# TAB 5 FDA Reviewer's Evaluation of the SDA/CTFA Submission (CP16) Regarding Benefit and Efficacy of Consumer Antiseptics

# CONSUMER ANTISEPTIC DRUG PRODUCTS REVIEW

**Office of Nonprescription Products (HFD-560)**
Center for Drug Evaluation and Research • Food and Drug Administration

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| REVIEWER: | Colleen Kane Rogers, Ph.D. |

## I. Purpose

This review provides a summary and evaluation of consumer antiseptic data submitted by the Soap and Detergent Association (SDA) and Cosmetic, Toiletry, and Fragrance Association (CTFA) Industry Coalition in a citizen petition to the healthcare antiseptic rulemaking. This citizen petition (CP16) complements a previous SDA/CTFA submission regarding healthcare antiseptic products and provides data to support the clinical benefit and efficacy of consumer antiseptics and food handler preparations. Submitted articles and technical reports pertaining to consumer products are reviewed here. Food handler preparations will be considered at a later date.

## II. Background

The Tentative Final Monograph (TFM) for Healthcare Antiseptic Drug Products (June 17, 1994) describes three categories of antiseptics: antiseptic handwashes and healthcare personnel handwashes, surgical hand scrubs, and patient preoperative skin preparations. Products labeled as antiseptic handwashes are intended to be used by consumers, while healthcare personnel handwashes are meant for professional use. The indication for an antiseptic handwash is "for handwashing to decrease bacteria on the skin." This may be

followed by one or more of the following phrases: "after changing diapers," "after assisting ill persons," or "before contact with a person under medical care or treatment."

The SDA/CTFA Industry Coalition's position is that the TFM is too restrictive and does not encompass the full antiseptic marketplace. The Coalition feels that antiseptic products should not be limited only to healthcare uses and, consequently, proposes a broader spectrum of uses in their Healthcare Continuum Model (HCCM). The HCCM includes six antiseptic product categories: consumer handwashes, consumer bodywashes, and food handler preparations, in addition to the three professional use categories in the TFM. The HCCM proposal includes product performance criteria, final formulation testing, and labeling for each of these product categories.

Under the TFM, antiseptic handwashes meant for consumer use are subject to the same testing requirements as healthcare personnel handwashes. This means that they must meet the same efficacy requirements (e.g., bacterial log reductions) as healthcare personnel handwashes, including a demonstration of cumulative microbial reduction.

The Coalition believes that the performance criteria specified in the TFM for antiseptic handwashes are overly stringent. The HCCM recommends lower bacterial log reduction criteria for in vivo testing of consumer products than proposed in the TFM. This recommendation is based in part on data submitted to FDA, which is reviewed here. The Coalition also proposes that antiseptic handwash efficacy be determined following a single handwash procedure (immediately after product use), with an option for similar sampling after multiple washes to demonstrate cumulative microbial reduction.

Listed in the table below are the current TFM bacterial log reduction criteria for in vivo testing of consumer antiseptic handwashes and the log reductions proposed in the HCCM.

**Effectiveness Criteria for Consumer Antiseptic Handwash**es

| | Bacterial Reduction after 1st wash | Bacterial Reduction after 10th wash |
|---|---|---|
| TFM proposal: Antiseptic handwash, all uses | 2 $\log_{10}$ | 3 $\log_{10}$ |
| HCCM proposal: Antiseptic handwash, domes use | 1 $\log_{10}$ | Optional |
| HCCM proposal: Antiseptic handwash, domes food preparation and food handler | 1.5 $\log_{10}$ | Optional |

The HCCM proposal does not provide specific bacterial log reduction criteria for antiseptic bodywashes. The Coalition recommends instead that a consumer body product should either a) show a significant reduction in resident flora compared to baseline levels as measured using the American Society for Testing and Materials (ASTM) pre-operative skin preparation

method, or b) show a significant reduction in transient flora compared to levels attained with use of placebo/bland (i.e., nonantimicrobial) soap as measured using the ASTM cup scrub technique for antibacterial washes. The TFM does not propose bacterial log reduction criteria for antiseptic bodywashes, since this category was not identified in any previous rulemakings.

Performance criteria for the three professional use categories of healthcare antiseptic products were discussed at a recent Nonprescription Drug Advisory Committee (NDAC) meeting (March 23, 2005). At that time, NDAC believed that there was not sufficient evidence to change the current performance criteria for professional use products. Although the current NDAC meeting will not focus on performance criteria for consumer antiseptics, knowledge of the current TFM criteria will help in assessing the efficacy of these products.

Many of the references submitted by SDA/CTFA in support of the HCCM for consumer antiseptics (handwashes and bodywashes) were also submitted in support of professional use products. These were previously reviewed as part of the background package for the March 23, 2005, Healthcare Antiseptic Advisory Committee meeting and will not be reviewed again here because they pertain to healthcare products rather than consumer antiseptics. Previously reviewed references are listed in Appendix A.

Consumer antiseptics would offer an advantage relative to nonantimicrobial soaps if they a) reduced the numbers of bacteria on the skin over and above the mechanical action of plain soap, b) provided a residual effect (i.e., persistence), or c) demonstrated both actions. The submitted efficacy studies were not designed to address either of these actions. The majority of clinical simulation studies, to test for bacterial log reduction effects, either did not include a vehicle control, or did not examine multiple time points for a residual effect. It should be noted that nonantimicrobial soap can generally achieve approximately a 2-log reduction in the ASTM handwash test. This may provide an appropriate benchmark for evaluation of the efficacy of consumer antiseptic products.

There is no clinical data to show that specific bacterial log reductions correlate with reduced disease transmission. Studies submitted to show a clinical benefit from use of consumer products also lacked adequate controls. The studies that examined infection rates utilized multiple interventions and did not employ placebo control arms. Other studies did not report infection rate data.

Overall, the submitted studies do not provide adequate data on which to base a regulatory decision that consumer antiseptics are effective.

## III. Review

The following review evaluates data submitted by the SDA/CTFA Industry Coalition to support either the clinical benefit or efficacy of consumer antiseptics. The review has been divided into three sections. The first section describes articles regarding clinical benefit. Clinical benefit is demonstrated by examining infection rates after use of a particular antiseptic product. These studies are conducted in consumer settings such as schools and day care centers. The second section describes studies submitted in support of the efficacy of antiseptic handwashes. Antiseptic efficacy is demonstrated through clinical simulation testing. The third section relates to the efficacy of antiseptic bodywashes, which also employ simulation testing.

### A. Clinical Benefit of Consumer Antiseptics – Effect of Antiseptic Use on Infection Rates

***Overview***

The Coalition submitted 31 journal articles and abstracts to demonstrate the clinical benefit of consumer antiseptic products. Most of the references relating to benefit are clinical studies of professional use products. These were reviewed previously and are not included here (see Appendix A). Of the remaining references, two assess the clinical benefit of hand sanitizer products in elementary schools, two describe microbial risk assessment models, and two describe other experimental models.

Most of these studies were not designed to demonstrate a clinical benefit from the use of a consumer antiseptic. The elementary school studies did suggest a trend toward reduced germ transmission. They were not, however, designed to demonstrate the efficacy of the antiseptic product compared to supervised hand hygiene alone. The school studies also had other limitations, such as a lack of controls, confounding due to multiple interventions, and failure to address cluster design in the data analysis. In summary, the results of these studies must be interpreted with caution. As a whole, the submitted studies may provide interesting experimental models, but do not support reduced infection rates as a result of using consumer antiseptic products.

***Study Evaluations***

**Dyer** and colleagues conducted an industry-sponsored 10-week, open-label crossover study of alcohol-free hand sanitizer use in conjunction with at-will soap-and-water handwashing in one elementary school.[6] All of the students received education before the study began about the importance of handwashing. Seven classrooms then received hand sanitizer (SAB; active ingredient: benzalkonium chloride), and seven were assigned to the control group. Hand sanitizer was used for 4 weeks, followed by a 2-week washout period, then test and control groups were switched. In addition to at-will handwashing with soap and water, children in the study group used the hand sanitizer under teacher supervision immediately after entering the classroom, before eating, after sneezing or coughing, and after using the restroom. Children in the control group were told only to wash before eating, after going to the

restroom, and as otherwise necessary during the day, but were not monitored for handwashing.

Absences were categorized as gastrointestinal (GI)-related (symptoms included vomiting, abdominal pain, and diarrhea), respiratory-related (symptoms included coughing, sneezing, fever, bronchitis, headache, mononucleosis, and acute exacerbation of asthma), or other (e.g., non-transmissible UTIs, broken limbs). In the first phase of the study, the total number of absences due to communicable illness was 33.6% lower in the hand sanitizer group than in the control group. Total GI- and respiratory-related absences were decreased by 37.5% and 30.9%, respectively, compared to controls. In the 2-week washout period, no significant difference was noted between the two groups. In the second phase of the study, there was a significant decrease in total illness-related absences in the hand sanitizer group, and the number of respiratory-related absences was 76% lower. The authors conclude that daily use of hand sanitizer with at-will handwashing was associated with significantly lower rates of illness-related absenteeism.

One limitation of this study is that the students were not formally randomized; they were grouped by classroom (i.e., clustered). The authors do not provide details of their statistical methods and do not account for the clustering. The use of a crossover design does help establish that the reduced illness rates are not due to differences in the composition of the two groups. This study was conducted at only one site, a private school. The socioeconomic diversity of the subjects may have been limited. Neither the subjects nor the study coordinators were blinded, and there was no placebo control. There was no monitoring of the students while washing with soap and water, compared to strict monitoring of the use of hand sanitizer. Consequently, there is no way to know if students complied with handwashing when they were in the control group. More importantly, there is no way to know if the decreased illness rates were due to monitoring of hand hygiene alone, rather than using a specific antiseptic.

**Guinan** and others conducted an industry-sponsored 3-month, open-label study of absenteeism in elementary school children using an alcohol-based gel hand sanitizer.[9] Children from five elementary schools were enrolled in the study for a total of 145 control and 145 test students. Students in the test classrooms received the interventions of education (video, pamphlet, and demonstration) and hand sanitizer, while control groups received no intervention. Absenteeism data was collected by the teachers for three months (March – May). Illness was defined as an infectious process, such as cold, flu, or gastroenteritis.

Overall, the test group had 50.6% fewer absences than the control group (140 vs. 277 absences; $p<.001$). The authors suggest that a hand hygiene program that incorporates both education and hand sanitizer use can lower student absenteeism and be cost-effective. However, this study had several limitations. Guinan et al. do not describe when hand sanitizer is used by the children or whether they are supervised or encouraged to use the sanitizer. Moreover, the study was not blinded and did not have a placebo control. The subjects were not randomized. They were divided by classroom, but clustering was not accounted for in the analysis. Although several schools were used for this study, they were

all in the same geographic location and had limited socioeconomic diversity. In addition, the authors do not mention which types of illnesses resulted in absenteeism (e.g. GI, respiratory).

**Chen** and colleagues performed laboratory experiments to investigate the extent of bacterial transfer between hands and other common surfaces involved in food preparation.[5] The secondary objective of the study was to provide cross-contamination data for quantitative microbial risk assessments. Fifty-two subjects were recruited, but only about 30 subjects were used for each transfer rate assessment, therefore each subject did not participate in every assessment. Subjects performed various food preparation tasks as described below.

To determine the bacterial transfer rate from chicken to hands, approximately $10^8$ colony forming units (CFU) of a nalidixic acid-resistant strain of *Enterobacter aerogenes* were inoculated onto 150 g of raw chicken breast meat and allowed to attach for 15 minutes. Subjects then diced the chicken on a sterile plastic cutting board. Afterwards, one of the hands was sampled using the glove juice method. The other hand was used to contaminate three sterile spigots. Before handling each of the spigots, the subject transferred the diced chicken back and forth from the cutting board to a tray three times. Subsequently, one of the spigots was sampled by swabbing with two moistened alginate swabs, dissolving the swabs in 1% sodium citrate, diluting, and plating the solution. The other two contaminated spigots were used to recontaminate the hands of the subject or contaminate the clean hands of other participants.

After hand contamination via chicken or spigots, two washing schemes were used. Subjects washed their hands with 0.5% para-chloro-meta-xylenol (PCMX) liquid antibacterial soap for at least 20 seconds, and then wiped them dry with a paper towel. In the conventional scenario, the subject handled two contaminated spigots after washing, but before wiping, to simulate turning off the faucet. In a non-hand-operated scenario, a technician turned on the water and provided soap and paper towels. One of the hands was then sampled using the glove juice procedure.

After dicing chicken and handwashing, subjects sliced clean lettuce for 1 minute using the non-sampled hand. The sliced lettuce was sampled for *E. aerogenes* by homogenization and plating. Contamination of the cutting board was also assessed. Subjects sliced contaminated chicken (~$10^6$ CFU) on cutting boards, which were then sampled by washing the board twice with phosphate buffered saline and swabbing four times. The wash fluid was combined with the extracted swabs and plated to enumerate the remaining bacteria.

The number of bacteria remaining on the chicken, spigot, lettuce, cutting board, and hands (after handling chicken and after washing) was determined and reported as $\log_{10}$ values. These values were then used to calculate transfer rates from chicken to hand, from hand to spigot, and from washed hand to lettuce. The reduction rate due to washing was also calculated.

After handling contaminated chicken, a mean of 7.43 $\log_{10}$ CFU of bacteria were recovered from subjects' hands. A mean of 4.42 $\log_{10}$ CFU were transferred from hands to a metal spigot, and between 1.90 and 6.46 $\log_{10}$ CFU (mean 4.68 logs) remained on the hands after

washing and drying. After handwashing, up to 3.81 logs of bacteria could be transferred to lettuce. The investigators found that bacterial transfer rates varied by more than five orders of magnitude, depending on the subject and surface. The highest degree of variability was seen with handwashing, while object-to-object cross-contamination (e.g., cutting board to lettuce) showed the least variability.

The authors conclude that bacterial transfer rates among hands, foods, and kitchen surfaces are highly variable. Moreover, handwashing does not completely eliminate bacteria from the hands when they are contaminated with large numbers of organisms. Therefore, additional measures to control bacterial cross-contamination are warranted. Notably, faucet spigots may be a significant source of cross-contamination in the kitchen.

Chen and colleagues provide useful data regarding bacterial transfer rates from contaminated food to different kitchen surfaces and hands. This study was not, however, adequately designed to assess the impact of an antimicrobial soap on bacterial transfer. In particular, the study compared two different handwashing methods, rather than comparing antibacterial and nonantibacterial soap. The authors concluded that measures in addition to handwashing are necessary to prevent cross-contamination in the kitchen. Although this study was well described, a few limitations were noted. Given the high degree of variability, more subjects should have been tested. Also, the authors do not mention any randomization schemes for handwashing or sampling. Finally, the bacterial reductions seen after handwashing may have been overstated because the authors do not mention using neutralizers[1] in their sampling solutions.

**Montville, Chen, and Schaffner**[12] developed a quantitative risk assessment model to examine the various factors that influence handwashing efficacy in the home or foodservice establishment, and determine the risk associated with different handwashing techniques. Data were collected from published literature and included bacterial counts on the hands of foodservice workers, healthcare workers, and research lab employees. The factors considered as input variables in the risk assessment model included initial bacterial count, soap type (bland, antimicrobial, or chlorhexidine gluconate [CHG]), method of drying (hot air or paper towel), hand sanitizer use (alcohol or alcohol-free), ring wearing, and bacterial density on faucet spigot. Data were translated into appropriate statistical distributions (e.g., normal, beta, or gamma), and Monte Carlo simulations were performed. It should be noted that data from all antibacterial ingredients, except CHG, were combined.

Analysis revealed that the top three most significant factors influencing final bacterial counts on the hands were use of hand sanitizer, use of soap, and drying method. Antibacterial soap was shown to be more effective than regular soap, but CHG was better than antibacterial soap. Hot air drying increased the amount of bacterial hand contamination, while use of paper towels decreased hand contamination slightly. There was essentially no difference between alcohol and alcohol-free hand sanitizer use. The simulations predict that a handwashing regimen which includes CHG soap, paper towels, alcohol-free hand sanitizer,

[1] A neutralizer stops the activity of the antimicrobial ingredient. Timely and adequate neutralization is important for proper assessment of the antimicrobial activity of an antiseptic.

no rings, and a touch-free faucet would leave no more than 3 $\log_{10}$ CFU on the hands approximately 92% of the time.

This study provides an intriguing risk assessment model, but is not designed to demonstrate the effectiveness of antibacterial soap. Furthermore, the data used as a basis for these simulations were derived from published studies conducted using a variety of different protocols. Notably, data from all antibacterial ingredients, except CHG, were pooled. This precludes the demonstration of a benefit from any particular active ingredient, with the exception of CHG. Data from different subject populations (i.e., healthcare, food service, and laboratory) were analyzed in combination. In addition to differences in bacterial contamination, the organic load for each of these subject populations varies. Also, other investigators have shown that the resident flora of healthcare personnel is different from that of homemakers.[1] Consequently, data derived from studies of healthcare personnel resident flora may not be appropriate for use in developing models for foodservice workers or the general population. Many of the studies examined resident flora, but a few used artificial contamination of the hands. Thus, data from gram-positive and gram-negative organisms were pooled. These organisms may not respond to antibacterials in the same way. Finally, some of the referenced studies had limitations of their own, such as inadequate numbers of subjects or a failure to neutralize the antimicrobial.

**Singh, Marples, and Kligman**[20] describe a method for inducing experimental skin lesions in the absence of prior skin traumatization. The study assessed the ability of *Staphylococcus aureus* to induce skin infections under both growth-promoting (i.e., occlusion) and lesion-promoting (i.e., ethanol pretreatment) conditions. Four of five subjects with alcohol-pretreated sites developed skin lesions by 4 days post-inoculation. In contrast, only one of five control subjects developed any lesions, and it was a mild skin reaction of unknown cause. Dose response studies showed an approximately linear relationship between inoculum size and lesion formation.

This study is an experimental infection model and does not attempt to evaluate the clinical benefit of consumer antiseptics. Singh et al. provide data to suggest that experimental *S. aureus* infections are difficult to produce without ethanol pretreatment of the skin. The authors also show that a relatively large inoculum is needed to produce a skin infection and the site must be occluded for bacterial proliferation. How these experimental manipulations (e.g., ethanol pretreatment, occlusion) relate to natural infection is unknown.

**Van** and others performed a 13-week, prospective study of the extent of fecal coliform contamination in day care centers.[21] Children under 24 months of age were enrolled from six day care centers for a total of 121 children. Consent was obtained from the day care center directors, caregivers, and parents. Data was collected for 13 weeks (Feb – May). Diarrhea was defined as the passage of unformed stools with twice the usual daily frequency. A diarrheal episode was defined as diarrhea following 7 or more days of being well. No attempts were made to change the day care environment or cleaning procedures prior to study initiation, but nurses observed cleaning, diapering, and housekeeping procedures for one week prior to the study.

Five areas from each room were cultured twice a week: the diaper-changing area, diaper pail handle, plastic toy, floor of the play area, and a high chair or chair seat. Cultures were obtained by swabbing a 10 x 10 cm area of the item for 15 seconds with a swab moistened in nutrient broth. The swab tip was placed in a tube containing 2.5 mL broth and kept cool until processed. Samples were vortexed and a 0.5-mL aliquot was plated on MacConkey agar to help identify coliforms. A 1-mL aliquot was also inoculated into lactose broth to test for the presence of fecal coliforms.

Once weekly, 1 hour after the morning nap, one hand of each caregiver and of five randomly selected children in each room were cultured by touching the palm and fingers to a MacConkey plate for 15 seconds. In addition, any child or caregiver who developed diarrhea had a stool specimen tested for *Shigella*, *Salmonella*, *Campylobacter*, *Aeromonas*, and *Plesiomonas*. Rotavirus and *Giardia* antigens were detected using enzyme-linked immunosorbent assays.

Significantly more coliform contamination was detected on children's hands and inanimate objects from toddler rooms compared to infant rooms. Coliforms were cultured significantly more often from rooms in which overclothes were not worn over diapers. However, when all sources of cultures were examined together, there was no association between the occurrence of diarrhea and fecal coliform contamination. During the study period, there were 73 episodes of diarrhea. More than half of the episodes (45) occurred as part of 11 outbreaks; six of the outbreaks were caused by rotavirus. The etiologic agents in the other outbreaks were not reported.

The authors conclude that there was no significant difference in fecal coliform contamination in childcare rooms with regard to observed hygiene practices, availability of handwashing facilities, or policy of accepting drop-in children. However, the authors suggested that significant differences may not have been noted because of the small number of rooms being compared. The authors did find that fecal contamination occurred more frequently with toddlers than with infants, and also with children that did not wear overclothes over their diapers. Ultimately, the study did not assess the role of antiseptics in reducing coliform contamination or episodes of diarrhea. Although the investigators tested stool samples for the causative agent of each episode of diarrhea, these data are not reported.

***Summary***

Although the elementary school studies suggest a trend toward reduced germ transmission, they are not designed to address the efficacy of the antiseptic product versus supervised hand hygiene alone. Also, there were no controls, such as washing with plain soap. Moreover, since these studies were only conducted during school hours, the influence of out-of-school hygiene practices on the outcomes cannot be determined. The studies were open-label and employed multiple interventions, such as educational programs. Furthermore, they were not formally randomized and did not address the cluster design in data analysis. Overall, the results of these studies must be interpreted with caution.

Of the remaining studies submitted to support the clinical benefit of consumer antiseptics, none of them were designed to address a clinical benefit. In fact, only the study by Van and colleagues provided infection rate data; however, these authors did not address antiseptic use. As a whole, these studies provide interesting experimental models, but do not demonstrate reduced infection rates as a direct result of consumer antiseptic product use.

## B. Efficacy of Consumer Antiseptics – Clinical Simulation Testing of Antiseptic Handwashes

***Overview***

The efficacy of antiseptic handwash products is often demonstrated using clinical simulation testing. The TFM describes clinical simulation testing for antiseptic handwashes, which is based on a previous American Society for Testing and Materials (ASTM) method. Both of these methods involve contaminating the hands with bacteria, washing, and sampling. The number of bacteria recovered from the hands is converted to $\log_{10}$ units and compared to a baseline value (sampling after contamination without washing). The difference between baseline counts and post-treatment counts is called the reduction factor and is used to demonstrate that a product meets a given performance criteria. The TFM performance criteria for antiseptic handwashes are a 2-$\log_{10}$ bacterial reduction after one wash and a 3-$\log_{10}$ reduction after the tenth consecutive wash.

Another important aspect of efficacy testing involves neutralization of the antimicrobial ingredient. Timely and adequate neutralization is important to properly assess the activity of the ingredient under the given conditions (e.g., a 30-second wash). Failure to adequately neutralize the active ingredient allows increased contact time between bacteria and the antimicrobial agent and falsely elevates the reduction factor generated during the washing procedure. The TFM recommends including neutralizers in all steps subsequent to sampling and in the last sampling solution. However, now it is believed that neutralizers should be included in all sampling solutions to insure proper neutralization of the active ingredient.

The SDA/CTFA Industry Coalition submitted 18 journal articles, technical reports, and other references to demonstrate the efficacy of consumer antiseptic products. Four of these references pertained to healthcare antiseptics and are not included here (see Appendix A). Nine references describe the efficacy of triclosan- or triclocarban-containing soaps, two references examined the efficacy of benzethonium chloride-containing products, and one article studied the efficacy of alcohol. For convenience, the reviews have been grouped by active ingredient. The remaining articles relate to antiseptic bodywashes and are described in section C.

Overall, the studies assessed product formulations and were not adequately controlled to demonstrate the contribution of the active ingredient to the effectiveness of the product. Differences in methodology also made it very difficult to compare data across studies. In general, the methods were poorly described and controls often were not used. Insufficient information was provided to be able to make any generalizations about the efficacy of triclocarban, triclosan, or alcohol. Two well-described studies were submitted to

demonstrate the efficacy of benzethonium chloride-containing soaps. The results of these studies suggest that products containing benzethonium chloride may have a difficult time meeting the TFM performance criteria. More data would be needed to establish the efficacy of this ingredient.

***Study Evaluations***

**Triclocarban**

The Industry Coalition referenced part of a citizen petition (CP) previously submitted to FDA by Bayer Corporation in support of the efficacy of triclocarban (TCC).[2] The CP provides summaries of published studies and data from a clinical simulation. The literature summaries do not include data or descriptions of the methods and cannot be fully evaluated. Moreover, some of the published studies use combination products and the contribution of TCC cannot be determined.

For the clinical simulation, a 1.5% TCC bar soap was compared to 4% chlorhexidine gluconate (CHG; Hibiclens) using a handwash test.[2] A modified version of the ASTM method was used. Five hand wash cycles were performed instead of eleven. *E. coli* was used as the test organism and the inoculation procedure was modified. The inoculum was applied to the hands in five 5-mL aliquots with 2 minutes of air-drying, compared to three 1.5-mL aliquots with 30 seconds of air-drying as recommended by ASTM. Descriptions of the washing and sampling procedures were not provided. The bacterial $\log_{10}$ reduction factors for each product are listed in the table below.

**Bacterial Reductions after Clinical Simulation Testing with TCC Soap or Hibiclens**

| Product | n | Reduction Factor ($\log_{10}$) | | |
|---|---|---|---|---|
| | | 1st wash | 5th wash | 10th wash |
| 1.5% TCC soap | 24 | 3.01 | 3.11 | Not tested |
| Hibiclens (4% CHG) | 24 | 3.34 | 5.21 | Not tested |

The study had design limitations. Although an active control was used, a vehicle control should have been included to demonstrate the contribution of TCC compared to the mechanical action of washing with a nonantimicrobial soap bar. The investigators also changed the protocol from the ASTM standard, but did not validate these changes. For instance, a larger volume of inoculum was applied to the hands (25 mL vs. 4.5 mL) and the effect of this increased inoculum on bacterial recovery is not known. In addition, the use of neutralizers is not mentioned, so the reduction factors may be artificially high. There was no description of subject randomization. The TFM efficacy criteria for consumer antiseptics require a 2-log reduction after the first wash and a 3-log reduction after the tenth wash. This study only examined five washes and would not fully meet the TFM efficacy criteria.

Several related **Procter & Gamble** technical reports were submitted to demonstrate the efficacy of TCC soap. Two reports provide data from Cade handwash studies that examined the amount of bacteria recovered after using 1.5% TCC soap for 5 or 12 days.[13, 15] In these studies, two separate baseline counts were determined from subjects who were using nonantimicrobial control bar soap prior to the start of the test regimen. Samples were

collected 5 and 12 days after starting the test regimen (1.5% TCC bar soap). Then, the geometric means of the baselines and test counts were used to calculate the percent reduction in bacterial count. No other information about the protocol was provided. A third report provides data from a similarly designed study, except that two soap formulations were used and subjects were only tested at 5 days post-treatment.[14]

In the first study, the $\log_{10}$ of the geometric means of recovered bacteria was 6.23 at baseline, 5.12 at 5 days, and 5.24 at 12 days. The geometric means for the second study were 6.36 at baseline, 5.29 at 5 days, and 5.14 at 12 days. The geometric means for the third study were 6.41 at baseline and 5.20 for the 1.5% TCC soap at 5 days, and 6.33 at baseline and 5.96 for the 0.25% TCC soap at 5 days. The $\log_{10}$ reduction factors are presented in the table below.

**Bacterial Reductions after Clinical Simulation Testing with TCC Soap**

| Study/Concentration/Reference | n | Reduction Factor ($\log_{10}$) | |
|---|---|---|---|
| | | Day 5 | Day 12 |
| Study 1 – 1.5% TCC [13] | 48 | 1.11 | 0.99 |
| Study 2 – 1.5% TCC [15] | 57 | 1.07 | 1.22 |
| Study 3 – 1.5% TCC [14] | 34 | 1.21 | Not tested |
| Study 3 – 0.25% TCC [14] | 34 | 0.37 | Not tested |
| Study 4 – soap B (1.5% TCC) [16] | 35? | Not tested | 1.12 |
| Study 4 – soap S (1.5% TCC) [16] | 35? | Not tested | 1.45 |

A fourth report from the same company describes a Cade handwash test that compared the efficacy of two 1.5% TCC bar soap formulations.[16] Seventy subjects were randomly assigned to one of two soap formulations, B or S. Subjects were asked to refrain from using antimicrobial products for 2 weeks prior to the start of the study. For the week prior to the study, subjects used placebo bar soap. Three baseline determinations were made: on the first and fifth day of placebo treatment, and on the first treatment day. Subjects used the assigned soap for 12 days. In addition, subjects returned to the test facility three times a day on weekdays to wash their hands. A final bacterial count was determined on day 12 after washing with placebo soap.

Subjects who used soap formulation B had a mean baseline count of 6.43 logs, and a post-treatment value of 5.31 logs. Subjects who used soap formulation S had a mean baseline count of 6.49 logs, and a post-treatment value of 5.04 logs. The $\log_{10}$ reduction factors are presented in the table above.

Use of TCC-containing soap for 5 or 12 days resulted in approximately a 10-fold (1-log) reduction of resident flora. Neither positive nor negative controls were included in any of the studies and they are not adequately designed to show the contribution of TCC in achieving the stated log reductions. With the exception of study 4, the studies were not randomized or blinded. Furthermore, the Cade method used in these four studies is very different from the TFM and ASTM methods, making comparisons between studies difficult. The methods are poorly described in all four technical reports. The pre-test period where subjects use only nonantimicrobial soap is not well defined, and the frequency and duration

of treatment washes is not provided. In addition, the sampling procedure is not described, and neutralizer use is not mentioned.

Another Procter & Gamble technical report describes the ability of two liquid soaps to reduce transient microbial flora on the hands after one wash.[17] Twelve subjects were recruited to participate in the study following a 1-week washout period. On test day, baseline determinations were made after a 30-second practice wash with bland soap. Hands were contaminated with 5 mL *S. marcescens* suspension and samples were taken using the glove juice method. For control washes, subjects' hands were contaminated and then six subjects washed with the control liquid soap for 30 seconds and rinsed for 15 seconds. The other six subjects only rinsed their hands under running tap water for 15 seconds. All 12 subjects performed a 30-second wash with the test soap.

The average baseline value was 8 logs. After washing with the test soap, 6.28 logs of bacteria were recovered, 6.8 logs were recovered after washing with the control soap, and 7.47 logs were recovered after only rinsing. The corresponding reduction factors are listed in the table below.

**Bacterial Reductions after Clinical Simulation Testing with Soap**

| Product | n | Reduction Factor ($\log_{10}$) | |
|---|---|---|---|
| | | 1st wash | 10th wash |
| Soap A (test) | 12 | 1.71 | Not tested |
| Soap B (control) | 6 | 1.20 | Not tested |
| Water rinse only | 6 | 0.53 | Not tested |

In contrast to the four previous technical reports from Procter & Gamble, this study uses artificial contamination of the hands. However, the methods are poorly described. The amount of bacteria used to contaminate the hands and the composition of the stripping solutions and plating media is not provided. Neutralizer use is not mentioned, which may lead to artificially high log reductions. Most importantly, the active ingredient in the test product and control soap, if any, was not provided. Even if detailed materials and methods were provided, this study would fail to meet the current performance criteria due to the small number of subjects and the low log reductions.

The last technical report submitted from Procter & Gamble describes a Healthcare Personnel Handwash test using a 1.5% TCC bar soap.[18] After a 1-week washout period, 16 subjects were reportedly tested according to the ASTM method. Only the wash procedure is described. Subjects picked up the bar of soap and wet their hands and the soap for 5 seconds under running water. The bar was lathered for 20 seconds, set down, and then subjects washed their hands with the lather for 30 seconds. Hands were rinsed for 15 seconds before sampling. The average baseline count was 7.6 logs and the post-treatment count was 4.82 logs, which corresponds to a reduction factor of 2.77.

This study was poorly described and has several limitations. The artificial contamination and sampling procedures were not described in detail and there was no mention of neutralizers. Due to the possible lack of neutralizers in this study, the reduction factor may be artificially

high. No controls were described. Placebo bar soap should have been included to demonstrate the contribution of the mechanical action of the soap and the contribution of TCC. Finally, because there was only one treatment arm, there was no randomization or blinding.

**Roman, Barnett, and Balske** performed a Cade handwash test using several concentrations of TCC soap.[19] Following a 2-week washout period, subjects washed with control soap and baseline determinations were made. Subjects then used the test soap (0.5, 1, or 2% TCC) for 12 days and were told to wash a minimum of three times a day. Test samples were taken 5, 11, and 12 days after starting treatment. The sampling procedure is not described.

The authors present the results as $\log_{10}$ of the bacterial counts in thousands, not as $\log_{10}$ of the original counts. Thus, the mean baseline value was reported as 3.2 logs, but would be 6.2 logs if calculated from the original bacterial counts. Furthermore, the authors used the mean of several hundred initial counts as the baseline value for all test subjects, but additional information about this data is not provided. The $\log_{10}$ reduction factors have been calculated by the reviewer and are presented in the table below. The bacterial reductions achieved by 2% TCC were significantly greater than the other concentrations of TCC. The authors conclude that 2% TCC is stable, effective, and superior to other biocides.

**Bacterial Reductions after Clinical Simulation Testing with TCC Soap**

| TCC Concentration | n | Reduction Factor ($\log_{10}$) | | |
|---|---|---|---|---|
| | | Day 5 | Day 11 | Day 12 |
| 0.5% | 7? | 0.87 | 0.81 | 0.94 |
| 1.0% | 11? | 0.84 | 1.17 | 1.08 |
| 2.0% | 25? | 1.45 | 1.69 | 1.66 |

The methods are poorly described in this article. The number of subjects that were used is unclear, the sampling procedure is not described at all, and there is no mention of the use of neutralizers. No placebo soap was tested, so the contribution of the active ingredient to the log reductions cannot be determined. The fact that 2% TCC appears to work well against resident flora may not be applicable to the regulatory evaluation of these products, because TCC is not allowed in concentrations exceeding 1.5% in antibacterial soap (1978 TFM). Most popular consumer soaps that contain TCC contain less than 1.5% of this ingredient.

## Triclosan

Data from a poster presented at an American Society for Microbiology meeting was submitted to support the efficacy of triclosan.[8] The investigators compared activated triclosan to 4% CHG and a traditional triclosan formulation using the ASTM Healthcare Personnel Handwash test. The hands of 30 subjects were contaminated with 4.5 mL *Serratia marcescens* at $10^8$ CFU/mL. Ten contamination/wash cycles were performed using 30-second washes with the product. Samples were taken after the first and tenth wash, and neutralizers were included in the sampling solution.

After one wash, all three products were able to exceed a 2-log reduction in bacterial counts. By the tenth wash, activated triclosan and 4% CHG reduced the bacterial counts significantly better than non-activated triclosan ($p<.001$), although there was no difference between activated triclosan and CHG. The authors conclude that an activated triclosan formula is superior to the non-activated triclosan handwash.

**Bacterial Reductions after Clinical Simulation Testing with Triclosan Handwash**

| Active Ingredient | n | Reduction Factor ($\log_{10}$) | |
|---|---|---|---|
| | | 1st wash | 10th wash |
| Activated triclosan | ? | 3.47 | 3.58 |
| Non-activated triclosan | ? | 2.13 | 2.20 |
| 4% CHG | ? | 2.54 | 3.78 |

The activated triclosan formulation, but not the traditional triclosan formulation, appears to be effective in this study and meets current TFM performance criteria. There was no vehicle control, so the contribution of triclosan over and above the mechanical action of the vehicle cannot be determined. Furthermore, it is difficult to compare these results to other studies without a more complete description of the study methods. Since this was a poster, most of the details of the methods and study design were not provided. For example, the neutralizers and neutralizer validation methods were not described. Although 30 subjects were involved in the trial, it is unclear whether a crossover design was used or there were only 10 subjects per treatment arm.

**Quaternary Ammonium Compounds**

The study described in the **Bioscience Laboratories** technical report compares a 0.2% benzethonium chloride (BZC) soap (Pure Cleanse Antimicrobial Handwash) to a 4% CHG reference product (Hibiclens).[4] After a 7-day washout period, 36 subjects were randomly assigned to use the test or reference product. Following a 30-second practice wash with bland soap, a baseline value was determined. Subjects rubbed 5 mL of bacterial suspension (approximately $10^9$ CFU/mL) on their hands and allowed them to air-dry for 2 minutes. Baseline samples were collected using the glove juice procedure and subjects performed a 30-second wash with bland soap. For product testing, hands were contaminated as described above and washed using 5 mL of test or reference product for 30 seconds, followed by a 30-second rinse. The contamination/wash cycle was repeated 10 times. For sampling, sterile gloves were placed on the hands while still wet. Seventy-five mL of stripping fluid (without neutralizers) were added to the glove and massaged for one minute. An aliquot was removed from the glove and diluted into an equal volume of buffer containing neutralizers. Samples were further diluted and plated in triplicate on tryptic soy agar with neutralizers.

Baseline values from the left and right hands were statistically equivalent ($p = 0.58$). For subjects who washed with 0.2% BZC soap, the mean $\log_{10}$ baseline value was 9.23 ± 0.28. After the first wash, the mean was 7.02 ± 0.25, and was 6.22 ± 0.28 after the tenth wash. Subjects who were assigned Hibiclens had a mean $\log_{10}$ baseline value of 9.44 ± 0.34, 6.25 ± 0.58 after the first wash, and 4.01 ± 0.57 after the tenth wash. Mean $\log_{10}$ reduction factors

are shown in the table below. The log reductions for both products meet the TFM requirements for antiseptic handwash.

**Bacterial Reductions after Clinical Simulation Testing with BZC Soap or Hibiclens**

| Product | n | Reduction Factor ($log_{10}$) | |
|---|---|---|---|
| | | 1st wash | 10th wash |
| Pure Cleanse (0.2% BZC) | 18 | 2.21 | 3.01 |
| Hibiclens (4% CHG) | 18 | 3.19 | 5.43 |

Overall, this study followed the TFM protocol closely. Some minor modifications were made to the procedure, but these were described. An active control arm was included and helped to validate the study conduct. Lack of a vehicle control prohibits assessment of the contribution of the active ingredient. Although the TFM allows for artificial contamination of the hands using at least $10^8$ CFU/mL, the inoculum used in this study was nearly 10-fold higher than what is commonly used for this test method. Generally, starting with a larger inoculum results in a greater reduction, and this may have resulted in slightly higher reduction factors. Furthermore, the reduction factors may be somewhat higher than actual values since neutralizers were not added during sampling, but only during the dilution step. The type of neutralizer used in the study was not described, although the investigators mention that the neutralizer was validated using the ASTM test method. Finally, a small number of subjects was used in this study.

The study described in the **Hill Top Research** technical report compares a 0.5% benzethonium chloride soap to vehicle and Hibiclens (4% CHG) using a revised ASTM handwash method.[10] After a 1-week washout period, 75 subjects completed the handwash testing. Thirty subjects were randomized to the test product (0.5% BZC), 30 to the vehicle, and 15 to the active control, Hibiclens. On test day, subjects performed a 15-second practice wash with bland soap and rinsed for 30 seconds. Next, subjects' hands were contaminated with three 1.5-mL aliquots of *S. marcescens* suspension at a minimum of $10^8$ CFU/mL. The inoculum was spread over the hands and allowed to air dry for 90 seconds. A baseline determination was made by placing the hands into plastic bags, adding 75 mL of stripping solution with neutralizer, and massaging for 1 minute. An aliquot was removed, diluted, and plated on trypticase soy agar. Hands were then rinsed to remove residual stripping fluid before the next contamination cycle. After each hand contamination, subjects washed with 5 mL test soap or vehicle for 30 seconds or with 5 mL Hibiclens for 15 seconds, followed by a 30-second rinse. Samples were collected after the first and eleventh washes; hands were dried with a paper towel after all other washes. The mean $log_{10}$ bacterial reductions are listed in the table below.

**Bacterial Reductions after Clinical Simulation Testing with BZC Soap or Controls**

| Product | n | Reduction Factor ($log_{10}$) | |
|---|---|---|---|
| | | 1st wash | 11th wash |
| 0.5% BZC soap | 30 | 1.87 | 2.61 |
| Soap vehicle | 30 | 1.82 | 2.10 |
| Hibiclens (4% CHG) | 15 | Not provided | Not provided |

The authors conclude that 0.5% BZC was significantly better at reducing the number of bacteria on the hands than vehicle. But, statistical analysis is not provided and it is not clear from the reduction factors that this is true, especially after a single wash. Overall, this study was well designed and followed the ASTM handwash protocol very closely. The log reduction data for the active control arm (Hibiclens) was not provided and cannot be used to to validate study conduct. The results show that the BZC soap does not meet the TFM criteria for an antiseptic handwash. In addition, a description of the neutralizers and the neutralization validation procedure were not provided. The number of subjects that were used still does not approach the number recommended in the TFM, however more subjects participated in this study than in most of the other submitted studies.

**Alcohol**

**Lilly and Lowbury** assessed the effectiveness of different hand hygiene methods on bacteria that were either rubbed or dried onto the skin.[11] Twenty-microliter drops of a *Staphylococcus aureus* suspension were deposited on the tips of the four fingers of the left hand. For the first study, a loopful of the suspension was transferred from each fingertip to the corresponding fingertip of the right hand, spread with the loop, and air-dried. In the second study, the opposing fingertips were rubbed together firmly for 30 seconds and allowed to dry for 1 minute. After allowing the inoculum to dry, each volunteer either 1) washed with bland soap and water for 30 seconds, 2) washed with 4% CHG (Hibiscrub) and water for 30 seconds, 3) rubbed two 5-mL aliquots of 70% ethanol on the hands until dry, or 4) washed with 4% CHG without water for 30 seconds. Four volunteers were used and each volunteer performed each type of wash procedure. Samples were collected by rubbing the fingertips against glass beads in a short glass tube containing Ringer's solution with neutralizers for 3 minutes. Samples were plated on horse blood agar for enumeration.

**Bacterial Reductions after Clinical Simulation Testing with Ethanol or Controls**

| Product | n | Mean $\log_{10}$ Reduction of Bacterial Counts | |
|---|---|---|---|
| | | Bacterial suspension: | |
| | | Dried on | Rubbed on |
| Bland soap | 4 | 1.76 | 0.53 |
| 70% Ethanol | 4 | 2.62 | 2.60 |
| 4% CHG with water | 4 | 1.35 | 2.07 |
| 4% CHG without water | 4 | 1.96 | 1.81 |

The authors conclude that antiseptics are more effective than soap and water; antiseptics are effective whether the bacteria are dried or rubbed on the skin; and soap is more effective when the inoculum is dried onto the skin. However, this study is not designed to demonstrate the contribution of the antiseptic ingredients to the observed effectiveness of the formulation. In addition, neither the inoculum nor the baseline values were provided, so the significance of reduction outcomes cannot be fully evaluated. Other studies suggest that the amount of inoculum applied to the skin may influence the reduction factors. Furthermore, these investigators use methods that are very different from the TFM and ASTM methods, although this article predates the TFM by 16 years. Finally, a small number of subjects were used and the subjects were not randomized.

***Summary***
Overall, the studies assessed product formulations and were not adequately controlled to demonstrate the contribution of the active ingredient to the effectiveness of the product. Five of eight references supporting the effectiveness of triclocarban used the Cade handwash test. The results from Cade studies, which measure resident flora, cannot be compared to studies using artificial contamination. Both the TFM and ASTM handwash tests use artificial hand contamination and six of the submitted studies followed the ASTM or TFM method. Of these, two studies tested triclocarban, one tested triclosan, two tested benzethonium chloride, and the active ingredient in the other study was not provided. Overall, the methods were poorly described and controls often were not used. In fact, in some cases the test methods were changed or the full number of washes was not performed.

Collectively, not enough information was provided to be able to make any generalizations about the efficacy of triclocarban. Only one study examined the efficacy of triclosan and suggests that triclosan does not meet the TFM performance criteria, although an activated form of triclosan does meet the log reductions.

Both studies that were submitted to demonstrate the efficacy of benzethonium chloride-containing soaps were conducted following established protocols. The studies were well described, tested a moderate number of subjects, and included an active control. The results of these studies suggest that products containing BZC may have a difficult time meeting the TFM performance criteria. In one study, the BZC product did not meet the TFM log reductions and, in fact, did not perform much better than vehicle. In the other study, the BZC product did meet the TFM performance criteria; however, a large inoculum and delayed neutralization may have resulted in elevated reduction factors. More data is needed to establish the efficacy of this ingredient.

## C. Efficacy of Consumer Antiseptics – Clinical Simulation Testing of Antiseptic Bodywashes

***Overview***
The SDA/CTFA Industry Coalition submitted two journal articles that relate to the efficacy of consumer antiseptic bodywashes. Both of the studies examine the ability of triclocarban to inhibit the growth of organisms associated with skin infections after a period of occlusion. These studies use experimental models whose relevance to the clinical setting is unclear.

***Study Evaluations***
**Billhimer** and colleagues examined the residual activity of a 1.5% TCC bar and vehicle bar soap in two simulated use studies.[3] Twenty subjects were recruited for each study and refrained from using antimicrobials for 7-14 days prior to study initiation. The TCC and vehicle soaps were randomized to each arm of the subject. Subjects performed a supervised wash of their forearms three times a day, at least 1 hour apart. The wash procedure was as follows: the arm and soap were wet under running tap water; the bar was rubbed on the volar

surface of the forearm in an up-and-down motion for 15 seconds; the lather was then rubbed on the arm for 45 seconds, rinsed for 15 seconds, and patted dry with a paper towel.

In the first study, immediate residual effectiveness was evaluated after a total of seven washes (three washes on days 1 and 2, and one wash on day 3). In the second study, prolonged residual effectiveness was evaluated after nine washes (three washes on days 1, 2, and 3). Subjects were allowed to bathe during the study; however they were instructed not to wash their arms with soap. Immediately after the seventh wash (study 1) or 24 hours after the ninth wash (study 2), three 3-cm diameter test sites on each arm were inoculated with *Staphylococcus aureus*. The sites were inoculated with 3.4-7.8 x $10^5$ (study 1) or 1.2-1.5 x $10^6$ (study 2) CFU of bacteria, which was spread within the test site. After inoculation, test sites were occluded with Hill Top chambers for 30 minutes, 2, or 5 hours. Sites were sampled by the cup scrub technique using sampling solution that contained letheen, a neutralizer, and Triton X-100 detergent. Samples were diluted and plated on trypticase soy agar containing blood.

Sample sites were inoculated immediately after the seventh wash and occluded for 30 minutes. Greater than 5 logs of bacteria were recovered from these sites, regardless of soap type (5.65 for vehicle and 5.19 for TCC). A greater difference was seen between TCC and vehicle after 2 or 5 hours of occlusion. When sample sites were inoculated 24 hours after the last wash and occluded, there was a statistically significant difference between TCC and vehicle at all three timepoints. Moreover, the majority of subjects had fewer CFUs recovered from the TCC-treated arm than from the vehicle-treated arm.

The authors conclude that sufficient TCC had remained on the skin for 24 hours after the final wash to inhibit the growth of *S. aureus* for as long as 5 hours. No baseline determinations were made and bacterial reduction factors are not reported for these subjects. Without baseline data, there is no way to know what reductions would be achieved. Occlusion encourages bacterial growth, and both residents and transients will grow under these conditions. Finally, the relevance of this experimental model to the clinical situation is not known.

**Finkey** and others performed two laboratory studies to demonstrate the efficacy of either 1.5% or 0.8% TCC bar soap against common skin pathogens.[7] Thirty subjects were tested, following a 2-week washout period. In the first study, the subjects' forearms were delipidized with acetone prior to application of the soap. In the second study, forearms were not delipidized and the test products were applied seven times over a 3-day period. Circular areas (2.7 cm diam.) were drawn on the flexor surface of both forearms. The soaps and placebo soap were each used as ten percent aqueous solutions. The soap solution (0.3 mL) was applied to each site and spread evenly. After 1 minute, sites were rinsed for 30 seconds. One hour after the final soap application, 0.01 mL of bacterial suspension was spread within the test area. The first study evaluated *S. aureus*, *Streptococcus pyogenes*, and *Corynebacterium minutissimum*. All but *S. pyogenes* were used in the second study. Each test site was occluded for 5 hours using a 1-5/8 inch plastic weigh boat. After 5 hours of occlusion, bacterial samples were taken using the detergent scrub method, diluted, and plated

on either trypticase soy agar containing tetracycline (*S. aureus*), 5% blood agar containing crystal violet (*S. pyogenes*), or brain heart infusion agar (*C. minutissimum*).

In the first study, 1.5% TCC was compared to placebo after one application to acetone-delipidized skin and 5 hours of occlusion. A statistically significant difference was seen between 1.5% TCC treatment and placebo in the recovery of both *S. aureus* ($p = .00005$) and *C. minutissimum* ($p = .03$). No difference was seen for *S. pyogenes*. However, the authors suggest that this organism survives poorly on the skin. The bacterial $\log_{10}$ reduction factors, as calculated by the reviewer, are listed in the table below.

**Reduction in Skin Organisms after Clinical Simulation Testing with TCC Soap**

| Organism | n | Reduction Factor ($\log_{10}$) | |
|---|---|---|---|
| | | 1.5% TCC soap* | Placebo* |
| *S. aureus* | 30? | 3.32 | 1.69 |
| *S. pyogenes* | 30? | 5.01 | 5.19 |
| *C. minutissimum* | 30? | 3.21 | 2.64 |

* Skin was delipidized prior to application of soap

In the second study, both 1.5% and 0.8% TCC were compared to placebo soap after seven applications to the skin in a randomized block design. No significant difference was seen between 1.5% and 0.8% TCC, but both TCC concentrations demonstrated significantly lower bacterial counts than placebo for the two organisms ($p \leq .05$). The calculated reduction factors are listed below.

**Reduction in Skin Organisms after Clinical Simulation Testing with TCC Soap**

| Organism | n | Reduction Factor ($\log_{10}$) | | |
|---|---|---|---|---|
| | | 1.5% TCC soap | 0.8% TCC soap | Placebo |
| *S. aureus* | 30? | 3.83 | 4.05 | 2.54 |
| *C. minutissimum* | 30? | 3.95 | 4.06 | 2.33 |

The authors conclude that TCC at either 0.8% or 1.5% demonstrates significant antibacterial activity against both *S. aureus* and *C. minutissimum*. Like the study described above, this is an experimental model whose relevance to the clinical situation is unclear. Consequently, it is difficult to compare these results to other studies since the methods are significantly different from other studies. For instance, the investigators delipidized the skin to enhance the persistence of *S. pyogenes* on the skin, but the authors do not describe what effect delipidization may have on persistence of the other two organisms. Actually, this treatment did not have the intended effect since very little *S. pyogenes* survived on the skin. Other limitations of the study include not providing a description of the detergent scrub method, the inocula, or whether neutralizers were used. Furthermore, the authors do not explain why test sites are not inoculated until 1 hour after soap treatment. Finally, the number of tests done on each subject is not stated and randomization is not mentioned for the first study.

***Summary***

Two studies were submitted to support the efficacy of consumer antibacterial bodywashes. Both of the studies examined the ability of TCC to inhibit the growth of organisms associated with skin infections after a period of occlusion. However, different methods were used and different organisms were tested. In one study, no baseline determinations were made, so the effect of application of the product cannot be determined. In the other study, the amount of inoculum was not reported and neutralizers were not used. In summary, neither of these studies provided sufficient information to determine the effectiveness of the antiseptic product under study.

## References


**1.** Aiello AE, Cimiotti J, Della-Latta P, and Larson EL. A comparison of the bacteria found on the hands of 'homemakers' and neonatal intensive care unit nurses. *J Hosp Infect.* 2003;54(4):310-315.

**2.** Bayer Corporation. Citizen Petition to classify triclocarban category I for efficacy in the Tentative Final Monograph for Healthcare Antiseptic Drug Products. Docket 75N-183H; 2001:1-5, 62-63.

**3.** Billhimer WL, Berge CA, Englehart JS, Rains GY, and Keswick BH. A modified cup scrub method for assessing the antibacterial substantivity of personal cleansing products. *J Cosmet Sci.* 2001;52:369-375.

**4.** BioScience Laboratories Inc. *Determination of the antimicrobial efficacy of one test product and one reference product using the health care personnel handwash procedure* Nov 30, 2000. 2002; Report No. 000918.

**5.** Chen Y, Jackson KM, Chea FP, and Schaffner DW. Quantification and variability analysis of bacterial cross-contamination rates in common food service tasks. *J Food Protect.* 2001;64(1):72-80.

**6.** Dyer DL, Shinder A, and Shinder F. Alcohol-free instant hand sanitizer reduces elementary school illness absenteeism. *Fam Med.* 2000;32(9):633-638.

**7.** Finkey MB, Corbin NC, Aust LB, Aly R, and Maibach HI. In vivo effect of antimicrobial soap bars containing 1.5% and 0.8% trichlorocarbanilide against two strains of pathogenic bacteria. *J Soc Cosmet Chem.* 1984;35:351-355.

**8.** Fuls JL, Fischler GE, Mulberry GK, Baxter KA, and Brady AR. Antimicrobial efficacy of activated 2,4,-tricloro-2'-hydroxy diphenyl ether (triclosan) in surfactant based formulations. Paper presented at: American Society for Microbiology Annual Meeting, 2003; Washington, DC.

**9.** Guinan M, McGuckin M, and Ali Y. The effect of a comprehensive handwashing program on absenteeism in elementary schools. *Am J Infect Control.* 2002;30(4):217-220.

**10.** Hill Top Research Inc. *HTR Study No. 01-109362-11* 2002.

**11.** Lilly HA and Lowbury EJL. Transient skin flora. Their removal by cleansing or disinfection in relation to their mode of deposition. *J Clin Path.* 1978;31:919-922.

**12.** Montville R, Chen Y, and Schaffner DW. Risk assessment of hand washing efficacy using literature and experimental data. *Int J Food Microbiol.* 2002;73(2-3):305-313.

**13.** Procter & Gamble. Hill Top Biolabs; 1977. Report No. 77-837-11.

**14.** Procter & Gamble. Hill Top Biolabs; 1979a. Report No. 79-1034-11.

**15.** Procter & Gamble. Hill Top Biolabs; 1979b. Report No. 79-0889-11.

**16.** Procter & Gamble. Hill Top Biolabs; 1991. Report No. BS-209-CLS-9111.

**17.** Procter & Gamble. Hill Top Biolabs, Inc.; 1993. Report No. BS-374-CLS-9308.

**18.** Procter & Gamble. Hill Top Biolabs, Inc.; 1994. Report No. BS-505-CLS-9410.

**19.** Roman DP, Barnett EH, and Balske RJ. New germicide for soap. *Soap Chem Spec.* 1958;34:35-37.

**20.** Singh G, Marples RR, and Kligman AM. Experimental *Staphylococcus aureus* infections in humans. *J Invest Dermatol.* 1971;57(3):149-162.

**21.** Van R, Morrow AL, Reves RR, and Pickering LK. Environmental contamination in child day-care centers. *Am J Epidemiol.* 1991;133(5):460-470.

**Appendix A – Submitted References, Previously Reviewed**

Clinical Benefit


1. Brown EJ. A povidone-iodine skin cleanser foam in the management of acne vulgaris. *Brit J Clin Prac* 1977; 31:218-219.
2. Butz AM, Larson EL, Fosarelli P, and Yolken R. Occurrence of infectious symptoms in children in day care homes. *Amer J Infect Control* 1990; 18:347-353.
3. Dubow E and Winter L, Jr. Effect of an antibacterial soap in the management of scratches, cuts, and abrasions. *Curr Therapeutic Res* 1967; 9:631-633.
4. Falsey AR, Criddle MM, Kolassa JE, McCann RM, Brower CA, and Hall WJ. Evaluation of a handwashing intervention to reduce respiratory illness rates in senior day-care centers. *Infect Control Hosp Epidemiol* 1999; 20:200-202.
5. Fendler E, Ali Y, Hammond B, Lyons M, Kelley M, and Vowell N. The impact of alcohol hand sanitizer use on infection rates in an extended care facility. *Amer J Infect Control* 2002; 30:226-233.
6. Franz E, Rohde B, and Weidner-Strahl S. The effectiveness of topical antibacterials in acne: a double-blind clinical study. *J Int Med Res* 1978; 6:72-77.
7. Gibson LL, Rose JB, Haas CN, Gerba CP, and Rusin PA. Quantitative assessment of risk reduction from hand washing with antibacterial soaps. *J Appl Microbiol Symp Suppl* 2002; 92:136S-143S.
8. Hammond B, Ali Y, Fendler E, Dolan M, and Donovan S. Effect of hand sanitizer use on elementary school absenteeism. *Amer J Infect Control* 2000; 28:340-346.
9. Hendley JO and Gwaltney JM. Mechanisms of transmission of rhinovirus infections. *Epidemiol Rev* 10:242-258.
10. Hoffman K, Winstead K, Edmundson M, Weber D, and Rutala W. Comparison of a novel triclosan hand protectant versus handwashing alone for reducing transient hand bacterial colonization and nosocomial infections. *Amer J Infect Control* 1999; 27:208ff [poster].
11. Jampani H, Newman J, Mulberry G, and Brady A. Clinical evaluations: transepidermal delivery of topical antimicrobials and moisturizers. *Amer J Infect Control* 2000; 28:92 [poster].
12. Jampani H, Newman J, Rizer R, and Trookman N. Bacterial inflammation: unique anti-inflammatory characteristics of a therapeutic antimicrobial hand gel. *Amer J Infect Control* 2000; 28:92 [poster].
13. Lucet JC, Rigaud MP, Mentre F, Kassis N, Deblangy C, Andremont A, and Bouvet E. Hand contamination before and after different hand hygiene techniques: a randomized clinical trial. *J Hosp Infection* 2002; 50:276-280.
14. MacKenzie AR. Effectiveness of antibacterial soaps in a healthy population. *JAMA* 1970; 211:973-976.
15. Marie JR, Haas CN, Rose JB, and Gerba CP. Quantitative assessment of benefits from using topical antimicrobial hand products: case study on *Salmonella* risk from handling raw chicken. Abstract American Society for Microbiology General Meeting; 2002.
16. Peters F and Flick-Fillies D. Hand disinfection to prevent puerperal mastitis. *The Lancet* 1991; 338:831.

17. Rose JB and Haas CN. A risk assessment framework for the evaluation of skin infections and the potential impact of antibacterial soap washing. *Amer J Infect Control* 1999; 27:526-533.
18. Samalonis L. Decreasing the incidence of external ocular eye disease. *Eye World* 1999; 4:52-53.
19. Shinder FS and Dyer DL. Alcohol-free instant hand sanitizer reduces illness absenteeism in an elementary school. Woodward Laboratories. No date.

Efficacy

1. Fischler GE, Fuls JL, and Mulberry GK. The use of *Escherichia coli* as an alternate test organism in the ASTM E1174 health care personnel wash method. Abstract American Society for Microbiology General Meeting; 2003 [poster].
2. Huntington Laboratories, Inc. *OR/Scrub – antimicrobial skin cleanser with 1% triclosan*. Research Bulletin HL-11173-030194. No date.
3. Sheena AZ and Stiles ME. Efficacy of germicidal hand wash agents against transient bacteria inoculated onto hands. *J Food Protect* 1983; 46:722-727.
4. Stepan Company. *Quat-based antibacterial hand soaps*. Stepan Report. No date.

## Appendix B – Acronyms and Abbreviations

| | |
|---|---|
| ASTM | American Society for Testing and Materials |
| cm | centimeter |
| BZC | benzethonium chloride |
| CHG | chlorhexidine gluconate |
| CFU | colony forming unit |
| CP | citizen petition |
| CTFA | Cosmetic, Toiletry, and Fragrance Association |
| GI | gastrointestinal |
| HCCM | Healthcare Continuum Model |
| mL | milliliter |
| OTC | over-the-counter |
| PCMX | para-chloro-meta-xylenol |
| SAB | surfactant, allantoin, and benzalkonium chloride |
| SDA | Soap and Detergent Association |
| TCC | triclocarban |
| TFM | Tentative Final Monograph |
| UTI | urinary tract infection |