

**TAB 9**

**FDA Reviewer's Evaluation of CTFA/SDA Submission  
(CP7 & C80) Regarding Clinical Benefit:**

- **Healthcare Personnel Handwashes – Steven Osborne, M.D.**
- **Patient Preoperative Skin Preparations -Steven Osborne, M.D.**

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| • <b>Surgical Hand Scrubs – Michelle M. Jackson, Ph.D.</b> |
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## HEALTHCARE ANTISEPTIC DRUG PRODUCTS REVIEW

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Food and Drugs Administration  
Center For Drug Evaluation and Research  
**Division of Over-the-Counter Drug Products (HFD-560)**

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<b>REVIEW DATE:</b>	June 7, 2004
<b>FDA DOCKET NO.:</b>	75N-183H
<b>SUBMISSION:</b>	CP7 and C80
<b>PHARMACOLOGICAL CATEGORY:</b>	Healthcare Antiseptic
<b>INDICATION:</b>	Surgical Hand Scrub
<b>REVIEWER:</b>	Michelle M. Jackson, Ph.D.

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This is an OTC microbiologist's review and reassessment of the performance criteria for effectiveness (*in vivo*) and clinical benefit for surgical hand scrubs for healthcare antiseptic drug products.

**Purpose:** The purpose of this review is to determine if data submitted by the Cosmetic, Toiletry, and Fragrance Association (CTFA) in a citizen petition and comment to the healthcare antiseptic rulemaking support their request to revise the performance and effectiveness criteria in the Healthcare Antiseptic Drug Products Monograph. CTFA requested that the log reduction criteria proposed in the 1994 tentative final monograph be lessened for ingredients marketed as healthcare antiseptics. They submitted journal articles to support their recommendations. This review focuses on surgical hand scrubs. The review first provides a brief synopsis of each literature report in a table format (page 5) followed by extensive review of each report.

**Background:** In the FEDERAL REGISTER of June 17, 1994, FDA published an amendment to the tentative final monograph (TFM) for over-the-counter (OTC) healthcare antiseptic drug products (59 FR 31402). The proposed rule defined performance expectations for surgical hand scrub as an antiseptic containing preparation that significantly reduces the number of microorganisms on intact skin; is broad spectrum, fast acting, and persistent. The indicated use for surgical hand scrub is that it significantly reduces the number of microorganisms on the skin prior to surgery. In order for an antiseptic ingredient to be generally recognized as effective for use as a surgical hand scrub, it must have existing data from well designed clinical studies demonstrating effectiveness.

FDA has proposed specific effectiveness criteria for final formulations of surgical hand scrubs that are based on the recommendations of the Panel and FDA experience in evaluating the effectiveness of this type of drug products approved through the new drug approval process. The 1994 TFM proposed the following criteria for surgical hand scrubs: reduces the number of bacteria 1 log<sub>10</sub> on each hand within 1 minute and bacteria cell count on each hand does not exceed baseline within 6 hours on the first day; produces a 2-log<sub>10</sub> reduction of the microbial flora on each hand within 1 minute of product use by the end of the second day; and 3-log<sub>10</sub> reduction of the microbial flora on each hand within 1 minute of product use by the end of the fifth day when compared to the established baseline. Sampling is taken on the second day and fifth day to demonstrate the substantive activity of antimicrobial products. These surgical hand scrub testing requirements and surrogate endpoints have served as the Agency’s basis for the evaluation of the effectiveness of OTC healthcare antiseptic drug products approved through the NDA process and are recommended in the TFM to be used for the demonstration of the effectiveness of the active ingredients seeking inclusion in the monograph.

In the preparation for the Nonprescription Drugs Advisory Committee (NDAC) meeting, a review of a Citizen’s Petition (CP7) and Comment to the Docket (C80) was conducted regarding clinical benefit. This review will focus on the criteria used to establish surgical hand scrub efficacy. CP7 contends the following:

- Surgical Scrub – A 1 log<sub>10</sub> reduction of the natural flora after a single wash as measured in American Society for Testing and Materials (ASTM) E1115 Standard Test Method for Evaluation of Surgical Hand Scrub Formulations reflects a level of efficacy that provides a benefit in the surgical suite. The criterion of a 1 log<sub>10</sub> reduction of the natural flora after a single wash is appropriate provided the baseline contamination level is greater than 5 log<sub>10</sub> and neutralizer is incorporated into all sampling fluids.

Table 1. Performance criteria proposed in the 1994 TFM vs. Industry’s proposed criteria.

	1994 TFM Current Reductions			Industry’s Proposed Reductions
Surgical Scrub Preparation	Day 1, Wash 1	Day 2*, Wash 2	Day 5*, Wash 11	Day 1**, Wash 1
	1 log <sub>10</sub> in 1 min AND bacterial count does not exceed baseline within 6 hours on day 1	2 log <sub>10</sub> in 1 min	3 log <sub>10</sub> in 1 min	1 log <sub>10</sub> in 1 min
<p>* Sampling is taken on the second day and fifth day to demonstrate the substantive activity of antimicrobial products.</p> <p>**Surgical scrubs should be effective following a single use. A cumulative effect should not be a requirement as alcohol, a Category 1 ingredient, and potentially other effective active ingredients may not provide a cumulative effect.</p>				

In support of this recommendation, CP7 provided the following table:

Table 2. Efficacy of Topical Antimicrobial Products after a Single Wash (Reduction from Baseline)

<b>Baseline Level (log<sub>10</sub>)</b>	<b>Range Log reduction after a single wash</b>	<b>Mean</b>	<b>Median</b>	<b>Number of Examples (references)</b>
<b>4% Chlorhexidine Gluconate</b>				
>6	0.29-1.88	0.97	0.84	10 (Aly & Maibach 1983; Reverdy et al. 1984; Larson et al. 1986; Larson et al. 1987; Cremieux et al. 1989; Hobson et al. 1998; Larson & Loughon 1987)
5-6	-0.127-1.5	0.68	0.57	7 (Larson et al. 1990; Larson & Bobo 1992; Butz et al. 1990b; Larson & Loughon 1987; Pereira et al. 1990)
<5	0.19-0.81	0.46	0.38	3 (Larson et al. 2001; Morrison et al. 1986; Sheena & Stiles 1985)
<b>60% Isopropyl Alcohol</b>				
>6	1.34-1.74	1.51	1.5	5 (Larson et al. 1986; Larson et al. 1987)
<5	1.4	-	-	1 (Morrison et al. 1986)
<b>70% Isopropyl Alcohol</b>				
>6	1.2-1.66	1.43	-	2 (Larson et al. 1986; Reverdy et al. 1984)
5-6	0.87	-	-	1 (Larson & Bobo 1992)
<5	0.05-0.5	-	-	2 (Morrison et al. 1986)
<b>7.5% Povidone-iodine</b>				
>6	0.7-1.22	1.05	1.14	4 (Larson et al. 1990; Aly & Maibach 1983; Cremieux et al. 1989; Hobson et al. 1998)
5-6	0.21-1.22	0.89	1.07	4 (Larson & Bobo 1992; Pereira et al. 1990; Kundsinn & Walter 1973)

CP7 stated that the data in Table 2 show how baseline contamination levels influence reductions in bacterial counts observed after a single wash. The comment further stated that in most examples, if the baseline level was greater than 6 log<sub>10</sub>, the mean reductions achieved after a single wash with chlorhexidine gluconate, isopropyl alcohol, and povidone-iodine containing surgical scrubs was approximately 1 log<sub>10</sub> or greater. As the baseline levels decreased, the observed mean reduction from use of these products decreased below 1 log<sub>10</sub>. The petition

contended that the expected contamination level on a surgeon's hands is approximately 3 to 6  $\log_{10}$ , and that depending on the baseline contamination, an efficacious product is one that reduces the bacterial population before a surgical procedure between 0.6 to 1.5  $\log_{10}$ . The comment concluded that based on the literature cited in Table 2, inclusion of a 1-  $\log_{10}$  reduction in the Final Monograph is appropriate for the surgical scrub category. The comment contends that the data presented provide ample evidence that an efficacious surgical scrub can be defined as one that causes a minimum 1  $\log_{10}$  reduction of the natural flora after one wash, as measured by ASTM E1115 (Standard Test Method for Evaluation of Surgical Hand Scrub Formulations), provided the baseline contamination level is greater than 5  $\log_{10}$  and neutralizer is incorporated into all sampling fluids. C80 provided additional data to support the petition's position.

### **Conclusions:**

Regarding clinical benefit, the studies have not shown a direct correlation between the use of any topical antiseptic agent for surgical hand disinfection and a reduction in surgical infection rates. There are numerous factors involved in surgical site infection development including: (1) patient's age, (2) nutritional status, (3) diabetes, (4) smoking, (5) obesity, (6) coexistent infections at a remote body site, (7) colonization with microorganisms, (8) altered immune response, (9) length of preoperative stay, (10) duration of surgical scrub, (11) skin antisepsis, (12) preoperative shaving, (13) preoperative skin prep, (14) duration of the operation, (15) type of antimicrobial used, (16) operating room ventilation, (17) inadequate sterilization of instruments, (18) foreign material in the surgical site, (19) surgical drain, and (20) surgical technique: poor hemostasis, failure to obliterate dead space and tissue trauma (1999 Guideline for Prevention of Surgical Site Infection). The studies evaluated were not adequately controlled to address the multifactorial nature of surgical site infection. The majority of the clinical simulation studies CTFA/SDA submitted contains many flaws and shows that many of the products tested do not meet the TFM criteria and contain many flaws. See Table on "Clinical Benefit of Surgical Hand Scrubs" on page 5. From the articles reviewed, none can clearly support a change in the efficacy criteria for surgical hand scrubs.

## Clinical Benefit of Surgical Hand Scrubs

Authors	Objective (Purpose)	Study Design (Endpoints)/ Setting	Active Ingredient (Dosage)	Population (Subjects)	Results	Deficiencies	Clinical Benefit
I. Aly & Maibach: <i>Curr Therap Res</i> , 1983	Evaluate comparative anti-microbial effects of CHG and PVP-I impregnated sponge brushes.  Phase 1 - Anti-microbial activity Phase 2 – Effects of blood on anti-microbial activity	Clinical Simulation Study  FDA TFM Glove Juice (1978)  Log Reduction Days 1, 2, & 5  Student's t-test  Randomized	4% CHG (Hibiclens)  7.5% PVP-I (E-Z Scrub)	22-54 years of age Total 38 subjects: Phase 1 12 – CHG 13 – PVP-I Phase 2 7 – CHG 6 – PVP-I	CHG Phase 1 - Anti-microbial activity (immediate) Day 1 = 1.88 Day 2 = 2.97 Day 5 = 3.78  CHG Phase 1 - Anti-microbial activity (delayed 3 hrs.) Day 1 = 1.52 Day 2 = 3.10 Day 5 = 3.60  CHG Phase 1 - Anti-microbial activity (delayed 6 hrs.) Day 1 = 1.00 Day 2 = 2.66 Day 5 = 3.22  CHG Phase 2 – Effects of blood on anti-microbial activity (delayed 3 hrs.) Day 1 = 1.63 Day 2 = 2.46 Day 5 = 1.74  CHG Phase 2 – Effects of blood on anti-microbial activity (delayed 6 hrs.) Day 1 = 1.29 Day 2 = 2.19 Day 5 = 2.94  ----- PVP-I Phase 1 - Anti-microbial activity (immediate) Day 1 = 1.21 Day 2 = 2.15 Day 5 = 2.75	<ul style="list-style-type: none"> <li>• No blinding of the study (subjects and data evaluations).</li> <li>• No demographics and disposition of the subjects provided.</li> <li>• No negative control.</li> <li>• Small sample size.</li> <li>• Neutralizer validation not described.</li> <li>• No randomization of sampling.</li> </ul>	No

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Authors	Objective (Purpose)	Study Design (Endpoints)/ Setting	Active Ingredient (Dosage)	Population (Subjects)	Results	Deficiencies	Clinical Benefit
2. Boyce et al: <i>J Infect Dis</i> , 1990	Outbreak of <i>S. epidermidis</i> related to cardiac surgery traced to surgeon's hands.	Case-control epidemiological study  Plasmid analysis, restriction endonuclease digests, antibiograms and biotyping used to identify organism.	Antimicrobial scrub (surgeon was required to use a CHG scrub preparation).	17 members of the cardiac surgery team	PVP-I Phase 1- Anti-microbial activity (delayed 3 hrs.) Day 1 = 0.81 Day 2 = 1.28 Day 5 = 1.73 PVP-I Phase 1- Anti-microbial activity (delayed 6 hrs.) Day 1 = -0.27 Day 2 = 0.44 Day 5 = 0.73 PVP-I Phase 2 – Effects of blood on anti-microbial activity (delayed 3 hrs.) Day 1 = 0.72 Day 2 = 0.84 Day 5 = 0.88 PVP-I Phase 2 – Effects of blood on anti-microbial activity (delayed 6 hrs.) Day 1 = 0.34 Day 2 = 0.38 Day 5 = 0.70	<ul style="list-style-type: none"> <li>Epidemic strain may come from a variety of sources: endogenous flora of the patient, surgical equipment, suction pump, operating room air, blood or other fluids, contaminated prosthetic valves, contaminated disinfectants, etc...</li> <li>Mechanism by which Surgeon A contaminated the operative field was not determined.</li> <li>Factors responsible for the sudden increase in infections caused by the epidemic strain was not determined.</li> <li>Numerous other factors that may have been responsible for the outbreak were not investigated.</li> <li>Only <i>S. epidermidis</i> was tracked.</li> </ul> Other infection control measures that may have been taken are not described.	No

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3. Butz et al: <i>Am J Infect Control</i> , 1990	Compare antimicrobial effectiveness of four handwash products.	Clinical Simulation Study Modified ASTM method for healthcare personnel handwash; 15 handwashes per day for 5 days NMS control Log Reduction Randomized Block ANOVA	Alcohol (30%) wipes; 1% triclosan; 4% CHG; NMS	48 healthy volunteers 12/arm	After the first handwash on day 1, mean log changes compared with baseline for each of the four treatment groups were alcohol wipe, +0.008; TCS, -0.151; CHG, +0.127; and control, +0.289. These changes were not significantly different among all four groups (F=0.254, p=0.86).  TCS and CHG products produced significant reductions in aerobic counts compared with the control after 75 washes (TCS, -1.523; CHG, -2.006; and control, -0.031), whereas results among subjects who used the alcohol wipes were not significantly different from those of the subjects who used the control soap (F=4.14, p=0.06).	<ul style="list-style-type: none"> <li>15 second handwash.</li> <li>Washout period was only for 3 days.</li> <li>Not blinded.</li> <li>Study focused mainly on promoting the use of alcohol wipes.</li> <li>Small sample size.</li> <li>No randomization in sampling as would be required for a surgical scrub.</li> <li>Neutralizer use or validation not described.</li> <li>Oral contraceptive use not excluded in a largely female population.</li> <li>No evaluation of persistence.</li> </ul>	No
4. Connell & Rousselot: <i>Am J Surg</i> , 1964	Evaluation of povidone-iodine in operating rooms, wards, and burn units.	- Aerosol spray was evaluated as an observational prep and wound treatment; 3-4 hr - Surgical scrub 4-minute scrubs - Liquid solution was evaluated as a soak to infected wounds - Patient observations - Bacterial counts - Graft success	PVP-I - 0.5% Aerosol Spray - 1.0%* Antiseptic solution - 0.75%* Surgical scrub - HEX	345 patients: 70 – burn wounds 125 – infected wounds or ulcers 150 – patient prep 50 – surgical scrub	Authors stated that PVP-I is effective degerming agent in any of the three forms studied.  Percentage bacterial reductions for scrub study: PVP-I = 98% (4-min.) PVP-I = 88% (1 ½ hrs.)  HEX = 84% (4-min.) HEX = 66% (1 ½ hrs.)	<ul style="list-style-type: none"> <li>Not blinded. Studies are not considered a well-controlled randomized clinical trial.</li> <li>No demographics and disposition of the subjects provided.</li> <li>No description on how the patients were cared for after the operation or the health of the patients before under going surgical procedures.</li> <li>PVP-I used in multiple area of treatment along with other measures.</li> <li>No statistical analyses.</li> <li>No description of how bacterial counts were performed.</li> <li>No discussion of neutralization for surgical scrub studies.</li> <li>No washout period.</li> </ul>	No

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5. Cremieux et al: <i>Appl Environ Microbiol</i> , 1989	Compare two antiseptic scrub formulations, PVP-I and CHG.	Clinical simulation study  Multi-center study  Scrubbing regimen involved two (Day 1 or 5) or three (Day 2 or 4) daily hand-washings for 5 consecutive and a single washing on Day 8.  NMS control  Log Reduction Welch test or Levene's test Fisher-Snedecor test Student's t-test	10% PVP-I (Betadine scrub) 4% CHG (Hibiscrub) NMS	125 adult volunteers: 49 – PVP-I 41 – NMS soap 35 – CHG	Test products Day 1: PVP-I = 0.70 CHG = 0.76 NMS = 0.57  Day 3: PVP-I = 0.52 CHG = 1.27 NMS = 0.35  Day 5: PVP-I = 0.40 CHG = 0.95 NMS = 0.51	<ul style="list-style-type: none"> <li>Nonrandomized, uncontrolled, and unblinded study.</li> <li>No demographics and disposition of the participants provided.</li> <li>No prescreening of subjects for adequate baseline counts.</li> <li>No wash out period.</li> <li>Study was limited to a quantitative evaluation of the bacteria reductions.</li> <li>No neutralizer validation.</li> <li>Bacterial sampling not randomized.</li> <li>Log reductions noted for one group (10 subjects).</li> <li>No evaluation of log reductions at 6 hours.</li> </ul>	No
6. Grinbaum et al: <i>Infect Control Hosp Epidemiol</i> , 1995	Investigate an outbreak of surgical site infections in vascular surgery unit related to the use of plain soap for surgical scrubbing.	Case-control epidemiological study  2 controls for each case matched for type of surgery and gender whose operations were performed within 30 days of the outbreak	NMS	9 patients with limb amputations or arterial reconstruction	Six of 9 case patients experienced surgical site infection, as compared with 3 of 18 control patients (P=0.026) and 28 of 244 patients in the pre-epidemic 9-month period (P=0.0002). Hand-scrubbing with plain soap yielded a statistical difference between the groups (P<.00001).  Analysis of other risk factors for the development of SSI	<ul style="list-style-type: none"> <li>Difficulties in the design of a case-control study in this outbreak because of a small number of operations were studied and all patients were exposed to the suspected risk factor.</li> <li>Not able to demonstrate definitely that scrubbing with plain soap was related to SSIs.</li> <li>No description of how patients were cared for.</li> </ul>	No

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7. Hobson et al. <i>Am J Infect Control</i> , 1998	Evaluate the <i>in vivo</i> antimicrobial efficacy of the new formulation in standardized handwashing tests recommended by the FDA test methods w/o using a brush with PVP-I and CHG.	2-tailed Fisher's exact test for continuous variables  Student's t test to compare pre-epidemic and epidemic SSI rates	70% alcohol (Triseptin) 4% CHG (Hibiclens) 7.5% PVP-I (Betadine)	90 volunteers (18 subjects per treatment group; 5 treatment groups)	such as age, sex, NNIS index, duration of surgery, ASA status, wound class, elective or emergency surgery, use of antibiotics, remote site infection, preoperative length of stay, underlying diseases (hypertension, diabetes), and substance used for handscrubbing. Handscrubbing with plain soap yielded a statistical difference between the groups ( $p < 0.00001$ ).  Mean log baseline values for all treatment groups ranged between 5.99 and 6.16 CFUs and no significant differences ( $P \leq .05$ ) exist between the groups. No significant differences ( $P \leq .05$ ) were observed in the test formulation treatments.  Immediate log reduction on days 1, 2, 5: 7.5% PVP-I = 1.2; 1.28; 1.27 4% CHG = 1.68; 1.99; 3.43 Brush = 2.86; 2.99; 4.63 Sponge = 2.35; 2.78; 4.46 Hands = 2.90; 3.40; 4.78  6 hour log reduction on days 1, 2, 5: 7.5% PVP-I = -0.21; 0.13; -0.04 4% CHG = 0.86; 1.49; 2.75 Brush = 1.80; 3.09; 4.32 Sponge = 1.33; 2.54; 3.32 Hands = 1.94; 2.70; 3.22  All except PVP-I did not exceed baseline at hrs.	<ul style="list-style-type: none"> <li>No demographics and disposition of the subjects provided.</li> <li>No information on the following: randomization of the subjects, blinding, detailing the neutralization use, etc...</li> <li>Small sample size.</li> <li>Baseline determination was not described.</li> <li>No description of washout period.</li> </ul>	No

CHG = Chlorhexidine gluconate; PVP-I = Povidone-Iodine; NMS = Nonmedicated Soap; IPA = Isopropyl Alcohol; HEX = Hexachlorophene; I = Iodophor; SSI = Surgical Site Infections; TCS = Triclosan; CFUs = Colony Forming Units; \* = available iodine

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8. Jackson: <i>Therap Adv New Clin Implic</i> , 1972	Use of PVP-I to prevent neurosurgical infections.	Observational study Naval Hospital  Liquid solution used as patient prep for craniotomy procedures and as a surgical scrub.	7.5% PVP-I (Betadine)	393 neurological operations Jan. 1968 through Mar. 1971	Out of 393 neurological operations only a single surgical infection was detected, <i>Staphylococcus aureus</i> (0.254%).	<ul style="list-style-type: none"> <li>No statistical outcome.</li> <li>No demographics and disposition of the subjects provided.</li> <li>No description on how the patients were cared for after the operation or the health of the patients before under going surgical procedures.</li> <li>Baseline infection rate with craniotomy?</li> <li>PVP-I used as part of a multiple approach to antiseptis. Therefore, the impact of PVP-I as a surgical scrub cannot be discerned.</li> </ul>	Maybe
9. Kundsinn and Walter: <i>Arch Surg</i> , 1973	Comparison of two scrubs: PVP-I and HEX.	Clinical simulation study  4-minute scrub with HEX  6-minute scrub with PVP-I  Bacterial counts	HEX (pHiso-Hex)  7.4% PVP-I (Betadine)	30 high school seniors (15-17 years of age): 20- boys 10-girls	PVP-I performs better in the immediate reduction of bacterial flora of the hands, but inside the gloved hand after one hour HEX has removed a significantly higher percent of bacteria. Percentage reductions for scrub study transformed from log reductions: PVP-I = 88% (immediately.) PVP-I = 89% (1 hr.)  HEX = 63% (immediately.) HEX = 96% (1 hr.)	<ul style="list-style-type: none"> <li>No statistical evaluation (p values).</li> <li>Washout period was only for three days.</li> <li>No demographics and disposition of the subjects provided.</li> <li>Limited information on the description on how the neutralizers were used.</li> <li>No randomization.</li> <li>No blinding.</li> <li>Small sample size.</li> <li>Only a single baseline determination.</li> <li>No details of neutralizer validation.</li> </ul>	No

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10. Larson et al: <i>Antimicrob Agents Chemother</i> , 1986	Antimicrobial efficacy and acceptability of five hand washing products,	Clinical simulation study 15 hand washes per day for 5 days 15 second scrubs sampling after first and last wash on days 1 and 5 Randomized block Log Reductions of aerobic and anaerobic bacteria Kruskal-Wallis to assess subjects differences in product acceptability Tukey technique for multiple comparisons Analysis of covariance on baseline counts	NMS control (5 mL); 60% IPA (5 mL) Calstat; 70% IPA/ 0.5% CHG (5 mL) Hibistat; 4% CHG/4% IPA (5 mL) Hibiclen; 70% IPA (2 mL)	50 volunteers 10/arm	All agents produced significant reductions in aerobic (P = 0.0002) and anaerobic (P = 0.002) counts over control soap. Log reduction of aerobic bacteria after the first wash on Day 1 NMS = 0.59 60% IPA = 1.34 70% IPA/ 0.5% CHG = 0.80 4% CHG/4% IPA = 1.09 70% IPA = 1.20 Log reduction of aerobic bacteria after the last wash on Day 5 NMS = 0.69 60% IPA = 3.01 70% IPA/ 0.5% CHG = 3.88 4% CHG/4% IPA = 4.34 70% IPA = 3.17	<ul style="list-style-type: none"> <li>No demographics and disposition of the participants provided.</li> <li>No prescreening of subjects for adequate baseline counts.</li> <li>Washout period was only for three days.</li> <li>Baseline count determination was not performed in triplicate.</li> <li>No neutralizer validation.</li> <li>Small sample size.</li> <li>No information on whether subjects on antibiotics and contraceptives were excluded.</li> <li>No evaluation of persistence at 6 hours.</li> <li>Scrub pattern substantially different from TFM.</li> </ul>	No

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11. Larson et al: <i>Am J Infect Control</i> , 1987	Evaluated the effect of stripping time on microbial yield from the hands.	Clinical simulation study  15-sec handwashing procedure done 15x for 5 days  Log reduction after first and 15 <sup>th</sup> wash  Randomized block  Tukey one-way analysis of variance	NMS control; 4% CHG (Hibiclen); 2 alcohol based hand rinses (CalStat and Hibistat containing 0.5% CHG)	40 healthy volunteers 10/arm	There was no significant differences in mean reductions in log CFU among subjects whose hands were sampled for 15 seconds or 3 minutes after one handwash (p=0.45) or after 15 washes (p=0.49).  Log reduction after 1 handwash 15 second sampling NMS = 0.45 4% CHG (Hibiclen) = 1.13 Alcohol rinses (CalStat) = 1.52 Alcohol rinses (Hibistat) = 0.63  Log reduction after 1 handwash 3 minute sampling NMS = 0.08 4% CHG (Hibiclen) = 0.71 Alcohol rinses (CalStat) = 1.50 Alcohol rinses (Hibistat) = 0.84  Log reduction after 15 handwashes - 15 second sampling NMS = 0.78 4% CHG (Hibiclen) = 1.78 Alcohol rinses (CalStat) = 2.60 Alcohol rinses (Hibistat) = 2.04  Log reduction after 15 handwashes 3 minute sampling NMS = 0.29 4% CHG (Hibiclen) = 1.45 Alcohol rinses (CalStat) = 2.83 Alcohol rinses (Hibistat) = 2.40	<ul style="list-style-type: none"> <li>No demographics and disposition of the participants provided.</li> <li>No prescreening of subjects for adequate baseline counts.</li> <li>Study was not blinded.</li> <li>No description of washout period.</li> <li>Limited description of neutralizers.</li> <li>No neutralizer validation.</li> <li>Baseline count determination was not performed in triplicate.</li> <li>Small sample size.</li> <li>Hand sampling not randomized.</li> <li>No evaluation of persistence at 6 hours.</li> </ul>	No

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12. Larson and Laughon: <i>Antimicrob Agents Chemother</i> , 1987	Compare antimicrobial efficacies and subject acceptance of four formulations of CHG and nonmedicated soap.	Clinical simulation study Handwashing 15 times per day for 5 days 15 second scrub Randomized Block Log reduction 7 point ordinal scale to assess skin condition after 5 days use Kruskal-Wallis	4% CHG liquid (Hibiclens) 4% CHG (Bacto-Foam) 2% CHG liquid (Bacto-Shield) NMS	50 volunteers: 42 females-84% 8 males-16% 5 treatment groups	Log reduction after 15 washes: 4% CHG (Hibiclens) = 1.31 4% CHG (Bacto-Shield) = 1.11 2% CHG (Bacto-Shield) = 1.24 4% CHG (Bacto-Foam) = 1.64 NMS = 0.84  Log reduction after 5 days: 4% CHG (Hibiclens) = 2.15 4% CHG (Bacto-Shield) = 1.80 2% CHG (Bacto-Shield) = 1.83 4% CHG (Bacto-Foam) = 2.36 NMS = 0.59	<ul style="list-style-type: none"> <li>No demographics and disposition of the participants provided.</li> <li>No prescreening of subjects for adequate baseline counts.</li> <li>No exclusion of subjects with antibiotics and contraceptives use.</li> <li>Study was not blinded.</li> <li>No description of neutralizers.</li> <li>Handwashing techniques were not described.</li> <li>Three day washout period.</li> <li>Products not used according to labeled directions. Bacto-Shield requires 6-min scrub and Hibiclens requires a two 3-min scrub.</li> <li>Baseline count determination was not performed in triplicate.</li> <li>No neutralizer validation.</li> <li>Small sample size.</li> <li>Hand sampling was not randomized.</li> <li>No evaluation of persistence at 6 hours.</li> </ul>	No
13. Larson et al: <i>Infect Control Hosp Epidemiol</i> , 1990	Test effects of four surgical scrub products: alcohol, triclosan, CHG, and PVP-I.	Clinical simulation study ASTM method surgical hand scrub 5-min. scrubs Log reduction on days 1 and 5 and at 4 hrs on day 1 7 point ordinal scale to assess hand condition Desquamation of hands Block randomization ANOVA	70% ETHOH/0.5% CHG; 1% Triclosan; 4% CHG; 7.5% PVP-I; NMS control	60 healthy volunteers (53 females and 7 males) 18-59 years of age 12/arm	Log counts after gloving day 1: 70% IPA/0.5% CHG = 1.21 1% Triclosan = 0.45 4% CHG = 0.59 7.5% PVP-I = 0.27 NMS = 0.01  Log counts after gloving day 5: 70% IPA/0.5% CHG = 2.42 1% Triclosan = 0.15 4% CHG = 1.76 7.5% PVP-I = 0.50 NMS = -0.22	<ul style="list-style-type: none"> <li>Limited description regarding the use of neutralizers in the samples.</li> <li>No neutralizer validation.</li> <li>Not blinded.</li> <li>3-day washout period.</li> <li>Small sample size.</li> <li>Only a single baseline determination.</li> <li>No exclusion of subjects to using oral contraceptives use.</li> <li>Hand sampling not randomized.</li> <li>No neutralizer validation.</li> <li>No evaluation of persistence at 6 hours.</li> </ul>	No

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14. Larson and Bobo: <i>J Emerg Med</i> , 1992	Evaluate the effect of blood on the antimicrobial activity of several agents.	Clinical simulation study 15 second scrub No product control Student's t-test Randomized Block Log reduction	70% IPA; 70% ETOH / 0.5%CHG; 7.5% PVP-I; 4% CHG; NMS	71 healthy volunteers 12/arm – except for IPA	In the presence of blood two alcohol products resulted in significantly greater reduction in numbers of CFU than other products. Log reductions w/blood after wash: 70% IPA = 0.86 70% ETOH / 0.5%CHG = 0.90 7.5% PVP-I = 0.26 4% CHG = 0.65 NMS = 0.32 Log reductions w/o blood after wash: 70% IPA = 0.87 70% ETOH / 0.5%CHG = 0.38 7.5% PVP-I = 0.21 4% CHG = 0.57 NMS = 0.07	<ul style="list-style-type: none"> <li>• Small sample size.</li> <li>• No blinding of study formulations.</li> <li>• Only a single baseline determination.</li> <li>• No exclusion of subjects using contraceptives.</li> <li>• No neutralizer validation.</li> <li>• Hand sampling not randomized.</li> <li>• No evaluation of persistence at 6 hours.</li> </ul>	No
15. Larson et al: <i>AORN J</i> , 2001	Compare the microbiology and skin condition of hands when using a traditional scrub versus a waterless alcohol based preparation.	6-week, single center, clinical trial (Operating Suites)  Randomized; Microbial counts and typing; Visual scoring of skin condition; Analysis of covariance; t-test; Mann-Whitney U test  Protocol submitted to FDA prior to study irritation.	4% CHG and 61% ETOH / 1% CHG (Avaguard)	27 surgical staff members recruited (18-65 years of age)  20 – treatment 5 – control	Waterless product was associated with less skin damage (p=.002) and lower microbial counts postscrub at days 5 (p=.002) and 19 (p=.02).	<ul style="list-style-type: none"> <li>• No blinding of the product used, so subject and/or investigator bias cannot be ruled out.</li> <li>• No demographics and disposition of the subjects provided.</li> <li>• Sample size determined based on desired difference to be detected in skin condition, not on variation of microbial assay.</li> <li>• Small sample size.</li> <li>• No washout period selected subjects with a previous history of CHG w/i 2 weeks of study.</li> <li>• Did not control for other confounders, like scrubbing frequency, hours in surgery or gloving.</li> <li>• No neutralizer validation.</li> <li>• No log reductions reported.</li> <li>• Hand sampling not randomized.</li> </ul>	No

CHG = Chlorhexidine gluconate; PVP-I = Povidone-Iodine; NMS = Nonmedicated Soap; IPA = Isopropyl Alcohol; HEX = Hexachlorophene; I = Iodophor; SSI = Surgical Site Infections; TCS = Triclosan; CFUs = Colony Forming Units; \* = available iodine

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16. Morrison et al: <i>Infect Control</i> , 1986	Evaluated several new handwash agents for efficacy in removing non-transient flora.	Clinical simulation study Log reduction Duncan's multiple comparison test 2. Phase study 1) traditional handwash products 2) evaporative products	70% IPA; 0.5%CHG/70% IPA (Hibistat); 60% IPA; 1% PCMX (Acute care); 0.05% PVP-I (Iodo care); 4% CHG	40 staff employees (21 years of age or older) 1 <sup>st</sup> phase of study. 14 additional subjects in the 2 <sup>nd</sup> phase of the study.	When compared with two other evaporative agents, the 60% IPA formulation demonstrated significant mean log <sub>10</sub> reduction for each handwash (p≤.03), with a total log <sub>10</sub> reduction of 2.9 over 4 handwashes (p= .0001).  Mean log reduction after fourth wash (handwash) 70% IPA = 0.04 1% PCMX = 0.14 0.05% PVP-I = 0.06 4% CHG = 0.29  Mean log reduction after fourth wash (evaporative handwash) 70% IPA = 0.2 0.5%CHG/70% IPA = 0 60% IPA = 0.5	<ul style="list-style-type: none"> <li>No description of washout period.</li> <li>No demographics and disposition of the subjects provided.</li> <li>No study blinding.</li> <li>10 mL broth used for sampling (normally 50 or 75 mL volumes are used).</li> <li>No description of exclusion criteria.</li> <li>No evaluation of persistence at 6 hours.</li> </ul>	No
17. Pereira et al: <i>Am. J Infect Control</i> , 1990	Determine whether a shorter duration scrub achieves the same reductions in CFU as a standard scrub.	Clinical simulation study Latin square design Randomized Analysis of covariance	4% CHG (Hibiclen); 7.5% PVP-I	34 subjects (operating room personnel), 6 M and 28 F (21-55) TREATMENTS 5-min initial / 3-min consec. scrub. (CHG)  3-min initial / 30-sec consec. scrub. (CHG)  5-min initial / 3-min consec. scrub. (PVP-I)  3-min initial / 30-sec consec. scrub. (PVP-I)	CHG was found to have lower numbers of CFU of bacteria than PVP-I. Optimal regimen was found to be the 5-minute initial and 3-minute consecutive scrubs with CHG.  Log reduction: 5-min initial / 3-min consec. scrub. (CHG) = 1.71  3-min initial / 30-sec consec. scrub. (CHG) = 1.20  5-min initial / 3-min consec. scrub. (PVP-I) = 0.73  3-min initial / 30-sec consec. scrub. (PVP-I) = 0.52	<ul style="list-style-type: none"> <li>No demographics and disposition of the participants provided.</li> <li>Washout period of one week, but were instructed to continue normal handwashing procedures during this period.</li> <li>No blinding of test materials to those analyzing the data</li> <li>No detailing of the use of neutralizers.</li> <li>No neutralizer validation.</li> <li>No exclusion of subjects on antibiotics or contraceptives.</li> <li>Small sample size.</li> <li>No randomization of hand sampling</li> <li>Significant difference between hand counts which made it necessary to calculate predicted microbial counts.</li> <li>No evaluation of persistence at 6 hours.</li> </ul>	No

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18. Reverdy and Fleurette; <i>Path Biol</i> , 1984 (French)	Compared the effects of nine soaps on bacterial flora of the hand 5 minutes after a surgical scrub.	Clinical simulation study Gaschen's bag method Log reductions in aerobic and anaerobic bacteria Student's t test	CHG 4 and 1.5% IPA 70% ETOH 70% NMS NMS and ETOH 70% NMS and IPA 70% NMS and Hydrogen peroxide	10 volunteers	Greatest reduction was produced by 70% IPA (1.7 log <sub>10</sub> reduction); 1.5 to 0.5 log <sub>10</sub> reductions were produced 70% ETOH, PVP-I, 4%, 1.5% CHG and NMS.  Log reduction for aerobic bacteria: CHG 4%, 0.88; CHG 1.5%, 0.67; IPA 70%, 1.66; ETOH 70%, 1.42; NMS 0.33; NMS and ETOH 70%, 0.62; NMS and IPA 70%, 0.39; NMS and Hydrogen peroxide, 0.22	<ul style="list-style-type: none"> <li>Article in French only abstract in English.</li> <li>Small sample size.</li> </ul>	No																														
19. Stiles and Sheena; <i>J Hyg Camb</i> , 1985	Compare the efficacy of antimicrobial products containing: iodophors, 2% CHG, 4% CHG, and nonmedicated soap and a tap water rinse against resident and transient bacteria.	Observational lab study 15 second scrub Latin square design Log reductions Randomized Analysis of variance Duncan's multiple range test	2% and 4% CHG (Hibitane); iodophors containing 0.75, 0.5, 0.3, 0.1, 0.01, and 0.005% available iodine; NMS control	28 Subjects 1/arm	Only 4% CHG and 0.75% PVP-I were significantly better than nonmedicated soap. Low concentrations of iodophor agents and 2% CHG fail to give results better than the NMS.  Uninoculated socially clean hands: <table style="margin-left: 40px;"> <thead> <tr> <th></th> <th>Initial</th> <th>Final</th> </tr> </thead> <tbody> <tr> <td>NMS</td> <td>1.1</td> <td>1.4</td> </tr> <tr> <td>4% CHG</td> <td>1.2</td> <td>0.5</td> </tr> <tr> <td>2% CHG</td> <td>1.0</td> <td>0.5</td> </tr> <tr> <td>0.75% I</td> <td>1.2</td> <td>0.5</td> </tr> <tr> <td>0.5% I</td> <td>1.1</td> <td>0.4</td> </tr> <tr> <td>0.3% I</td> <td>1.3</td> <td>1.0</td> </tr> <tr> <td>0.1% I</td> <td>1.1</td> <td>0.9</td> </tr> <tr> <td>0.01% I</td> <td>1.3</td> <td>1.0</td> </tr> <tr> <td>Water</td> <td>2.3</td> <td>1.9</td> </tr> </tbody> </table>		Initial	Final	NMS	1.1	1.4	4% CHG	1.2	0.5	2% CHG	1.0	0.5	0.75% I	1.2	0.5	0.5% I	1.1	0.4	0.3% I	1.3	1.0	0.1% I	1.1	0.9	0.01% I	1.3	1.0	Water	2.3	1.9	<ul style="list-style-type: none"> <li>Demographics were not provided.</li> <li>This article focused on food handling instead of clinical setting of a hospital.</li> <li>No demographics and disposition of the subjects provided.</li> <li>No blinding (subjects and data evaluations).</li> <li>No neutralizers were mentioned.</li> <li>Broth used for sampling.</li> <li>No mention of washout periods.</li> <li>Small sample size.</li> <li>Reported results as mean of 3 days.</li> <li>Plating not done in triplicate.</li> <li>No statement of inclusion criteria.</li> </ul>	No
	Initial	Final																																			
NMS	1.1	1.4																																			
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20. Bryce et al: <i>Infect Control Hosp Epidemiol</i> , 2001	Determine whether alcohol hand disinfection is an effective alternative traditional agents for pre-surgical scrub.	Prospective clinical trial  Two hospital sites in British Columbia  Cross-over study  CFUs  Fingertip impressions  Glove-juice test  Unpaired t test  Welch/Mann-Whitney U test	70% IPA; 7.5% PVP-I; 4% CHG	22 physicians and 3 surgical nurses from one site.  10 nurses and 6 surgeons at the second site	There was no statistical difference between the microbial hand counts following use of the alcohol-based product or the current agents, for cases less than 2 hours duration.  Less than 2 hour duration 70% IPA = 0.21 7.5% PVP-I & 4% CHG = 0.33  Greater than 3 hour duration 70% IPA = -1.19 7.5% PVP-I & 4% CHG = -0.69	<ul style="list-style-type: none"> <li>No demographics and disposition of the participants provided.</li> <li>There were many variables (factors) in the studies such as glove type, glove liners, other skin agent use, and use of antibiotics and contraceptives were not controlled for.</li> <li>No washout between periods and no instructions were given regarding the use of antimicrobials at home.</li> <li>Not blinded.</li> <li>Not randomized.</li> <li>Results for CHG and PVP-I combined.</li> </ul>	No

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21. Parienti et al: <i>JAMA</i> , 2002	Compare the effectiveness of hand-cleansing protocols in preventing surgical site infections during routine surgical practice.	6 surgical services from teaching and nonteaching hospitals in France.  Randomized crossover study  Multi-site study  Nosocomial infection rates (prospective & post discharge)  Compliance by surgical teams & acceptance  Surgical site infections were prospectively diagnosed by a surgeon, infectious disease specialist, or hygiene specialist on a standard data-collection form.	75% propanol-1/propanol-2/mece-tronium etilsulfate  4% PVP-I (Betadine)  4% CHG (Hibiscrub)	4387 consecutive patients  278 surgeons and nurses  77 staff members assessed for skin tolerance	SSI rates were 55 of 2252 (2.44%) in the hand-rubbing protocol and 53 of 2135 (2.48%) in the hand scrubbing protocol, for a difference of 0.04%.	<ul style="list-style-type: none"> <li>Because unblinded nature of the study bias cannot be ruled out.</li> <li>No description on how the patients were cared for after the operation or details on the health of the patients or antibiotics use before undergoing surgical procedures.</li> <li>No assessment of glove tears or punctures.</li> <li>Other risk factors to take in for consideration such as aseptic techniques, sterilization of surgical instruments used, type of wound dressing applied, etc... were not addressed.</li> <li>Inconsistent use of a non-medicated soap.</li> </ul>	No

## Literature Review

1. **Aly, R and Maibach, HI. "Comparative evaluation of chlorhexidine gluconate (hibiclens) and povidone-iodine (E-Z scrub) sponge/brushes for presurgical hand scrubbing." *Curr Therap Res* 1983 (34):740-745.**

The objective of this study was to evaluate the comparative antimicrobial effectiveness of chlorhexidine gluconate and povidone-iodine sponge/brushes on the normal flora of the hands under the conditions simulating operating room use.

**DESIGN & METHODS:** This study was conducted in two phases: in the first, 25 subjects were randomly assigned to two groups to determine basic antimicrobial activity and, in the second, another 13 subjects were randomly assigned to determine the effect of blood on antimicrobial activity. This study evaluated the following characteristics of these products: 1) immediate effect in reducing the resident bacterial flora of the hands; 2) persistent, or residual, effect in maintaining bacterial reduction; 3) effect of blood, which commonly penetrates through punctured surgical gloves, on residual antimicrobial efficacy; and 4) irritation potential after repeated use.

Thirty-eight subjects whose left-hand and right-hand baseline counts were  $>10^6$  microorganisms/hand were selected to continue. Days 5 and 7 baseline counts also were obtained for these subjects. For subjects in the second phase, day 28 baseline counts also were obtained to ensure that bacterial counts had not changed in the delayed interval before testing. All baseline counts were combined to obtain an average count. Subjects were assigned randomly to specific groups in the two phases.

In the first phase, 12 subjects were assigned to the chlorhexidine gluconate group and 13 to the povidone-iodine group. In the second phase, seven were assigned to the chlorhexidine gluconate group and six to the povidone-iodine group. Neutralizers for chlorhexidine gluconate (Tween 80 and Azolectin) and for povidone-iodine (sodium thiosulfate) were added to the stripping, diluent, and culture media to ensure against carryover of the antimicrobial agents. Neutralization control checks against typical skin microorganisms were made to ensure validation.

**RESULTS:** Table 1 and Table 2 below summarize the results for mean  $\log_{10}$  bacterial count reductions. Both the chlorhexidine gluconate and povidone-iodine sponge/brushes proved to be effective presurgical scrub products, significantly reducing resident bacterial counts. The chlorhexidine gluconate sponge/brush was statistically significantly more effective at every evaluation point in reducing bacterial counts in both phases of the study, i.e., in both the absence and the presence of blood. It maintained significant reductions over the 6-hour period of each test day. However, this was not the case for the povidone-iodine sponge/brush, for which, at some evaluation points, the six-hour counts approached or were greater than baseline counts. The chlorhexidine gluconate sponge/brush was significantly more effective in preventing reestablishment of bacteria under surgical gloves, providing greater duration of action. No significant differences in

irritation potential between the products were observed. Two subjects in the chlorhexidine gluconate group experienced one-grade increases during the study compared to three in the povidone-iodine group. However, five subjects in each group who had been graded as having some degree of erythema or scaling on entrance into the study experienced decreases of one grade. No significant dermal irritation was noted with either product when used in the study.

Table 1. Immediate and delayed postwash mean reductions in bacterial counts and percent kill (basic antimicrobial effects)

	Chlorhexidine Gluconate			Povidone-iodine		
	No. Hands Sampled	Log10 Reduction	Percent Kill	No. Hands Sampled	Log10 Reduction	Percent Kill
Day 1						
Immediate	12	1.8887*	97.57	13	1.2183	87.51
Delayed 3 Hr.	6	1.5224**	93.21	7	0.8184	56.86
Delayed 6 Hr.	6	1.0013*	86.98	6	-0.2740	-243.75
Day 2						
Immediate	12	2.9744*	99.80	13	2.1574	96.34
Delayed 3 Hr.	6	3.1041*	99.63	7	1.2893	87.53
Delayed 6 Hr.	6	2.6679*	99.67	6	0.4480	35.72
Day 5						
Immediate	12	3.7860*	99.97	13	2.7509	99.60
Delayed 3 Hr.	6	3.6098*	99.92	7	1.7313	91.01
Delayed 6 Hr.	6	3.2266*	99.75	6	0.7354	39.54

\* The chlorhexidine gluconate sponge/brush was significantly (P<0.01) more effective than the povidone-iodine sponge/brush

\*\* P<0.07

Table 2. Delayed postwash mean reductions in bacterial counts and percent kill (effects in presence of blood)

	Chlorhexidine Gluconate			Povidone-iodine		
	No. Hands Sampled	Log10 Reduction	Percent Kill	No. Hands Sampled	Log10 Reduction	Percent Kill
Day 1						
Delayed 3 Hr.	7	1.6317*	90.62	6	0.7233	74.57
Delayed 6 Hr.	7	1.2956*	86.11	6	0.3409	52.65
Day 2						
Delayed 3 Hr.	7	2.4683*	99.38	6	0.8477	82.23
Delayed 6 Hr.	7	2.1910*	98.86	6	0.3814	47.99
Day 5						
Delayed 3 Hr.	7	1.7422*	96.59	6	0.0682	-37.95
Delayed 6 Hr.	7	2.9454*	99.71	6	0.7090	75.09

\* The chlorhexidine gluconate sponge/brush was significantly (P<0.01) more effective than the povidone-iodine sponge/brush in the presence of blood

**Reviewer's comments:** *CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the CHG met all the TFM required log reductions and the 6-hr persistence and that PVP-I partially met the criteria.*

*The authors concluded that chlorhexidine gluconate sponge/brush is microbiologically more efficacious than the povidone-iodine sponge/brush for presurgical hand scrubbing. This was due to chlorhexidine gluconate meeting all three time points and povidone-iodine failing to meet the third time point on the fifth day. This reviewer agrees that chlorhexidine gluconate is an excellent antimicrobial agent for surgical hand scrubs due to its persistent effect. However, demographics and disposition of the subjects were not provided. No blinding of the studies (subjects and data evaluations). Although appropriate neutralizers were added to the stripping solution, diluents, and culture media, it is not clear how long before the samples were plated. No details about neutralizer validation were provided. Given that the study used brush/sponges the lack of a negative control is a deficiency. There is also the lack of persistent for povidone-iodine. The study was not designed to demonstrate a correlation between infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

2. **Boyce, JM, Potter-Bynoe, G, Opal, SM, Dziobek, L, and Medeiros AA. "A common-source outbreak of *Staphylococcus epidermidis* infections among patients undergoing cardiac surgery." J Infect Dis. 1990 (161):493-9.**

This article reported a common-source outbreak of infections related to cardiac surgery that was traced to colonization of a surgeon's hand by a strain of *Staphylococcus epidermidis*.

**DESIGN & METHODS:** A single strain of *S. epidermidis* caused an outbreak of postoperative wound infections and endocarditis during a 6-month period. Infections caused by the epidemic strain developed more frequently in valve surgery patients than in those undergoing coronary artery bypass graft surgery ( $P = .03$ ) and occurred only in patients operated on by surgeon A. None of 17 members of the cardiac surgery team carried the epidemic strain in their anterior nares, axillae, or inguinal folds. Hand cultures were performed on 8 surgical personnel, and only surgeon A carried the epidemic strain on his hands. Isolates from cardiac surgery patients, bypass pump blood cultures, and the hands of the implicated surgeon all had identical antimicrobial susceptibility patterns, plasmid profiles, and EcoRI restriction endonuclease digest patterns.

**RESULTS:** The investigation revealed that surgeon A had been using a nonantimicrobial preparation for scrubbing his hands for several years because he had previously developed a dermatitis attributed to an antimicrobial scrub solution. Surgeon A recently adopted the practice of applying sterile mineral oil to his hands before donning on gloves at the time of surgery. Surgeon A was not allowed to perform cardiac surgery until the epidemic strain was eradicated from his hands. He was required to use an antimicrobial

scrub solution containing chlorhexidine daily for 2 weeks. Sampling was taken after scrubbing and after he had been gloved for 3-4 hours.

**Reviewer's comments:** *CTFA cited this reference to demonstrate that CHG surgical hand scrub could eradicate an epidemic strain of S. epidermidis from a carrier. The study shows that there was eradication of S. epidermidis from the surgical field 24 months after implementation of the infection control measures described. However, this can not be directly attributed to the use of CHG.*

*The findings suggest that the common-source outbreak of infections among cardiac surgery patients was due to carriage of a strain S. epidermidis on the hands of a cardiac surgeon. The epidemic strain may come from a variety of other sources: endogenous flora of the patient, members of the cardiac team and technicians, surgical equipment, suction pump, operating room air, blood or other fluids, contaminated prosthetic valves, contaminated disinfectants, etc...However, this was not evaluated. The mechanism by which Surgeon A contaminated the operative field was not determined. Surgeon A was advised not to add mineral oil to his hands. Since the epidemic strain was isolated from blood cultures after the surgery, it was concluded that contamination may have resulted from glove tears during the surgery. However, this was not documented. Other factors that may have been responsible for the sudden increase in infections caused by the epidemic strain were also not determined. Further, details about the use of chlorhexidine gluconate as a surgical hand scrub were not provided. It is also not clear what if any infection control measures for other staff were instituted.*

**3. Butz, AM, Laughon BE, Gullette DL, Larson EL. "Alcohol-impregnated wipes as an alternative in hand hygiene." Am J Infect Control 1990 (18):70-6.**

This article presents data that compare the immediate antimicrobial effectiveness of four handwash products for healthcare professional use, including a 30% ethyl alcohol-impregnated hand wipe, after extended use of 15 handwashes per day for 5 consecutive days to determine if alcohol-impregnated hand wipes are an acceptable alternative to soap-and-water handwashing.

**DESIGN & METHODS:** A sample of 48 healthy adult volunteers who had no history of allergies, sensitivity to soap, eczema, psoriasis, or other skin diseases and who reported no current oral or topical antibiotic use was recruited. Three days before the testing period all subjects were provided with a mild nonmedicated liquid soap. Subjects were instructed in a standardized 15-second handwash technique. All subjects were assigned by means of block randomization to one of the four handwash products for healthcare professional use: (1) ethyl alcohol-impregnated hand wipes, 30% w/w plus emollients (alcohol wipes), (2) a liquid detergent base that contained 1% triclosan (TCS), (3) a liquid detergent base containing 4% chlorhexidine gluconate (use of this product was not as directed i.e., a 15-second was used), and (4) nonmedicated soap. The handwashing protocol was adapted from the ASTM method 1174-87 for healthcare personnel handwashes. Microorganisms of the hands were assayed by means of a modification of the glove juice technique. Each subject inserted the dominant hand into a sterile

polyethylene bag that contained 50 mL sterile sampling solution (sterile distilled water containing per liter: lecithin, 20 gm; sodium thiosulfate, 6 gm; sodium oleate, 6 gm; protease peptone, 1 gm; and Tween 80, 50 mL, pH 7.2 to 7.4). Colony-forming units (CFUs) were counted, and total CFUs counts per hand were calculated and compared across product formulations. Sampling of the hands were assayed four times during the study: immediately before the test period after a brief handwash with control soap (baseline); after the first and last handwash on the first testing day, and after the last handwash on the last testing day.

**RESULTS:** The baseline mean log CFU counts from the hands of the 12 subjects in each treatment group ranged from 5.37 to 6.01 with no significant differences among groups (F=2.55, p=0.07). After the first handwash on day 1, mean log changes compared with baseline for each of the four treatment groups were alcohol wipe, + 0.008; TCS, - 0.151; CHG, +0.127; and control, +0.289. These changes were not significantly different among all four groups (F=0.254, p=0.86). By the end of test day 5 (total 15 handwashes), TCS and CHG products produced significant reductions in aerobic counts compared with the control (TCS, -1.523; CHG, -2.006; and control, -0.031), whereas results among subjects who used the alcohol wipes were not significantly different from those of the subjects who used the control soap (F=4.14, p=0.06). TCS was associated with significantly greater CFU reductions compared with the alcohol wipe (F=25.5, p=0.0005), and CHG was associated with significantly greater reductions than was TCS (F=5.79, p=0.02).

Table 1. Mean log counts ( $\pm$  SD) from hands of 48 subjects among the four treatment groups (handwash products for health care personnel)

Active Ingredient	Baseline	After one wash (day 1)	After 15 washes (day 1)	After 75 washes (day 5)
Alcohol wipe	5.754 (0.425)	5.762 (0.525)	5.978 (0.348)	5.719 (0.353)
Triclosan	6.011 (0.471)	5.860 (0.553)	6.379 (0.530)	4.488 (0.728)
Chlorhexidine	5.760 (0.726)	5.887 (0.470)	5.157 (0.569)	3.754 (0.702)
Control	5.367 (0.540)	5.656 (0.786)	5.354 (0.428)	5.336 (0.515)
ANOVA comparing The four treatment Groups at each interval	F= 2.55 p = 0.07	F = 0.254 p = 0.86	F = 15.38 p = <0.0001	F = 24.17 p = 0.0001

**Reviewer's comments:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows is that the CHG did not meet the required log reduction or the 6-hr persistence.

*The authors concluded that alcohol wipes are an acceptable alternative to soap-and-water handwashing in nonacute healthcare settings. There were no significant differences among the treatment and control groups. Immediately after the first wash none of the four groups met the 1-log reduction. It wasn't until after 15 washes that the*

*TCS and CHG meet a 1-log reduction. Thirty percent ETOH is not recognized as an effective antiseptic. The study contained a small sample size of subjects. Demographics and disposition of the subjects were not provided. Washout period was only for 3 days. As recommended by the TFM, washout period should be for at least two weeks prior to sampling the first baseline. The study was not blinded. While, neutralizers were in the sampling solution, there was limited description of their use. No details about neutralizer validation were provided. Overall, the information gathered from this study focused mainly on promoting the use of alcohol wipes. The study was not designed to demonstrate a correlation between infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

4. **Connell, JF and Rousselot, LM. "Povidone-iodine: Extensive surgical evaluation of a new antiseptic agent." Am J Surg 1964 (108):849-55.**

This article evaluated the use of iodine, complexed with polyvinyl-pyrrolidone (PVP), in the operating room, ward and burn research laboratory.

**DESIGN & METHODS:** Povidone-iodine is available in a number of forms. Those which are examined in this study were the aerosol spray, surgical scrub, and the liquid antiseptic solution. Three hundred forty-five patients were included in the study: 70 subjects had burn wounds, 125 subjects had ulcers, 150 patients were preoperative patients, and 50 subjects were used for surgical scrub studies. The available iodine for the product varied from 0.5% in the spray, 0.75% in the surgical scrub, to 1.0% in the antiseptic solution.

The three forms of povidone-iodine were used in various procedures as follows: Aerosol Spray: aerosol was sprayed onto the skin over the area selected for the incision. After one or two spray applications the antiseptic was allowed to dry for 4 minutes. Antiseptic Solution: solution was applied as a skin preparation in the treatment of open wounds. Solution was applied full strength as a wet compress or by instillation every 4 hours via a catheter inserted into the dressing. Surgical Scrub: subjects washed their hands for 4-minute periods eight to ten times daily while performing their assigned duties about the wards and laboratories. Cultures were taken from fingernail beds and palm surfaces before and after scrubbing, as well as at fifteen minute and one hour intervals after scrubbing. The comparative effectiveness of hexachlorophene to povidone-iodine was also evaluated. Bacterial reduction 4 minute post scrub and one and a half hours postoperative (preoperative) and operating time (gloved hands) were the endpoints used to evaluate bacterial counts. Graft success rates were also assessed.

**RESULTS:** A page was missing from the article. The FDA journal request line was unable to retrieve a copy of the article. There was limited information on the results of the use of the aerosol spray used on infected wounds. Overall, the study reported a decrease in the number and variety of organisms cultured from the unprotected echar surface. The application of povidone-iodine every 4 hours by either aerosol spray or as a wet dressing of antiseptic solution resulted in a marked reduction or organism proliferation in the wounds. In the preoperative procedure, results demonstrated a 98%

bacterial reduction at the 4-minute post application using povidone-iodine versus 96% bacterial reduction using hexachlorophene. Bacterial reduction after 1 ½ hours was 78% using povidone-iodine and 68% using hexachlorophene.

In the surgical scrub procedure, the predominating organisms cultured from the hexachlorophene group and povidone-iodine group were gram negative rods and non-hemolytic *S. aureus*. The povidone-iodine surgical scrub had more effective rate of bacterial reduction and did not require a previous, 72 hour constant use to achieve excellent results. Results of the scrub study demonstrated 98% (less than one log) bacterial reduction at the 4-minute post application using povidone-iodine versus 84% bacterial reduction using hexachlorophene and 88% bacterial reduction at the 1 ½ hour post application using povidone-iodine versus 66% bacterial reduction using hexachlorophene.

*Reviewer's comment: CTFA cited this reference to demonstrate clinical benefit with the use of antimicrobial products in invasive procedures. The study shows that there was a lower incidence of post-operative wound infection with the use of 10% PVP-I antiseptic solution and a 7.5% PVP-I surgical scrub as part of a multifaceted approach to infection control.*

*The study was not blinded. The studies were not considered a well-controlled randomized clinical trial. There was no description on how the patients were cared for after the operation or the health of the patients before under going surgical procedures. No statistical analyses were evaluated in the studies. There were no demographics and disposition of the subjects provided. No description of how bacterial counts were performed. No description of neutralization for surgical scrub studies. No washout period. Povidone-iodine was used in multiple areas of treatment along with other measures. Trial does not provide evidence to show the correlation of clinical outcome of infection rates to the reduction of bacteria on the surgeon's hands. Overall, there was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

- 5. Cremieux, A, Reverdy, ME, Pons, JL, Savage, C, Chevalier, J, Fleurette, J, Mosse, M. Standardized method for evaluation of hand disinfection by surgical scrub formulations. Appl Environ Microbiol 1989;55:2944-2948.**

The objective of the study was to assess the validity of a protocol on the basis of statistical analysis and to compare the two antiseptic scrub formulations (povidone iodine (PVI) and chlorhexidine (CHX)) with each other and with nonmedicated soap (NMS). A standardized protocol for the evaluation of hand disinfection by surgical scrub formulations was applied to volunteers in a multicenter trial.

**METHODS:** Adult volunteers were gathered for each of the three studies (PVI, CHX, and NMS) in seven groups corresponding to distinct centers. All centers were involved in the PVI study (49 subjects, seven groups of 10, 6, 8, 6, 10, 6, and 3 subjects), while one center was missing for the NMS study (41 subjects, six groups of 10, 6, 7, 6, 6, and 6

subjects) and two centers were missing for the CHX study (35 subjects, five groups of 10, 6, 8, 8, and 3 subjects). All subjects were instructed to avoid the use of antiseptics, detergents, and gloves during the experiment. Subjects were not prescreened for an adequate baseline count. The scrubbing procedure involved three daily hand washings occurring on days 2-4 and 2 washings on days 1 and 5. Surviving bacteria were counted daily after being collected in a suitable neutralizing solution. Immediate efficacy (IE 5 minutes after product use), cumulative efficacy (CE after 2<sup>nd</sup> wash on day 5), and remanent effect (RE after last wash on day 5 and after 3 days in eruption) were calculated by reference to the control hand. Hand flora was recovered in a sterile plastic bag containing 400 ml of a neutralizing solution which has previously been demonstrated as convenient for the two scrub formulations and the soap. Five minutes after the end of the scrubbing procedure, the appropriate hand (left hand for control counts and right hand for test formulation) was plunged into the bag and agitated for 5 minutes. The solution was then transferred into a sterile bottle. Samples were placed in 15 ml tryptic soy agar. Colonies were counted after 48 hours of aerobic incubation at 37°C. All counts were conducted in duplicate.

**RESULTS:** Statistical analyses of IE, CE and RE showed significant differences among the three scrub formulations. IEs of PVI and CHX were equivalent and different from IE of NMS; CE and RE of CHX were higher than those of PVI and NMS. Statistical analysis was limited to IE on day 1, CE on day 5 and RE on day 8.

TABLE 2. Results of IE, CE, and RE with three scrub formulations for one group (10 subjects)

Day	Scrub formulation	Control (C1* or Cd*)	Test (T1* or Td*)	IE (C1 - T1; Cd - Td)	CE (C1 - Td)	RE (C1 - Cd)
1	PVI	6.48 ± 0.98*	5.78 ± 1.07	0.70 ± 0.79		
	CHX	6.51 ± 0.58	5.75 ± 0.69	0.76 ± 0.53		
	NMS	6.58 ± 0.58	6.01 ± 0.75	0.57 ± 0.23		
2	PVI	5.69 ± 1.01	5.22 ± 0.81	0.47 ± 0.51	1.26 ± 0.62	0.80 ± 0.28
	CHX	5.44 ± 0.46	4.76 ± 0.54	0.68 ± 0.49	1.75 ± 0.48	1.08 ± 0.50
	NMS	6.23 ± 0.51	5.93 ± 0.41	0.30 ± 0.32	0.65 ± 0.41	0.35 ± 0.45
3	PVI	5.47 ± 0.59	4.95 ± 0.79	0.52 ± 0.58	1.53 ± 0.86	1.01 ± 0.71
	CHX	4.93 ± 0.82	3.66 ± 1.36	1.27 ± 1.19	2.85 ± 1.08	1.58 ± 0.79
	NMS	6.21 ± 0.40	5.86 ± 0.67	0.35 ± 0.48	0.72 ± 0.69	0.37 ± 0.52
4	PVI	5.09 ± 1.03	4.59 ± 0.75	0.50 ± 0.73	1.89 ± 0.78	1.40 ± 0.54
	CHX	5.12 ± 0.76	3.38 ± 1.44	1.75 ± 1.24	3.13 ± 1.22	1.39 ± 0.64
	NMS	6.29 ± 0.39	5.88 ± 0.39	0.41 ± 0.20	0.70 ± 0.45	0.29 ± 0.57
5	PVI	5.50 ± 0.78	5.10 ± 0.77	0.40 ± 0.42	1.39 ± 1.03	0.98 ± 0.97
	CHX	5.06 ± 0.57	4.12 ± 0.45	0.95 ± 0.51	2.39 ± 0.58	1.45 ± 0.61
	NMS	6.31 ± 0.31	5.81 ± 0.66	0.51 ± 0.42	0.77 ± 0.41	0.27 ± 0.47
8	PVI	6.56 ± 0.60	5.63 ± 1.13	0.92 ± 0.76	0.85 ± 1.04	-0.08 ± 0.83
	CHX	6.02 ± 0.38	4.50 ± 0.79	1.53 ± 0.92	2.02 ± 0.86	0.49 ± 0.52
	NMS	6.59 ± 0.42	6.05 ± 0.48	0.54 ± 0.28	0.53 ± 0.43	-0.01 ± 0.56

\* C1, Count obtained on day 1 with the control hand (base line count).  
\* Cd, Count obtained from day 2 to day 8 with the control hand.  
\* T1, Count obtained on day 1 with the test hand.  
\* Td, Count obtained from day 2 to day 8 with the test hand.  
\* Mean ± standard deviation of log<sub>10</sub> number of microorganisms per hand.

TABLE 4. IE, CE, and RE of PVI, CHX, and NMS and comparison by Student's *t* test<sup>a</sup>

Scrub formulation and comparison	No. of subjects	IE (day 1)	CE (day 5)	RE (day 5)	RE (day 8)
PVI	49	0.94 ± 0.57	1.67 ± 0.78	0.99 ± 0.76	0.20 ± 0.74
CHX	35	1.08 ± 0.57	2.42 ± 0.81	1.33 ± 0.62	0.45 ± 0.58
NMS	41	0.62 ± 0.36	0.78 ± 0.55	0.39 ± 0.55	0.06 ± 0.49
NMS < PVI <sup>b</sup>		0.002	0.000	0.000	0.281
NMS < CHX <sup>b</sup>		0.000	0.000	0.000	0.008
PVI < CHX <sup>b</sup>		0.251	0.000	0.024	0.077

<sup>a</sup> Values are means ± standard deviation.

<sup>b</sup> Student's *t* test.

**Reviewer's Comments:** CTFA cited this reference to demonstrate that the products tested could almost meet a 1-log reduction. What the study reported, despite its deficiencies is that the CHG and PVP-I almost came close to meeting the required log reduction. However, other TFM effectiveness endpoints were not addressed.

*This article mainly focused on describing a standardized method for evaluation of hand disinfection by various surgical scrub formulations. The aim of the study was to assess the validity of the protocol on the basis of statistical analysis and to compare the two antiseptic scrub formulations with each other and with the non-medicated soap. The authors concluded based on their analyses of the data that the protocol described may be considered satisfactory for the comparison of scrub formulations because it allows sorting between ineffective, bactericidal, and bactericidal plus remanent scrubs. Their analyses of data indicate that the population size required for further studies aimed at detecting significant differences between surgical scrub formulations could be estimated.*

*There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. The data were generated from a nonrandomized, uncontrolled, and unblinded study. There was no demographics and disposition of the participants provided (ratio of males to females and ages). The study does not provide description of the baseline determination. Normally baseline counts are performed in triplicate (days 1, 3, and 5) using a non-antimicrobial soap. The baseline count of the resident microbial populations is performed to evaluate eligibility of the study, as well as establish baseline values for each subject. Subjects with baseline counts of at least  $1.5 \times 10^5$  organisms per hand are selected to continue the study. This article mentions that the mechanical effect of repeated scrubbing and bactericidal effect of the antiseptics differentially reduced hand flora, but their study was limited to a quantitative evaluation of the bacteria.*

6. **Grinbaum, RS, de Mendonca, JS, Cardo, DM. "An outbreak of handscrubbing-related surgical site infections in vascular surgical procedures." Infect Control Hosp Epidemiol 1995;16:198-202.**

The objective of the study reported in this publication was to investigate an outbreak of surgical site infections in vascular surgery unit related to handscrubbing with non-antimicrobial soap.

**DESIGNS & METHODS:** The study was conducted at a 60-bed unit of vascular surgery, where surgeons performed an average of 30 operations per month at a 1,000-bed tertiary care hospital in Sao Paulo, Brazil. The study included in the case group nine patients who had limb amputations or arterial reconstructions from October 16 through 23, 1992. The study included in the control group patients (two controls for each case) whose operations were performed within 30 days of the outbreak period. Control patients were matched for sex and type operation.

**RESULTS:** Six of nine case patients experienced surgical site infection, as compared with 3 of 18 control patients ( $P=0.026$ ) and 28 of 244 patients in the 9-month pre-epidemic period ( $P=0.0002$ ). Several risk factors were balanced for case and control groups. Factors assessed were American Society of Anesthesiology status, duration of surgery, wound class, emergency status, remote site infections, preoperative length of stay, use of prophylactic antibiotics, and underlying diseases (hypertension and diabetes). Possible common sources also were analyzed. No differences were observed concerning hair removal, preoperative shower, wound dressing, and surgical team present in the operating room.

During the outbreak period, the operating room was not provided with povidone-iodine, used in the hospital for skin cleansing and handscrubbing. Surgeons from all departments, including vascular surgery, used 2% iodine with 70% alcohol for skin cleansing. Surgeons from other departments used this iodine solution for hand scrubbing, but the vascular surgeons used plain soap for handscrubbing. No increases in surgical site infection rates were reported in other services. Comparison of case and control groups for handscrubbing was statistically significant ( $P<0.00001$ ). After reinstatement of povidone-iodine, only one surgical site infection was diagnosed in 13 vascular procedures. Overall, the conclusions drawn by the authors based on their analyses of data indicate that they could not demonstrate definitely that scrubbing with plain soap was related to surgical site infections, but they found a strong suggestion of this association.

*Reviewer's comments: CTFA cited this reference to demonstrate clinical benefit with the use of antimicrobial products in invasive procedures. What the study reports, despite its deficiencies is that the use of PVP-I surgical scrub in a vascular surgery unit controlled an outbreak of surgical site infections.*

*Basically the data presented is not able to demonstrate definitely that scrubbing with plain soap was related to surgical site infections. There were difficulties in the design of a case-control study in this outbreak because a small number of operations were studied and all patients were exposed to the suspected risk factor. Because of the unblinded nature of the study, bias cannot be ruled out. There were other risk factors to take in for consideration such as the presence of a particular surgeon, aseptic techniques, sterilization techniques, type of wound dressing applied etc... Overall, there was no valuable information regarding the correlation of infection rates to the reduction of bacteria.*

7. **Hobson, DW, Woller, W, Anderson, L, and Guthery, E. "Development and evaluation of a new alcohol-based surgical hand scrub formulation with persistent antimicrobial characteristics and brushless application." Am J Infect Control 1998 (26):507-512.**

The objective of this study was to: (1) evaluate the *in vivo* antimicrobial efficacy of the new formulation (70% alcohol) in standardized handwashing tests recommended by the FDA for evaluation of new healthcare antiseptic handwashing products with 7.5% povidone iodine (PVPI) and 4% CHG as comparison control formulations and (2) investigate the feasibility of use of the formulation without a brush, either by using a sponge or the hands alone.

**DESIGN & METHODS:** The study was conducted in accordance with the design, procedures, and methods described in the 1994 Tentative Final Monograph (TFM) for healthcare antiseptics. The human subjects included 90 subjects (18 subjects per treatment group; 5 treatment groups) who met the pre-study hand microbe count criteria as required by the TFM criteria. The relative efficacy of a new alcohol-based surgical scrub formulation that contains ingredients that provide surfactant and antimicrobial persistence characteristics was compared with that of commercial 4% CHG and 7.5% PVPI formulations with use of human subjects. Hand antimicrobial count sampling was performed by using standardized "glove juice" methodology.

**RESULTS:** The efficacy and persistence results of the new formulation showed statistically significant improvement over both CHG and PVPI at a substantially lessened scrub time (3 minutes). In addition, use of the new formulation without a scrub brush produced results statistically similar to 3-minute applications with either a brush or a sponge.

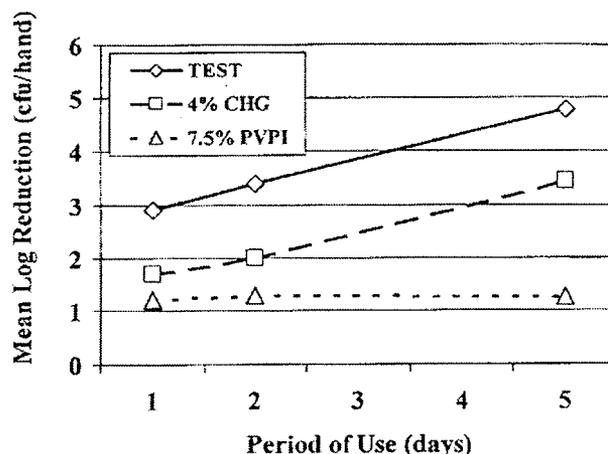
**Table 1.** Summary of hand count data for all treatments

Treatment	1 min	SD	3 h	SD	6 h	SD
Day 1						
7.5% PVPI	1.2	0.68	0.71	0.66	-0.21	0.82
4% CHG	1.68	0.85	1.08	0.51	0.86	0.88
TEST (Brush)	2.86cp	0.54	2.05cp	0.66	1.80cp	0.87
TEST (Sponge)	2.35cp	0.75	1.99cp	0.83	1.33p	0.85
TEST (Hands)	2.90cp	0.84	1.58cp	0.82	1.94cp	0.83
Day 2						
7.5% PVPI	1.28	0.62	0.65	0.62	0.13	1.01
4% CHG	1.99	1.69	1.1	0.62	1.49	1.20
TEST (Brush)	2.99p	0.62	2.74cp	0.65	3.09cp	1.50
TEST (Sponge)	2.78cp	0.59	3.27cp	1.17	2.54cp	0.66
TEST (Hands)	3.40cp	0.80	3.13cp	1.12	2.70cp	0.75
Day 5						
7.5% PVPI	1.27	0.88	0.69	0.56	-0.04	1.08
4% CHG	3.43	1.26	2.81	1.06	2.75	1.25
TEST (Brush)	4.63p	1.32	4.27cp	1.30	4.32cp	0.96
TEST (Sponge)	4.46p	1.48	3.84cp	1.66	3.32p	1.07
TEST (Hands)	4.78p	1.50	4.60cp	1.10	3.22p	1.17

All values shown are mean logarithmic reductions from baseline counts.

N = 12 hand microbial values per treatment time point

p: significantly greater logarithmic reduction ( $P < .05$ ) than the 7.5% PVPI formulation; c: significantly greater logarithmic reduction ( $P < .05$ ) than the 4% CHG formulation.



**Fig 2.** Contrasting mean logarithmic reduction results in (CFU) per hand at 1 minute after applications of the 7.5% PVPI, 4% CHG, and TEST formulations on study days 1, 2, and 5 according to the manufacturer's recommended modes of application. Note the lack of persistence observed for the 7.5% PVPI formulation in contrast with the persistence shown by the other 2 formulations.

**Reviewer's comments:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the CHG met all of the TFM endpoints and PVP-I met the required 1-log reduction and the 6-hr persistence.

The study finding showed that the mean logarithmic baseline values for all treatment groups ranged between 5.99 and 6.16 CFU/hand, and no statistically significant differences ( $P \leq .05$ ) existed between groups. All three types of applications of the TEST formulation met the microbial reduction criteria required under the TFM for a surgical hand scrub. The authors concluded, that the new alcohol-based formulation used in this study demonstrates promise as a new surgical hand scrub formulation with antimicrobial and use characteristics that are significantly improved over current CHG and PVPI formulations. However, there was lack of detail and small sample size. The study does not provide description of the baseline determination. Normally baseline counts are performed in triplicate (days 1, 3, and 5) using a non-antimicrobial soap. The baseline count of the resident microbial populations is performed to evaluate eligibility of the study, as well as establish baseline values for each subject. Subjects with baseline counts of at least  $1.5 \times 10^5$  organisms per hand are selected to continue the study. This information is useful in that, the use of alcohol formulated leave-on surgical hand scrub drug products are being used as an alternative to traditional surgical hand-scrubbing. This study was not designed to demonstrate a correlation between the numerical reductions of bacteria and reduction in hospital infection rates.

8. **Jackson, FE. "The utilization of povidone-iodine in the prevention of neurosurgical infections." In: Polk HC Jr, Ehrenkranz NJ , eds. Therapeutic Advances and new Clinical Implications: Medical and Surgical Antisepsis with Betadine Microbicides. Yonkers , NY: Purdue Frederick, 1972:79-86.**

This 1972 article discusses povidone-iodine used by the military, in Vietnam and in the United States on a large number of neurosurgical operations. Povidone-iodine has been used exclusively for preoperative scrubbing of the hands of the surgeons (Betadine Surgical Scrub), preparation of the patient's skin prior to surgery (Betadine Solution), and postoperatively to cover the wound (Betadine-soaked dressing).

**DESIGN & METHODS:** Three hundred ninety three neurosurgical patients were included in the case series. Prior to a scheduled craniotomy, the patient's hair was shampooed with Betadine Shampoo. The hair was clipped the evening preceding the craniotomy and the scalp again washed with Betadine Solution, which was blotted dry. Betadine Surgical Scrub was used for scrubbing surgeons' hands and was not rinsed off following the 10-minute scrub period but is blotted dry with sterile towels prior to the surgeon donning the gown and gloves. The patient's scalp was prepped with Betadine Surgical Scrub and Solution, and the operation was performed. Following the operation, a Telfa strip soaked in Betadine Solution was placed over the incision and covered with a sterile gauze dressing.

**RESULTS:** The causative organism in the majority of the neurosurgical infections was *Staphylococcus aureus*. There was a positive correlation between the duration of an operation and the number of infections. Any surgical technique which would materially decrease the exposure time of the wound to aerial contamination would reduce infections. There have been no infections in any of these neurosurgical cases operated upon in the operating room. In 393 neurological operations performed from January 1, 1968, through March 10, 1971 there was only a single surgical infection, an infection rate of 0.254%.

**Reviewer's comment:** *CTFA cited this reference to demonstrate clinical benefit with the use of antimicrobial products in invasive procedures. What the study reports, despite its deficiencies is that there was a lower incidence of infection rate of 0.254% after 393 neurological operations using a 7.5% PVP-I formulation for surgical scrubbing and preoperative preparation as part of a multifaceted approach to infection control.*

*There were no statistical outcomes (P values) and no demographics and disposition of the subjects provided. There were no descriptions on how the patients were cared for after the operation or the health of the patients before under going surgical procedures. PVP-I was used in a multifaceted approach to antisepsis. Therefore, the effectiveness of PVP-I as a surgical scrub cannot be discerned. The authors provide no discussion of what infection rates for neurosurgeries are.*

9. **Kundsin, RB and Walter, CW. "The surgical scrub-practical consideration." Arch Surg 1973 (107):75-7.**

The objective of this study is to compare two surgical hand scrubs, hexachlorophene detergent (pHisoHex) and povidone-iodine (Betadine) under simulated conditions.

**DESIGN & METHODS:** There were 30 high school senior participants in a summer program. Twenty boys and ten girls aged 15 to 17 years participated, and of these, 26, used both scrubs. The method consisted of a prescribed exposure to the preparation under test, using a prescribed number of strokes with a nylon bristled surgeon's brush to skin surfaces, nails, and the subungual spaces. A 4-minute scrub with hexachlorophene detergent (pHisoHex) and 6-minute scrub with povidone-iodine (Betadine) were performed. All cultures were made in duplicate, 1 ml of four dilutions ( $10^0$ ,  $10^{-1}$ ,  $10^{-2}$ , and  $10^{-3}$ ) of the fluid collected from the interior of the glove to ensure a good quantitative bacterial evaluation. Plates containing between 30-300 bacterial colonies were considered valid.

**RESULTS:** Comparison of the median counts at all test times show the same trend as shown in the Table 1 below. The median of prescrub bacterial counts was very close in all the tests. The immediate postscrub count is lower for the povidone-iodine than for the

	Hexachlorophene Detergent		Povidone-Iodine	
	F (10)	M (20)	F (8)	M (17)
Prescrub	$3 \times 10^4$	$3 \times 10^4$	$4 \times 10^4$	$4 \times 10^4$
Postscrub	$6 \times 10^4$	$8 \times 10^4$	$8 \times 10^4$	$4 \times 10^4$
1 hr postscrub	$3 \times 10^4$	$3 \times 10^4$	$2 \times 10^4$	$2 \times 10^4$

	Hexachlorophene Detergent		Povidone-Iodine	
	F (9)	M (20)	F (7)	M (17)
Immediately following scrub	66	63	95	88
1 hr after scrub	97	96	88	89

Time, min	Organisms/ml	
	H <sub>2</sub> O, 100 ml	0.1% Sodium Thiosulfate (100 ml) in Saline
0	1,850	1,850
30	1,850	1,900
60	1,600	2,000

hexachlorophene detergent. The povidone-iodine count remained within one logarithm of the original prescrub counts in males and rose in the females, indicating bacterial regeneration. Table 3 is neutralizer validation data.

*Reviewer's comment: CTFA cited this reference to demonstrate that the products tested could almost meet a 1-log reduction. What the study shows, despite its deficiencies is that the PVP-I almost met the required initial 1-log reduction. Other TFM effectiveness endpoints were not addressed.*

*The authors concluded that iodine preparation produced a greater immediate reduction in bacterial count than the hexachlorophene preparation. However, this advantage was lost after one hour. The bacterial count inside the gloves following the iodine preparation increased after 1 hour and was higher than the count 1 hour following the hexachlorophene preparation. There are some limitations to this study. No statistical evaluation (p values). The study contained small sample size of subjects. Washout period was only for 3 days. TFM requires 2 weeks are required. No demographics and disposition of the subjects are provided. No randomization and blinding of subjects. The study provided only a single baseline determination. Normally baseline counts are performed in triplicates (days 1, 3, and 5) using a non-antimicrobial soap. The baseline count of the resident microbial populations is performed to evaluate eligibility of the study, as well as establish baseline values for each subject. Subjects with baseline counts of at least  $1.5 \times 10^5$  organisms per hand are selected to continue the study. There was limited information on the description on how the neutralizers were used. No description about neutralization validation was provided. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

**10. Larson, EL, Eke, PI, and Laughon, BE. "Efficacy of alcohol-based hand rinses under frequent-use conditions." Antimicrob Agents Chemother 1986 (30): 542-544.**

This article reports the results of in vivo tests of the antimicrobial efficacy and user acceptance of five hand washing products after extended use, 15 hand washes per day for 5 consecutive days.

**DESIGN & METHODS:** Fifty volunteers randomly assigned to one of five hand washing agents (10 subjects per agent)--a nonantiseptic liquid soap (control), an antiseptic hand rinse containing 60% isopropyl alcohol (IPA) with emollients (Alc A; Calstat), an antiseptic hand rinse containing 70% IPA and 0.5% chlorhexidine gluconate with emollients (Alc B; Hibistat), an antiseptic containing 4% chlorhexidine gluconate and 4% IPA (CHG), and 70% IPA (Hibiclens)--washed their hands 15 times per day for 5 days under supervision by using a standardized technique and measured amounts of test agent. Microbiologic samples of hand flora were obtained at baseline and after hand washes 1 and 15 on test days 1 and 5.

**RESULTS:** After the initial hand wash there were significant reductions over base line in aerobic and anaerobic log CFU among those using Alc A, CHG, and IPA. By the end of the first day of hand washing (15 washes), there were 2-log or greater reductions in aerobic counts among subjects using all antiseptics, but no significant reductions in controls. By the end of day 5, all agents produced significant reductions in aerobic (P = 0.0002) and anaerobic (P = 0.002) counts over control soap. Subject assessment of effects of hand washing on the skin and overall satisfaction varied significantly by product (P = 0.04 and 0.05, respectively).

TABLE 1. CFUs from hands in five treatment groups

Type of bacteria	Treatment group	Base line	Log <sub>10</sub> CFU (% reduction)*			
			Day 1		Day 5	
			After hand wash 1	After last hand wash	After hand wash 1	After last hand wash
Aerobes	Control	7.00	6.41 (8.4)	6.19 (11.6)	6.67 (4.7)	6.31 (9.9)
	Alc A	6.25	4.91 (21.4)	2.63 (57.9)	3.04 (51.4)	3.24 (48.2)
	Alc B	6.91	6.11 (11.6)	3.47 (49.8)	3.89 (43.7)	3.03 (156.2)
	CHG	7.02	5.93 (15.5)	4.29 (38.9)	3.89 (44.6)	2.68 (61.8)
	IPA	7.09	5.89 (16.9)	4.26 (39.9)	5.11 (27.9)	3.92 (44.7)
Anaerobes	Control	6.88	6.38 (7.3)	5.96 (13.4)	6.26 (9.0)	6.18 (10.2)
	Alc A	6.70	5.44 (18.8)	3.77 (43.7)	4.14 (38.2)	3.26 (51.3)
	Alc B	6.24	6.13 (1.8)	3.43 (45.0)	4.97 (20.4)	2.79 (55.3)
	CHG	6.66	5.64 (15.3)	4.49 (32.6)	5.17 (22.4)	3.83 (42.5)
	IPA	7.07	6.05 (14.4)	5.62 (20.5)	5.31 (24.9)	4.49 (36.5)

\* Percent reductions from base line calculated as (base line count - test count)/base line count} x 100.

**Reviewer's comments:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the CHG and IPA met the required initial 1-log reduction. Other TFM effectiveness endpoints were not evaluated.

The authors concluded that alcohol-based hand rinses are highly efficacious, and such products are recommended as a health care personnel hand wash, particularly when sink and running water are inaccessible. However, there were limitations with the study. The study contained small sample size of subjects. The scrub patterns are different i.e., 15 scrubs in one day versus 11 over 5 days in the TFM. No demographics and disposition of the participants provided. Only a single baseline count was determined in the study. Normally baseline counts are performed in triplicates (days 1, 3, and 5) using a non-antimicrobial soap. The baseline count of the resident microbial populations is performed to evaluate eligibility of the study, as well as establish baseline values for each subject. Normally those subjects with baseline counts of at least  $1.5 \times 10^5$  organisms per hand are selected to continue the study. No description about neutralization validation was provided. No description of whether subjects on antibiotics and/or oral contraceptives were included in the study. Washout period was only for three days (normally 2 weeks are required). There was no description of whether sampling was

*randomized. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

**11. Larson, EL, Eke, PI, and Laughon, BE. “Effect of sampling time on bacterial yield from the hands.” Am J Infect Control 1987 (15):272-3.**

The objective of this study was to evaluate the effect of stripping (sampling) time on microbial yield from the hands.

**DESIGN & METHODS:** Forty healthy adult volunteers were assigned by randomization to one of four handwashing products, 10 subjects per product: a nonmedicated liquid soap (control); an antiseptic containing 4% chlorhexidine gluconate, and two alcohol-based hand rinses (one of the alcohol rinse contains 0.5% chlorhexidine gluconate). Within each of the four groups, subjects were assigned by randomization to a 15-second or a 3-minute stripping time. Fifteen scrubs per day for 5 days were conducted. For each of the subjects, logarithms of the differences in microbial counts from baseline sampling to samples collected after one and 15 consecutive handwashes were calculated. A Tukey one-way analysis of variance was used to compare these differences for each product, between the group whose hands were sampled for 15 seconds and the group whose hands were sampled for 3 minutes.

**RESULTS:** Initial aerobic log CFU from hands of the 40 subjects ranged from 5.9 to 8.5. There was no significant differences in the mean reductions in log CFU among subjects whose hands were sampled for 15 seconds or 3 minutes after one handwash ( $p = 0.45$ ) or after 15 washes ( $p = 0.49$ ) shown in the table below.

Table 1. Reductions from baseline in mean aerobic CFU (log 10) by handwashing agent and sampling time

	CHG		AlcA		AlcB		Control	
	15 sec	3 min	15 sec	3 min	15 sec	3 min	15 sec	3 min
Baseline counts	6.63	6.20	6.80	7.06	6.81	6.41	6.63	6.18
Reduction after 1 handwash	1.13	0.71	1.52	1.50	0.63	0.84	0.45	0.08
Reduction after 15 handwashes	1.78	1.45	2.60	2.83	2.04	2.40	0.78	0.29

No significant differences in counts between the two sampling times were found after one handwash ( $p=0.45$ ) or after 15 handwashes ( $p=0.49$ ).

**Reviewer’ comment:** *CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the CHG and IPA met the required 1-log reduction. However, other TFM endpoints were not evaluated.*

*The authors concluded that the difference in bacterial harvest from the skin of the hands with sampling time longer than 1 minute probably adds little information of clinical importance and stated that a 1-minute sampling should be sufficient for most studies.*

*The study contained small sample size of subjects. There was no exclusion of subjects taking antibiotics and/or oral contraceptives. The study did not provide enough details regarding the use of neutralizers. No description about neutralization validation was provided. It does not appear that the products were used as directed. Hibiclens currently has two 3-minute scrubs for directions. No demographics and disposition of the participants provided. The study was not blinded. No description of washout period was conducted. Hand sampling was not randomized. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

**12. Larson, EL and Laughon, BE. “Comparison of four antiseptic products containing chlorhexidine gluconate.” Antimicrob Agents Chemother. 1987 Oct;31(10):1572-4.**

The purpose of this study was to compare the antimicrobial efficacies and subject acceptance of four formulations of chlorhexidine gluconate (CHG) for handwashing under frequent-use conditions.

**DESIGN & METHODS:** Fifty volunteers were assigned by block randomization to one of five products: one of two liquid detergents containing 4% CHG, a liquid detergent containing 2% CHG, a foam containing 4% CHG, and a non-antiseptic soap (control). Subjects washed their hands by a standardized 15-second wash technique 15 times per day for 5 days. A 7-point scale was used by subjects to assess the appearance, intactness, moisture content, and sensation of the skin on their hands at baseline and again after 5 days of handwashing. Analysis of variance was used to test the significance of differences in log CFU between the five treatment groups at baseline, on days 1 and 5 for each product.

**RESULTS:** Mean CFU counts in all five treatment groups decreased at every testing interval, although reductions were very small in the control group as shown in the table below. After days 1 and 5 of handwashing, there was a significant reduction in log CFU for subjects using all four CHG-containing products compared with subjects using control soap and for subjects within each group after days 1 and 5 compared with the base-line CFU counts (all P less than 0.05). There were no significant differences between the four CHG products at any testing time.

Table 1. Results of handwashing with four CHG-containing products

Product Group	Base-line CFU	Change in mean log CFU on hands after:			
		Initial wash	8 Washes	15 Washes	5 Days
CHG4	5.94 + 0.51 <sup>a</sup>	-0.34	-0.76	-1.31	-2.15
CHG2	5.67 + 0.54	-0.07	-0.62	-1.14	-1.80
Foam	5.88 + 0.49	-0.20	-0.88	-1.24	-1.83
CHG4a	6.28 + 0.60	-0.88	-1.16	-1.64	-2.36

Control	5.89 + 0.47 (P=0.09 <sup>b</sup> )	-0.11 (P=0.92 <sup>b</sup> )	-0.59 (P=0.43 <sup>b</sup> )	-0.85 (P<0.05 <sup>c</sup> )	-0.59 (P<0.001 <sup>c</sup> )
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<sup>a</sup> Mean + standard deviation.

<sup>b</sup> Analysis of variation, comparing difference between treatment groups at each sampling time.

<sup>c</sup> Difference between control and other products statistically significant, but no significant difference between the four antiseptic products.

**Reviewer’s comment:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the CHG met the required log reduction after 15 washes. Other TFM effectiveness endpoints were not evaluated.

*The author concluded that the four tested formulations are satisfactory for clinical use. Although, these products are considered satisfactory using in vivo test methods, other studies such as in vitro (MIC and time kill) should be conducted also. In evaluating this study there were several limitations to the study. No demographics and disposition of the participants were provided. The study was not blinded. The study contained small sample size. Subjects using antibiotics and/or oral contraceptives were not excluded. Limited information regarding the use of neutralizers. Handwashing techniques were not described in detail. There was only a 3-day washout period in this study (TFM requires 2 week washout period). Only a single baseline count was determined in the study. Normally baseline counts are performed in triplicate (days 1, 3, and 5) using a non-antimicrobial soap. The baseline count of the resident microbial populations is performed to evaluate eligibility of the study, as well as establish baseline values for each subject. Subjects with baseline counts of at least  $1.5 \times 10^5$  organisms per hand are selected to continue the study. The subjects were instructed to scrub for 15 seconds, however the products are labeled for significantly longer scrubs. The study was not designed to provide information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

**13. Larson, EL, Butz, AM, Gullette, DL, Laughon, BA. “Alcohol for surgical scrubbing?” Infect Control Hosp Epidemiol 1990 (11):139-143.**

The purpose of the study was to compare the immediate and sustained antimicrobial effectiveness and user acceptability of surgical scrub preparations containing either alcohol, triclosan, chlorhexidine gluconate or povidone iodine.

**DESIGN & METHODS:** Sixty healthy adult volunteers were selected who were not receiving systemic or topical antibiotics, and who reported no history of skin disease or sensitivity to soaps. The subjects were assigned by block randomization (12 subjects per group) to use one of the following formulations: 70% ethyl alcohol with 0.5% chlorhexidine gluconate (ALC); a liquid detergent base containing 1% triclosan (TRI); a liquid detergent base containing 4% chlorhexidine gluconate (CHG); a liquid detergent base containing 7.5% povidone-iodine (PI); or a nonantimicrobial liquid soap (control).

Using a standard scrub protocol (ASTM method), subjects performed a 5-minute surgical scrub daily for 5 consecutive days. Hand cultures were obtained at baseline and on test days 1 and 5 immediately after the scrub and following four hours of gloving.

**RESULTS:** After the first and last scrubs, ALC, CHG and PI resulted in significant reductions in colonizing flora when compared to the control. Additionally, by day 5 ALC was associated with an almost 3-log reduction as compared to an approximate 1.5-log reduction for CHG and PI and less than a 1-log reduction for TRI and the control (p = .009). After 4 hours of gloving on both days 1 and 5, microbial counts on hands of subjects using ALC, TRI and CHG were significantly lower than counts for the control (p less than .001), whereas there was no significant difference in counts between the PI and control groups (p = .41). None of the test products exceeded baseline on days 1 and 5. Skin assessment by study subjects rated products from least to most harsh as follows: control, TRI, CHG, ALC and PI p = .00001).

Mean Log Count ( $\pm$ Standard Deviation) From Hands of 60 Subjects Using Surgical Scrub Protocol					
Active Ingredient	Baseline	After Scrub 1	After 4 hrs Gloving Day 1	After Scrub 5	After 4 hrs Gloving Day 5
Alcohol	6.04 (0.49)	4.06 (1.20)	4.83 (1.10)	3.19 (0.72)	3.62 (1.34)
Triclosan	5.84 (0.67)	5.28 (0.58)	5.39 (0.96)	5.28 (0.54)	5.69 (0.44)
Chlorhexidine	5.80 (0.58)	4.94 (0.95)	5.21 (1.10)	4.24 (0.63)	4.04 (1.11)
Povidone-Iodine	6.18 (0.39)	5.10 (0.47)	5.91 (0.46)	4.61 (0.49)	5.68 (0.31)
Control	6.07 (0.57)	5.68 (0.42)	6.06 (0.47)	5.65 (0.46)	6.29 (0.51)
ANOVA 5 groups	F:104 p .39	6.89 <.001	4.13 <.001	32.9 <.0001	23.3 <.0001

**Reviewer's comment:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the CHG met the required initial 1- log reduction. Other TFM effectiveness endpoints were not evaluated.

The authors concluded that alcohol could be an efficacious and acceptable alternative for surgical scrubbing. There were limitations in the studies. There were limited description regarding the use of neutralizers in the samples. No description about neutralization validation was provided. No exclusion of subjects using oral contraceptives. No demographics and disposition of the participants provided. The study was not blinded. The study contained small sample size of subjects. Only a 3-day washout period was conducted. Only a single baseline count was determined in the study. Normally baseline counts are performed in triplicates (days 1, 3, and 5) using a non-antimicrobial soap. The baseline count of the resident microbial populations is performed to evaluate eligibility of the study, as well as establish baseline values for each

*subject. Normally those subjects with baseline counts of at least  $1.5 \times 10^5$  organisms per hand are selected to continue the study. Hand sampling was not randomized. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

**14. Larson, E and Bobo, L. "Effective hand degerming in the presence of blood."  
J Emerg Med 1992 (10):7-11.**

This study evaluated the effect of blood on the antimicrobial activity of several agents used for handwashing.

**DESIGN & METHODS:** Seventy-one healthy adult volunteers without a history of allergies or sensitivity to soaps or detergents, eczema, psoriasis, or other skin diseases were recruited primarily from among staff and students at the study institution. Subjects were required to have intact skin and not be receiving systemic antibiotic therapy within 30 days prior to testing. Subjects used one of six products: 70% isopropyl alcohol [IPA]; a liquid hand rinse containing 70% ethyl alcohol and 0.5% chlorhexidine gluconate [EA]; a detergent containing 7.5% povidone-iodine [PI]; a detergent containing 4% chlorhexidine gluconate [CHG]; a nonantimicrobial soap; and a control group that used no product in two tests: with and without 1.2 mL of dried sterile sheeps' blood on the hands. Hands were cultured at four intervals: before and after application of the test product, with or without blood on the hands. Prior to baseline sampling, subjects performed a brief handwash with nonantimicrobial liquid soap to remove dirt and transient contaminants. A 15-second hand wash was used. A Student's t-test was used to assess the significance of differences between  $\log_{10}$  reductions in CFU on each subject's hands in the presence and absence of blood.

**RESULTS:** In the presence of blood, the two alcohol products (IPA and EA) resulted in significantly greater reductions in numbers of colony-forming units than other products (P less than 0.001). When no blood was present, IPA was associated with significantly greater reductions, whereas soap and control groups had significantly lower reductions (P = 0.008).

Table 1. Mean Log<sub>10</sub> Counts on Hands by Handwashing Product, with and without Blood on the Hands (n = 12 subjects per product)

Handwashing product	Mean Log Counts (± standard deviation)					
	With Blood		Before-After Log change	Without Blood		Before-After Log change
	Before wash	After wash		Before wash	After wash	
70% isopropyl alcohol	5.83 (.44)	4.97 (.66)	-.86*	5.91 (.58)	5.04 (.72)	-.87
70% ethyl alcohol/0.5% chlorhexidine gluconate	5.52 (.66)	4.62 (.85)	-.90*	5.44 (.43)	5.06 (.45)	-.38†
Detergent with 7.5% povidone-iodine	5.76 (.59)	5.50 (.72)	-.26	5.52 (.46)	5.31 (.44)	-.21
Detergent with 4% chlorhexidine gluconate	5.54 (.76)	4.89 (.57)	-.65	5.32 (.49)	4.75 (.63)	-.57
Non-antimicrobial liquid soap	5.97 (.36)	5.65 (.34)	-.32	5.68 (.50)	5.75 (.48)	+.07†
No soap (control)	5.49 (.43)	5.32 (.46)	-.17	5.44 (.49)	5.34 (.42)	-.10

\*Significantly greater reductions than with other products (P < 0.001).

†Significantly greater reductions with blood on hands than without blood (P < 0.01).

*Reviewer's comment: CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. Other TFM effectiveness endpoints were not evaluated.*

*The authors concluded that hands were effectively degermed with a variety of products in the presence of blood, and that alcohols give greater initial reductions in colonizing flora. They stated that this was of particular relevance in emergency situations during which contamination with blood is likely and handwashing facilities are inaccessible. However, the initial reduction showed less than 1-log reduction. Only a single baseline count was determined in the study. Normally baseline counts are performed in triplicate (days 1, 3, and 5) using a non-antimicrobial soap. The baseline count of the resident microbial populations is performed to evaluate eligibility of the study, as well as establish baseline values for each subject. Normally those subjects with baseline counts of at least 1.5 x 10<sup>5</sup> organisms per hand are selected to continue the study. Validation of neutralization studies would have been desirable as required by the TFM. No description about neutralization validation was provided. There was no exclusion of subjects using oral contraceptives as required by the TFM. The study contained a small sample size of subjects. There was no randomization of hand sampling. There was no blinding of test formulations. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

15. **Larson, EL, Aiello, AE, Heilman, JM, Lyle, CT, Cronquist, A, Stahl, JB, Della-Latta, P. "Comparison of different regimens for surgical hand preparation." AORN J 2001 (73):412-432.**

The objective of this clinical trial was to compare the traditional surgical scrub with a waterless alcohol-based hand preparation in terms of antimicrobial effectiveness, effect on skin condition, and time required.

**DESIGN & METHODS:** This study was a 6-week, single center, clinical trial. Twenty-five surgical staff members participated in a clinical trial. The subjects were of either gender, ranged in age from 18 to 65, and met the following inclusion criteria: 1) had been using a traditional scrub product as their preoperative scrub for at least 2 weeks before enrollment; 2) were expected to be available throughout the course of the study; 3) agreed not to use lotions on their hands during the course of the study, except when prescribed by study staff members; and 4) were willing to comply with the requirements of the study and give informed consent. The study was designed to compare the microbiology and skin condition of hands when using a traditional surgical scrub (TSS) with a detergent-based antiseptic containing 4% chlorhexidine gluconate(CHG) and a short application without scrub of a waterless hand preparation (HP) containing 61% ethyl alcohol, 1% CHG, and emollients. The subjects used the HP for 3 consecutive weeks and, after a 1-week hiatus, used the TSS for 3 consecutive weeks.

**RESULTS:** The visual scoring of the skin (VSS) measurements revealed no mean changes greater than 0.6 and no observable trends. The change scores for VSS were significantly better during the HP protocol. The HP was associated with less skin damage ( $P = .002$ ) and lower microbial counts postscrub at days 5 ( $P = .002$ ) and 19 ( $P = .02$ ). The HP protocol had shorter contact time (HP mean [M] = 80.7 seconds; TSS M = 144.9 seconds;  $P < .0001$ ), and more subjects preferred the HP regimen ( $P = .001$ ). The HP performed better than the TSS, was less costly, and should be evaluated in larger trials and considered for widespread implementation.

Table 7

Time period	Mean log <sub>10</sub> counts (± standard deviation)		P value (paired t tests)
	Hand preparation regimen	Traditional surgical scrub regimen	
Prescrub, week 1, day 1	4.80 (.92)	5.15 (1.11)	.21
Postscrub, week 1, day 1	3.86 (.84)	4.34 (1.24)	.054
Prescrub, week 1, day 5	4.32 (.98)	4.41 (.53)	.67
Postscrub, week 1, day 5	3.09 (.54)	3.68 (.83)	.002
Prescrub, week 3, day 5	4.26 (.86)	4.64 (.86)	.08
Postscrub, week 3, day 5	3.43 (.98)	4.09 (1.29)	.02

***Reviewer's comment:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows that the CHG did not meet the required log reduction.*

*The authors recommended that combinations of chlorhexidine gluconate and alcohol be evaluated in larger clinical trial and considered for OR use. The authors recognized that there were several limitations in the studies such as not blinding the product used, so subject and/or investigator bias cannot be ruled out. Subjects knew they were being observed and it is possible they may have modified their scrub practices. No description about neutralization validation was provided. There were no demographics and disposition of the subjects provided. There was no controlling for other confounding factors. The study contained a small sample size of subjects. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

16. **Morrison, AJ, Gratz, J, Cabezudo, I, Wenzel, R. "The efficacy of several new handwashing agents for removing non-transient bacterial flora from hands." Infect Control 1986 (7):268-72.**

This article describes several new handwash agents for efficacy in removing non-transient flora from the hands of medical personnel using the sterile bag technique of quantitative hand culture after brief contact times, while incorporating an effective handwash agent neutralizer.

**DESIGN & METHODS:** Forty subjects participated in a study of six handwashing agents evaluated for their efficacy in removing non-transient bacteria: 70% isopropanol, 0.05% stabilized iodine, 4% chlorhexidine gluconate, 1% para-chloro-meta-xyleneol, 0.5% chlorohexidine gluconate in 70% isopropyl alcohol, and 60% isopropyl alcohol with emollients. Phase one of the study involved each subject performing a non-medicated handwash to remove transient flora. Afterwards, three consecutive experimental handwashes were performed using a 10-second contact time, and a fourth handwash employed a 1-minute contact time. Quantitative post-handwash cultures were obtained using the sterile bag technique incorporating an effective agent neutralizer. Phase two of the study involved obtaining subject's baseline bacterial flora. Then four consecutive evaporative agent applications were performed. Hand culturing was performed between each agent application using a sterile bag technique. After culturing, a tapwater rinse without friction was performed to eliminate residual broth, and then the hands were air-dried without friction prior to the next application of agent.

**RESULTS:** Significant mean log<sub>10</sub> reductions were documented for 4% chlorhexidine gluconate, but only after the third (P = .05) and fourth (p = .004) handwash. However, the total log<sub>10</sub> reduction was less than 1.0 for any single agent. Subsequently, three evaporative handwash agents, including 70% isopropanol, 0.5% chlorhexidine in 70% isopropanol, and a 60% isopropanol formulation containing evaporative retardants, were tested in 14 subjects. Contact time was prolonged to the point of evaporation prior to culturing. Four consecutive post-handwash cultures were obtained after performing a

baseline pre-handwash culture. When compared with the other two evaporative agents, the 60% isopropanol formulation demonstrated significant mean log<sub>10</sub> reductions for each handwash (p less than or equal to .03), with a total log<sub>10</sub> reduction of 2.9 over all four handwashes (p = .0001).

**Table 1.**  
Inter-agent comparisons of mean log<sub>10</sub> bacterial reduction / mean after each of four consecutive handwashes with four handwashing agents (N=40)

Handwash Number	MLR IA	MLR AK	MLR IK	MLR HC
1	0.05	0.15	0.12	0.19
2	0.17	0.23	0.12	0.21
3	0.07	0.11	0.08	0.25*
4	0.04	0.14	0.06	0.29†
<b>Total (1-4)</b>	<b>0.33</b>	<b>0.63</b>	<b>0.38</b>	<b>0.94‡</b>

\*p=0.05; HC more efficacious than IA/AK/IK  
†p=0.004; HC more efficacious than IA/AK/IK  
‡p=0.0001; HC more efficacious than IA/AK/IK  
Key:  
IA=70% isopropyl alcohol with 1% glycerin  
AK=Acute-Kare; 1% PCMX; Calgon Corporation, St.Louis, MO.  
IK=Ido-Kare; 0.05% stabilized iodine; Calgon Corporation, St. Louis, MO.  
HC=Hibiclens; 4% Chlorhexidine gluconate; Stuart Pharmaceuticals

**Table 2.**  
Inter-agent comparisons of mean log<sub>10</sub> bacterial reduction (MLR) after each of four consecutive handwashes with three evaporative handwashing agents (N=14)

Handwash Number	MLR IA	MLR HS	MLR CS
1	-0.5	-0.15	1.4*
2	0.3	0.0	0.5†
3	0.0	0.1	0.5
4	0.2	0.0	0.5**
<b>Total (1-4)</b>	<b>0.0</b>	<b>-0.3</b>	<b>2.9††</b>

\*p=0.0001; CS more efficacious than IA/HS  
†p=0.02; CS more efficacious than IA/HS  
‡p=0.03; CS more efficacious than IA/HS  
\*\*p=0.0001; CS more efficacious than IA/HS  
Key:  
IA=70% isopropyl alcohol with 1% glycerin  
HS=0.5% chlorhexidine gluconate in 70% isopropyl alcohol; Stuart Pharmaceuticals, Wilmington, DE  
CS=60% isopropyl alcohol with evaporative retardants; Calgon Corporation, St. Louis, MO  
HC=Hibiclens; 4% Chlorhexidine gluconate; Stuart Pharmaceuticals

**Reviewer's comment:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, is that the CHG and IPA did not meet the required initial 1-log reduction.

*The authors suggested that data from this study do not suggest any agent preference for the reduction of non-transient flora with the possible exception of 60% isopropyl alcohol. The authors also suggest that further studies are needed to substantiate the importance of non-transient bacteria in nosocomial infections. No description of the type of neutralizers that were used was provided. No description of the length of the washout period was provided. There were no demographics and disposition of the subjects provided. The study contained a small sample size of subjects. There is no mention in the exclusion criteria of subjects admitted into the study who is currently using topical or systemic antimicrobials, or any other medication (such as contraceptives) known to affect the normal flora of the skin. There was no blinding of test formulations. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

17. **Pereira LJ, Lee GM, and Wade KJ. "The effects of surgical handwashing routines on the microbial counts of operating room nurses." Am J Infect Control 1990 (18):354-364.**

The objective of the study reported in this publication was to determine whether a shorter duration surgical scrub achieves the same reductions in CFU as a standard scrub.

**DESIGNS & METHODS:** This study examined two interdependent factors: the time taken to wash the hands and the type of antiseptic solution used. A 3-minute initial scrub and 30-second consecutive scrub regimen was compared with a current standard regimen of a 5-minute initial scrub and a 3-minute consecutive scrub. Chlorhexidine gluconate 4% and povidone-iodine 7.5% were the antiseptics used in the two regimens. The sample (n = 34) was drawn from nurses employed in the operating room suite of a 950-bed hospital.

**RESULTS:** Chlorhexidine gluconate was found to be responsible for lower numbers of colony-forming units of bacteria than povidone-iodine. The duration of the scrub had no significant effect on the numbers of bacteria when povidone-iodine was used. The optimal regimen was found to be the 5-minute initial and 3-minute consecutive scrubs with chlorhexidine gluconate.

**Reviewer's Comments:** CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the PVP-I met the required initial 1-log reduction. Other TFM effectiveness criteria were not evaluated.

*The authors based on their analyses of the data indicate that although the shorter-duration surgical scrub is apparently adequate with either of the scrub antiseptics tested, the longer-duration surgical scrub with chlorhexidine gluconate achieves and maintains*

*the best microbial reductions. The study did not provide any demographics and disposition of the subjects. The study contained a small sample size of subjects. The study included a washout period of 1 week, but were instructed to continue normal handwashing procedures during this period. There was no information regarding blinding of the test materials and those analyzing the data. There was no use of a baseline non-antimicrobial control soap. No description of neutralization validation was provided. There was significant difference between hand counts which made it necessary to calculate predicted microbial counts. Overall, the information gathered from this study focused mainly on comparing two surgical hand disinfectants povidone iodine and chlorhexidine gluconate and the optimal scrub time. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

- 18. Reverdy, ME and Fleurette, MJ. “A comparison study of nine disinfectants and/or soaps for surgical disinfection of hands.” (In French). Path Biol 1984 (32):591-595. Effectiveness of 9 soaps and/or antiseptics on hand flora after surgical-type washing**

The article studied the effect of nine soaps and/or antiseptics on the bacterial flora of hands 5 minutes after a surgical scrub.

**DESIGN & METHODS:** Each agent was used by 10 healthy volunteers, free of skin lesions. The following agents were used: chlorhexidine gluconate 4% and 1.5%, povidone iodine 4%, ethanol 70%, isopropanol 70%, a non-antiseptic soap, and another soap followed by either ethanol 70%, isopropanol 70% or a preparation containing H<sub>2</sub>O<sub>2</sub>. The surgical scrub procedure varied slightly according to whether or not the agent was soapy and required rinsing. Sampling was carried out using Gaschen's bag method with 400 ml of neutralizing solution. Counts were made after 48 hours aerobic incubation at 35°C on tryptic soy agar with 1% Tween 80, and after 8 days anaerobic incubation at 35°C on Brewer's yeast agar with 1% Tween 80.

**RESULTS:** Results were expressed as the log<sub>10</sub> of the number of bacteria per hand. Statistical significance was determined using the Student's t-test. The greatest reduction in aerobic flora was produced by isopropanol 70% (1.7 log<sub>10</sub>). 1.5 to 0.5 log<sub>10</sub> reductions were produced, in the following decreasing order, by ethanol 70%, povidone iodine, chlorhexidine gluconate 4% and 1.5% and a soap with ethanol 70%. A reduction of less than 0.5 log<sub>10</sub> was produced by a soap with isopropanol 70%, and soaps with H<sub>2</sub>O<sub>2</sub>. Similar results were obtained with the facultative anaerobes.

**Reviewer's comment:** *CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, despite its deficiencies is that the CHG and IPA met the required initial 1-log reduction. This article was in French and could not be evaluated. Only the abstract was in English.*

19. **Stiles, ME and Sheena, AZ. "Efficacy of low-concentration iodophors for germicidal hand washing." J Hyg Camb 1985 (94):269-277.**

The purpose of the study was to evaluate the efficacy of iodophor (0.75, 0.5, 0.3, 0.1, 0.01, and 0.005% available iodine) germicides against transient (inoculated) bacteria and the natural hand microflora and comparing it to chlorhexidine gluconate (2 and 4%) liquid detergent (Hibitane), non-germicidal soap, and a tap water rinse.

**DESIGN & METHODS:** Total of 8 agents was tested. Latin square designs were used so that each subject used each agent once during the course of each experiment. Total of 28 subjects participated in the study. Agents were randomly assigned according to the procedure specified. A 5 ml aliquot of the agent was applied to wetted hands and used in a standardized washing procedure during a 15-second exposure time, supervised by one of the researchers. The washing procedure included 4 different series of movements, each repeated five times. After a 15-second exposure hands were rinsed. There were 3 testing days each week. Subjects with socially clean hands were sampled by the standard rinsing technique immediately before and after the hand wash treatments, but there was no mention of a prewash.

**RESULTS:** Regarding efficacy against resident flora, an analysis of variance of the  $\log_{10}$  transformed change ratios indicated a significant effect ( $P < 0.01$ ) attributable to agents. The differences were less distinct than those observed for transient bacteria. 4% chlorhexidine was significantly better than the tap water rinse, non-germicidal soap and iodophor product containing 0.1% available iodine, but compared with other germicidal agents it did not give a significantly better reduction in numbers of bacteria released from hands. Baird-Parker medium and standard aerobic plate counts were highly correlated ( $r = 0.82$ ), so that for studies of gram-negative bacteria inoculated onto hands as a transient microflora. The low-concentration iodophor products and the product containing 2% chlorhexidine gluconate failed to give results significantly better than the non-germicidal control soap.

**Reviewer's comment:** *CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows, is that the CHG did not meet the required initial 1-log reduction.*

*The authors concluded that only the 4% chlorhexidine gluconate and 0.75% iodophor products significantly reduced the number of natural bacterial released from hands and that 0.5% iodophor product gave an intermediate effect. There were several limitations to this study. This article focused on food handling instead of the clinical setting of a hospital. There was no demographics and disposition of the subjects provided. No blinding of the studies (subjects and data evaluations). Used broth for sampling. No neutralizers were mentioned in the study. There was no mention of washout periods. Over all, there was no valuable information regarding the correlation of infection rates to the reduction of bacteria. Clinical relevance was not demonstrated.*

Two additional studies on surgical scrubs (Bryce et al. 2001 and Parienti et al. 2002) are from C80.

### **Literature Review**

**Bryce, EA, Spence, D, and Roberts, F. "An in-use evaluation of an alcohol-based pre-surgical hand disinfectant." Infect Control Hosp Epidemiol 2001 (22):635-639.**

The objective of this study was to determine whether alcohol hand disinfection is an effective alternative to traditional agents for the pre-surgical scrub.

**DESIGN & METHODS:** A prospective clinical trial of a 70% isopropanol pre-surgical hand disinfectant (Manorapid) involving the operating room suites at two hospital sites in British Columbia. The cases were selected to evaluate both short and longer procedures. The hand disinfectant was compared to agents in current use as surgical scrubs (4% chlorhexidine and 7.5% povidone-iodine). Surgical technique and glove use were not modified. Surgical personnel scrubbed (using traditional solutions and brushes) for 3 minutes after cleaning under the fingernails with a nail pick, according to operating room guidelines. The alcohol hand antiseptic was used as follows: hands were washed with a mild neutral soap for 1 minute prior to the first case of the day, hands were dried, and approximately 5 mL of the alcohol product was dispensed into a cupped hand. Staff were instructed to dip their opposing fingernails into the solution, then transfer the Manorapid to the other hand and do the same to the other fingernails; the remaining product was used to rub all areas of the hands to the wrist. A second 5 mL of solution was dispensed and the liquid dispersed up both arms to the elbows and rubbed into the skin. A third 5 mL of product then was rubbed into the hands. Total time for the surgical hand rub was approximately 3 minutes. Pre- and postoperative fingertip impression and "glove-juice" cultures were used to determine microbial burden, and hands were evaluated for skin integrity.

**RESULTS:** There was no statistical difference between the microbial hand counts following use of the alcohol-based product or the current agents, for cases less than 2 hours' duration. Comparison of longer surgical cases revealed significantly better pre- and postoperative culture results with the alcohol hand rinse, but analysis of matched pairs showed no significant difference in microbial counts. The alcohol hand rinse was equivalent to the operative scrub in terms of skin integrity and user acceptability.

**Reviewer's comments:** *CTFA cited this reference to demonstrate that the products tested could meet a 1-log reduction. What the study shows that IPA did not meet the required log reduction.*

*The authors concluded that an alcohol hand rinse was equivalently effective in reducing microbial hand counts as the traditional pre-surgical scrub, both immediately after hand*

*disinfection and at the end of the surgical procedure. There were several limitations in the study. There was no demographics and disposition of the subjects provided. There were many variables (factors) in the studies such as glove type, glove liners, other skin agent use, and use of antibiotics and contraceptives that were not controlled for. There was no washout between periods and no instructions were given regarding the use of antimicrobials at home. The washout period is important because they crossed over from more persistent antimicrobials to the alcohol. The participants were given no specific instructions regarding their use of antimicrobial-containing products such as deodorants, shampoos, lotions, or soaps, nor were they provided with kits containing non-antimicrobial personal-care products for use during the evaluation. Overall, the information gathered from this study just showed that alcohol-based product was a comparable agent to those that were currently in use and effective if used according to recommendations. There was no valuable information regarding the correlation of infection rates to the reduction of bacteria. There was no clinical relevance depicted in the study.*

**Parienti JJ, Thibon P, Heller R, LeRoux Y, von Theobald P, Bensadoun H, Bouvet A, Lemarchand F, Le Coutour X. “Hand-rubbing with an aqueous alcoholic solution vs traditional surgical hand-scrubbing and 30-day surgical site infection rates.” JAMA 2002 (288):722-727.**

The purpose of this study was to compare the effectiveness of hand-cleansing protocols in preventing surgical site infections during routine surgical practice.

**DESIGNS & METHODS:** This is a randomized equivalence trial comparing hand-scrubbing and hand-rubbing protocols with a multiple service crossover experimental design. Six surgical services from teaching and nonteaching hospitals in France included a total of 4387 consecutive patients who underwent clean and clean-contaminated surgery between January 1, 2000, and May 1, 2001. Surgical services used two hand-cleansing methods alternately every other month: a hand-rubbing protocol with 75% aqueous alcoholic solution containing propanol-1, propanol-2, and metronidazole; and a hand-scrubbing protocol with antiseptic preparation containing 4% povidone iodine or 4% chlorhexidine gluconate. Thirty-day surgical site infection rates were the primary end point. Operating department teams' tolerance of and compliance with hand antisepsis were secondary end points. A non-medicated soap was used in conjunction with the first wash of the day and also when the hands were visibly soiled. Surgical site infections were prospectively diagnosed by a surgeon, infectious disease specialist, or hygiene specialist on a standard data-collection form. Post-discharge surveillance was based on chart review of visits and telephone contacts with the surgeons.

**RESULTS:** The authors report that the two protocols were comparable in regard to surgical site infection risk factors. The Table below shows that the surgical site infection rates were 55 of 2252 (2.44%) in the hand-rubbing protocol and 53 of 2135 (2.48%) in the hand-scrubbing protocol, for a difference of 0.04% (as treated 95% confidence interval, -0.88% to 0.96%). During the study period, 278 individual compliance assessments were made of the operating teams (174 in the hand-rubbing group),

corresponding with 160 surgical procedures (102 in the hand-rubbing group). On the average, the first hand-cleansing protocol of the day, excluding the simple non-antiseptic hand wash prior to hand-rubbing, lasted significantly longer in the hand-rubbing group than in the hand-scrubbing group (mean [SD], 313 [80] seconds vs 287 [75] seconds;  $P=.01$ ). Scrub nurses complied better with the recommended duration of hand antiseptics than did surgeons and assistants (56% vs 33%;  $P<.001$ ). Based on subsets of personnel, compliance with the recommended duration of hand antiseptics was better in the hand-rubbing protocol of the study compared with the hand-scrubbing protocol (44% vs 28%, respectively;  $P=.008$ ), as was tolerance, with less skin dryness and less skin irritation after aqueous solution use.

**Table 2. Surgical Site Infection (SSI) Rates and Differences Between Hand-Scrubbing and Hand-Rubbing\***

Alteimeier Class of Contamination	No. SSI/No. Operations (%)		SSI Rate Difference (Hand-Scrubbing–Hand-Rubbing), % (95% Confidence Interval)	$\chi^2$ Test of Equivalence (P Value)
	Hand-Scrubbing Protocol	Hand-Rubbing Protocol		
Clean	29/1485 (1.95)	32/1520 (2.11)	-0.15 (-1.16 to 0.85)	16.0 (<.001)
Clean-contaminated	24/650 (3.69)	23/732 (3.14)	0.55 (-1.36 to 2.46)	1.9 (.09)
All	53/2135 (2.48)	55/2252 (2.44)	0.04 (-0.88 to 0.96)	19.5 (<.001)

\*The 95% confidence interval of the SSI rate difference was calculated according to Wallenstein<sup>12</sup> and the  $\chi^2$  test was the lowest  $\chi^2$  value of the Dunnett and Geff<sup>13</sup> continuity corrected double 1-sided test for equivalence at -2% and +2%.

**Table 3. Compliance With the Recommended Duration of Hand Antiseptics During the First Procedure of the Day\***

Operating Room Personnel	Hand-Scrubbing Protocol	Hand-Rubbing Protocol	P Value†
Duration of hand antiseptics, mean (range), s	287 (100-480)	313 (60-510)	.01‡
No. of hand antiseptics $\geq$ 5 min/total no. of hand antiseptics (%)			
Surgeon/assistant	20/83 (24)	51/133 (38)	.04
Scrub nurse	9/21 (42)	26/41 (63)	.18
All	29/104 (28)	77/174 (44)	.008

\*Time required for the nonantiseptic hand wash prior to hand rubbing with aqueous alcoholic solution has been excluded.

†Analyzed using Fisher exact test.

‡Analyzed using Mann-Whitney test.

**Reviewer’s Comments:** CTFAs cited this reference to demonstrate clinical benefit with the use of antimicrobial products in invasive procedures. What the study shows, despite its deficiencies is that 75% alcoholic solution (propanol-1, propanol-2 and mecetronium etilsulfate) with PVP-I and CHG in actual surgical situations showed no statistical difference in the surgical site infection rates.

*This is the first randomized trial to compare hand-rubbing with alcohol-based solution and traditional hand-scrubbing in the routine surgical setting. The authors mention that according to CDC guidelines, all surgical site infections had to be confirmed by the surgeon or the physician in charge of the patient. Therefore, observers of the clinical outcome could not be blinded to the hand antisepsis protocol. Because of the unblinded nature of the study bias cannot be ruled out. There was no description on how the patients were cared for after the operation or details on health of the patients or antibiotics use before undergoing surgical procedures. There was no microbiological evaluation of SSI on the patients. This would be difficult to link the source of infection to the surgeon. There were no reports of glove tears or punctures. Other risk factors to take in to consideration such as aseptic techniques, sterilization of surgical instruments used, type of wound dressing applied etc... In conclusion, the trial does not provide absolute evidence to show that the correlation of clinical outcome of infection rates to the reduction of bacteria on the surgeon's hands.*

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