elucidating the role of quaternary ammonium compounds in infection control, including its usefulness in inpatient clinical settings, especially in the intensive-care unit, as well as its efficacy against transient flora.

The adherence to hand hygiene measures has been directly related to the decreased prevalence of healthcare-associated infections.(17, 18)The results of this study are critical in that they demonstrate that a long-acting hand sanitizer is not only as effective as soap-and-water and alcohol-based sanitizers, but also appears to improve hand condition in comparison to soap-and-water handwashing. Considering that lack of compliance with hand hygiene in clinical settings is secondary to inconvenience, lack of time, and skin irritation, a hand sanitizer that reduces the number of required uses and improves hand condition may increase overall compliance, and thus decrease health-care associated infections. Importantly, implementation of a long-acting sanitizer would also potentially reduce costs compared to other methods that require expensive technology or large numbers of additional personnel to monitor hand hygiene compliance. This is significant considering the cost of healthcare-associated infections results in an additional \$5-16.6 billion in the US.

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