

TAB 6

Excerpt of comments from CTFA/SDA in regards to the relationship of benefit to efficacy (75N-183H – CP7, section 3)

SECTION 3
THE RELATIONSHIP OF BENEFIT TO EFFICACY

- **Surgical Scrub** - A 1 log₁₀ reduction of the natural flora after a single wash as measured in 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 log₁₀ reduction of the natural flora after a single wash is appropriate provided the baseline contamination level is greater than 5 log₁₀ and neutralizer is incorporated into all sampling fluids.
- **Pre-operative Skin Preparation** - As measured in ASTM E1173 Standard Test Method for Evaluation of a Pre-operative Skin Preparation, bacterial reductions of 1 log₁₀/cm² for injection sites and 2 log₁₀/cm² for a moist site reflect a level of efficacy that provides a benefit in preparation of skin immediately prior to invasive procedures. These criteria are appropriate provided the baseline contamination level is greater than 4 log₁₀ and neutralizer is incorporated into all sampling fluids.
- **Healthcare Antiseptic Handwash** - As measured in ASTM E1174 Standard Test Method for Evaluation of the Effectiveness of Health Care Personnel or Consumer Handwash Formulations, bacterial reductions of 1.5 log₁₀ after a single wash reflect a level of efficacy that provides a benefit in a healthcare setting. This criterion is appropriate provided neutralizer is incorporated into all sampling fluids.
- **As shown in the HCCM, the uses and benefits of Topical Antimicrobial Products** are not limited to these three product categories. Additional product category descriptions and efficacy criteria for Topical Antimicrobial Products containing appropriate active ingredients are necessary for the proper regulation of claims.

Citations specific to the efficacy of Topical Antimicrobial Products were retrieved during the review of the scientific literature, company brochures and industry submissions to the FDA. In addition, previous Industry Coalition submissions to the FDA were reviewed including unpublished company data that was submitted in 1995 and 1996.

Theoretically, the incidence of infection would be directly related to a specified dose of organisms that cause that infection. However, there are numerous mitigating factors that influence whether an infection can establish, including immunological status of the host, viability and virulence of the infectious agent, and route of infection. These factors make it difficult to calculate precisely the level of bacterial reduction needed to demonstrate the benefit of a prophylactic agent. However, it is possible to demonstrate a significant incremental benefit from the use of topical antimicrobial products.

While there are many studies demonstrating the benefit of using topical antimicrobial products, few present data on the reduction of bacteria at the treated site. In reviewing these benefit studies, we especially noted the bacterial reduction of established topical antimicrobial products that are known to be efficacious. There are many other studies, without a clinical endpoint, that measure the reduction of bacteria on treated skin using topical antimicrobial products that are known to be efficacious and shown to provide a benefit. Many of these studies evaluate these topical antimicrobial products using methods based on the pertinent ASTM method. More importantly, there are some studies that evaluate their performance versus the natural flora in situations that mimic typical use patterns. This makes it possible to extrapolate the results from an efficacy study to a benefit study that uses a clinical endpoint. However, many of the other factors cited earlier affecting the benefit are not taken into consideration.

We have reviewed the literature on alcohol, Chlorhexidine gluconate and povidone-iodine using this approach.

Baseline

For two categories, surgical scrub and patient pre-operative skin preparation, the level of bacteria on the skin at baseline significantly impacts the resulting measurement of efficacy. In both cases, if the numbers of bacteria on the skin are high, the potential efficacy of the product that can be measured is also higher. If the numbers of contaminating bacteria are low, while the reduction of bacteria by product use may be as efficient as when the contaminating bacteria are high, the absolute reduction in numbers will be lower. For example, the data in Table I show how baseline contamination levels influence reductions in bacterial counts observed after a single wash using the surgical scrub protocol. In most examples, if the baseline level was greater than $6 \log_{10}$, the mean reductions achieved after a single wash with Chlorhexidine gluconate, isopropyl alcohol and povidone-iodine containing surgical scrubs was approximately $1 \log_{10}$ or greater. As the baseline levels decreased, the observed mean reduction from use of these products decreased below $1 \log_{10}$. Thus it is important that the baseline level of contamination be considered in the determination of efficacy. This is discussed below for those two product categories.

Neutralization

Neutralization status must be considered in reviewing the performance data of surrogate endpoint tests (surgical scrub, healthcare personnel handwash) in the literature. Neutralization of the active ingredient in all sampling fluids is critical when the active ingredient remains on the skin, that is, substantive to the skin. Without the incorporation of a neutralizer in the sampling fluid, there may be an overestimation of the efficacy of substantive active ingredients as the ingredient can be removed from the skin during the sampling process and continue to damage or kill bacteria during the period between sampling and enumeration of the surviving bacteria. For Chlorhexidine gluconate, in particular, this effect can be substantial. For example, using all of the available data for surgical hand scrubs containing 4% Chlorhexidine gluconate

(Appendix D, Table 4), the range of bacterial reduction from a surgical scrub test after a single wash is -0.127 to $4.8 \log_{10}$, the mean reduction is $1.58 \log_{10}$, and the median reduction is $1.41 \log_{10}$. When only those studies, which use neutralizer in the sampling glove are evaluated, the mean drops to $0.96 \log_{10}$ and the median to $0.81 \log_{10}$. This illustrates the importance of knowing the status of neutralization in evaluating the data from these studies.

The Industry Coalition is preparing a separate submission using the literature and a new study to further support this recommendation discussed in the September 29, 1999 proposal on finished product testing.

While neutralization is not as critical in the testing of non-substantive active ingredients such as alcohol compared to substantive actives, the Industry Coalition recommends that neutralizer be incorporated in all sampling fluids as part of standardizing the method for future testing. Incorporation of neutralizer in all sampling fluids should allow for greater confidence in the comparison of data.

In the discussion below, the incorporation of neutralizer in the sampling fluids was considered critical for evaluation of products containing substantive ingredients, i.e., all ingredients except alcohols. Thus, for povidone-iodine or Chlorhexidine gluconate only, those examples that incorporated neutralizers in the glove during hand sampling or in the cup for body sampling were considered.

Surgical Scrubs

- **A $1 \log_{10}$ reduction of the natural flora after a single wash as measured in 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 $1 \log_{10}$ reduction of the natural flora after a single wash is appropriate for inclusion in the Final Monograph provided the baseline contamination level is greater than $5 \log_{10}$ and neutralizer is incorporated into all sampling fluids.**

The Standard Test Method for Evaluation of Surgical Hand Scrub Formulations evaluates the topical antimicrobial product versus the resident flora of the test subject. Studies using this method are detailed in Appendix D Tables 4-6.

When evaluating these studies for use in this context, baseline contamination levels should be considered. Only examples from studies that reported baseline contamination levels were used. Higher contamination levels in some cases result in greater reductions than when lower contamination levels are used (see below).

The efficacy of topical antimicrobial products after a single wash is summarized in Table 1.

Table 1
Efficacy of Topical Antimicrobial Products after a Single Wash
Reduction from Baseline (\log_{10})

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

The level of activity of a surgical scrub depends upon the baseline bacterial level, topical antimicrobial product used, and other factors such as amount of product, scrub time, etc. The data in Table I show how baseline contamination levels influence reductions in bacterial counts observed after a single wash. In most examples, if the baseline level was greater than 6 log₁₀, the mean reductions achieved after a single wash with Chlorhexidine gluconate, isopropyl alcohol and povidone-iodine containing surgical scrubs was approximately 1 log₁₀ or greater. As the baseline levels decreased, the observed mean reduction from use of these products decreased below 1 log₁₀.

The expected contamination level on a surgeon's hands is approximately 3 to 6 log₁₀. The data in Table I indicate 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 log₁₀.

Grinbaum *et al.* showed the importance of a povidone-iodine surgical scrub in preventing surgical site infections. Upon comparison of risk factors such as duration of surgery, wound class, use of antibiotics, remote site infection and hand scrubbing procedure, Grinbaum *et al.* concluded that the only significant factor related to an outbreak of surgical site infections was hand scrubbing. A prospective study was conducted to compare surgical site infection cases that occurred during a period when povidone-iodine was not provided to surgeons for preoperative scrubbing to times when povidone-iodine was used. Scrubbing with bland soap by surgeons in the vascular surgery unit was the only factor that could be linked to the outbreak (p<0.00001). 100% of cases displaying surgical site infections (9/9) were those where bland soap was used, as opposed to control cases (povidone-iodine used) where the infection rate was 0% (0/18). Further support of the authors' findings was the fact that no increase of surgical site infections was detected in other departments where 2% povidone-iodine in alcohol was used when povidone-iodine surgical scrub was unavailable. Finally, when povidone-iodine again became available for pre-surgery scrubs, the outbreak was controlled. (Grinbaum *et al.* 1995) Two additional benefits studies implicate the use of 7.5% povidone-iodine surgical scrubs in conjunction with povidone-iodine pre-operative preparations as playing a major role in the reduction of surgical wound infections (Jackson 1972; Connell and Rousselet 1964).

In another study, routine use of a Chlorhexidine gluconate surgical hand scrub eradicated an epidemic strain of *S. epidermidis* from a carrier. Investigation of post-operative wound infections and endocarditis caused by a single strain of *S. epidermidis*, including examination of surgical equipment, staff and unaffected patients, revealed the outbreak was related to the identical strain on one surgeon's hands. The surgeon was prohibited from performing cardiac surgery and required to use a Chlorhexidine surgical scrub routinely. Two weeks later cultures taken immediately after scrubbing and 3-4 hours after gloving failed to grow the epidemic strain and the surgeon was reinstated. No infections related to the epidemic strain were detected for 24 months after implementation of the infection control measures (Boyce *et al.* 1990).

Based on the literature cited above, inclusion of a 1 log₁₀ reduction in the Final Monograph is appropriate for the surgical scrub category. The data presented provide ample evidence that an efficacious surgical scrub can be defined as one that causes a minimum 1 log₁₀ 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 log₁₀ and neutralizer is incorporated into all sampling fluids.

Pre-operative Skin Preparations

- **As measured in ASTM E1173 Standard Test Method for Evaluation of a Preoperative Skin Preparation, bacterial reductions of 1 log₁₀/cm² for injection sites and 2 log₁₀/cm² for a moist site reflect a level of efficacy that provides a benefit in preparation of skin immediately prior to invasive procedures. These criteria are appropriate for inclusion in the Final Monograph provided the baseline contamination level is greater than 4 log₁₀/cm² and neutralizer is incorporated into all sampling fluids.**

The Standard Test Method for Evaluation of a Pre-operative Skin Preparation evaluates the topical antimicrobial product versus the resident flora of the test subject. Studies using this method are compiled in Appendix D Tables 7-9.

The efficacy of topical antimicrobial products, as measured by log₁₀ reduction from baseline after a typical application, is summarized in Table 2.

Table 2
Efficacy of Topical Antimicrobial Products after a Typical Application
Reduction from Baseline (\log_{10}/cm^2)

Baseline Level (\log_{10}/cm^2)	Range	Mean	Number of Examples (References)
4% Chlorhexidine Gluconate			
Abdomen 3-4	1.81-1.98	1.9	2 (Aly <i>et al.</i> 1998)
Groin 4->5	2.13-3.81	2.97	2 (Vorherr <i>et al.</i> 1988; Aly <i>et al.</i> 1998)
Perineum >5	4.31	-	1 (Vorherr <i>et al.</i> 1988)
60% Isopropyl Alcohol			
Abdomen >5	3.25	-	1 (Leyden & Kligman 1981)
70% Isopropyl Alcohol			
Injection Site >3	2.18-2.95	2.41	4 (SDA/CTFA 1995)
70% Ethanol			
Abdomen >5	3.88	-	1(Leyden & Kligman 1981)
60% Ethanol			
Abdomen 2-3	2.3-2.77	2.53	2 (Jampani <i>et al.</i> 2000)
Groin ~4	2.04-3.12	2.58	2 (Jampani <i>et al.</i> 2000)
7.5% Povidone-iodine			
Abdomen 3-4	1.17	-	1 (Arata <i>et al.</i> 1993)
10% Povidone-iodine			
Groin 3-4	3.42-3.66	3.54	2 (Vorherr <i>et al.</i> 1988)
Perineum 4-5	3.65-3.74	3.7	2 (Vorherr <i>et al.</i> 1988)

The baseline bacterial population should be large enough to allow demonstration of bacterial reductions of $2 \log_{10}/\text{cm}^2$. Therefore, a baseline population of at least $4 \log_{10}/\text{cm}^2$ is recommended where possible. The mean reduction for most sites and active ingredients is approximately $2 \log_{10}/\text{cm}^2$ or greater for all abdominal, groin or perineum sites tested. The mean bacterial reduction for injection site preparations meets the $1 \log_{10}/\text{cm}^2$ reduction in all cases.

In practical terms, injection sites are usually very dry sites that have a low bacterial population ($3 \log_{10}/\text{cm}^2$ or less). Therefore, the performance standard as measured in a surrogate test should reflect that lower reductions, i.e. $1 \log_{10}/\text{cm}^2$ reduction, are appropriate with lower baseline population. Dry surgical sites such as the abdomen also have a low bacterial population. Mulberry surveyed 68 test subjects who had a mean abdominal bacterial count of $2.16 \log_{10}/\text{cm}^2$ covering a range from 0.08 to $4.9 \log_{10}/\text{cm}^2$ (Mulberry *et al.* 1994). However, as the risk of infection from transfer of the bacteria from the skin's surface into the surgical wound is much greater (due to the

greater size of the incision) it is logical that a higher performance standard be applied to that site, i.e. a $2 \log_{10}/\text{cm}^2$ reduction is appropriate. However, as pre-operative preparations are marketed for all surgical site preparations, not just dry or moist sites, it is recommended that the worst case scenario be evaluated, i.e. a moist site where the bacterial population exceeds $4 \log_{10}/\text{cm}^2$, with the same performance standard of a $2 \log_{10}/\text{cm}^2$ reduction.

Klovekorn reported a reduction in skin population by 97% (approximately $1.5 \log_{10}/\text{cm}^2$) following use of a 10% povidone-iodine preparation prior to thoracic surgery. In this study the overall rate of infection following median sternotomy was reduced to less than 0.5% (Klovekorn *et al.* 1985). A number of other studies describe the use of 7.5% povidone-iodine surgical scrubs and 10% povidone-iodine pre-operative skin preparations as playing a major role in the reduction of surgical wound infections (Beaton, undated; Jackson 1972; Georgiade *et al.* 1990).

A number of studies record the reduction in bacteria prior to surgery without documenting a change in the clinical outcome. Using a 4% Chlorhexidine gluconate preparation produced a mean $2.7 \log_{10}/\text{cm}^2$ bacterial reduction at the operation site for 28 orthopedic patients (Gilmore *et al.* 1984). A $1.89-5.7 \log_{10}/\text{cm}^2$ bacterial reduction was reported on umbilici treated with 4% Chlorhexidine gluconate. In other studies skin was treated with various topical antimicrobial agents and then biopsied. Reductions vs. baseline of 83%, 83%, 88%, and 96% ($0.7-1.4 \log_{10}/\text{cm}^2$ bacterial reduction) were reported with the use of 4% Chlorhexidine gluconate, 70% ethanol, 60% isopropyl alcohol, and povidone-iodine, respectively (Stuart 1986; Selwyn *et al.* 1985).

Therefore, based on the data presented, bacterial reductions of $1 \log_{10}/\text{cm}^2$ for injection sites and $2 \log_{10}/\text{cm}^2$ for a moist site as measured in the Standard Test Method for Evaluation of a Preoperative Skin Preparation are appropriate for inclusion in the Final Monograph provided the baseline contamination level is greater than $4 \log_{10}/\text{cm}^2$ and neutralizer is incorporated into all sampling fluids.

Healthcare Personnel Hand Products

- **As measured in ASTM E1174 Standard Test Method for Evaluation of the Effectiveness of Health Care Personnel or Consumer Handwash Formulations reparations, bacterial reductions of $1.5 \log_{10}$ after a single wash reflect a level of efficacy that provides a benefit in a healthcare setting. This criterion is appropriate for inclusion in the Final Monograph provided neutralizer is incorporated into all sampling fluids.**

In the Standard Test Method for Evaluation of the Effectiveness of Health Care Personnel or Consumer Handwash Formulations, hands are artificially contaminated with a marker strain. As these products are largely designed for removal of transient species, this is an appropriate mechanism for evaluation of these products. However, the literature was reviewed to determine the level of natural bacterial flora commonly

encountered in this use situation and the level of antimicrobial efficacy needed to show a benefit. Studies using this method are detailed in Appendix D Tables 1-3.

Four studies demonstrated the ability of alcohol products to reduce the natural flora by greater than 1 log₁₀ following use. In two studies Larson evaluated the effect of a single use of isopropyl alcohol. Use of 60% isopropyl alcohol resulted in a 1.34 or a 1.74 log₁₀ reduction immediately after use. Use of 70% isopropyl alcohol resulted in a 1.2 log₁₀ reduction immediately after use. Leyden also evaluated 70% isopropyl alcohol and found a 98.7% reduction (approximately 1.89 log₁₀). Lilly evaluated 95% ethanol and found a 2 log₁₀ reduction immediately after use (Larson *et al.* 1986 1987; Leyden *et al.* 1991; Lilly *et al.* 1979).

Six studies evaluated the impact on the natural flora of a single wash with 4% Chlorhexidine gluconate products. Reductions of 76.4% (approximately 0.63 log₁₀) (Field and Martin 1986), 87.1% (approximately 0.89 log₁₀) (Lilly and Lowbury 1974), and 92.6% (approximately 1.13 log₁₀) (Leyden *et al.* 1991) are presented. Larson *et al.* 1986 found a reduction of 0.75 log₁₀; Lilly *et al.* (1979) found a 0.75 log₁₀ reduction and Sheena and Stiles (1983) found reductions of 0.37 to 0.99 log₁₀.

Two data points were found for 7.5% povidone-iodine: Leyden *et al.* 1991 reported a 50.2% reduction (approximately 0.3 log₁₀); and Lowbury 1963 reported a 60% reduction (approximately 0.4 log₁₀).

In summary, the data indicate that a single wash with a known efficacious material reduces the resident and transient flora on the hand between 0.2 and 2.5 log₁₀. The efficacy is dependent upon the amount of product applied, wash duration, baseline bacterial population and potentially other factors. The use of a marker strain in the Standard Test Method for Evaluation of the Effectiveness of Health Care Personnel or Consumer Handwash Formulations is important as it provides for consistency and reproducibility in that method.

Handwash products have been shown to play an important role in infection control. Central venous line related infections, ventilator-associated pneumonias as well as infections at all body sites have been reduced through the use of alcohol hand products (Gould 2000; Brooks *et al.* 1999; Jones & Newman 2000). Alcohol-based products significantly reduced the aerobic Gram negative bacteria on patient's skin and the transfer of those bacteria to caregiver's hands (Eckert *et al.* 1989b; Ehrenkranz *et al.* 1991).

Ehrenkranz demonstrated that a bland soap handwash failed to prevent the transfer of Gram negative bacteria to a catheter in 11 of 12 experiments while a 30 second rinse with 70% isopropyl alcohol failed in 2 of 12 experiments. Soap failed to prevent transient colonization in 12 of 12 experiments; Ethyl alcohol, in 5 of 12. A single Gram negative species carried at source levels greater than 5.5 x 10³ established transient colonization in 23 of 30 exposures following a soap handwash. If the contamination level was less than 3.5 x 10³, colonization was established in 1 of 22 exposures (after

soap) (Ehrenkranz *et al.* 1991). Reverdy reported that a 1 minute exposure to 70% isopropyl alcohol in a surgical scrub reduces the resident flora by approximately 1.4 log₁₀ (Reverdy *et al.* 1984).

Significant reductions in skin graft donor body contamination, nosocomial infection rates and staff colonization with pathogens were found with use of Chlorhexidine gluconate hand preparations (May *et al.* 1991; Klausner *et al.* 1999; Doebbeling *et al.* 1992; Maki and Hecht 1982; Maki 1989; Casewell and Phillips 1977; Stuart 1986).

Povidone-iodine solutions were also shown to significantly reduce staff colonization with pathogens and nosocomial infection rates (Maki and Hecht 1982; Maki 1989, Amortegui and Buffenmyer 1978; Knittle *et al.* 1975).

A 10% povidone-iodine solution (Betadine Scrub, Purdue-Frederick), 4% Chlorhexidine gluconate (Hibiclens, Stuart), and a non-medicated soap were studied in a surgical intensive care unit in a sequential comparative design with a team of 38 personnel. Povidone-iodine and Chlorhexidine gluconate demonstrated a 50% reduction in nosocomial infections over the non-medicated soap ($p > 0.001$) (Maki and Hecht 1982; Maki 1989). During the six-week use period personnel were randomly cultured and the average skin flora and *S. aureus* reported (See Table 3).

Table 3
Average Skin Flora (log₁₀) After Six weeks Using a
Topical Antimicrobial Product

Treatment	Total Flora (log₁₀)	<i>S. aureus</i> (log₁₀)
10% Povidone-iodine	4.18 ± 0.11 cfu/hand	0.54 ± 0.21 cfu/hand
4% Chlorhexidine gluconate	3.56±0.09 cfu/hand	0.13±0.78 cfu/hand
Plain soap	4.22±0.12 cfu/hand	0.22±0.09 cfu/hand

Therefore, in this case, the reduction in total aerobes required to effect a clinical benefit for Chlorhexidine was approximately 0.66 log, which is less than the 1.5 log₁₀ reduction proposed for the surrogate endpoint test. There was no change in the total flora (-0.04 log₁₀) observed with the 10% povidone-iodine, yet a clinical benefit was still detected.

Based on the data presented, bacterial reductions of 1.5 log₁₀ after a single wash is appropriate provided neutralizer is incorporated into all sampling fluids, as measured in the Standard Test Method for Evaluation of the Effectiveness of Health Care Personnel or Consumer Handwash Formulations.

Other Categories

- **The uses and benefits of topical antimicrobial products are not limited to the actives currently found to be Category I for safety and efficacy, nor are they limited to the three product categories detailed above. The development of additional product category descriptions and efficacy criteria for topical antimicrobial products containing appropriate active ingredients is necessary for the proper regulation of claims.**

There are a number of use situations that are not described by the current categories. One example is detailed below as an illustration.

Whole body washing of the surgical patient

A number of studies discuss the use of topical antimicrobial products for total body washing in the days surrounding a surgical procedure. In two studies using two 4% Chlorhexidine-gluconate washes prior to surgery, Paulson showed a bacterial reduction of $0.86 \log_{10}/\text{cm}^2$ at the abdominal site and $0.41 \log_{10}/\text{cm}^2$ at the inguinal site (Paulson *et al.* 1993); and Kaiser showed a bacterial reduction of $1.61 \log_{10}/\text{cm}^2$ at the subclavian site and $2.07 \log_{10}/\text{cm}^2$ at the inguinal site (Kaiser *et al.* 1998).

Garibaldi showed in two separate trials that showering twice with 4% Chlorhexidine gluconate after the operation led to $2.44 \log_{10}/\text{cm}^2$ and $2.1 \log_{10}/\text{cm}^2$ reductions at the surgical site (Garibaldi *et al.* 1988). The effect of similar use of 7.5% povidone-iodine and 1% Triclocarban (TCC) was also followed in these same trials. The bacterial reductions seen were 1.62 and $1.1 \log_{10}/\text{cm}^2$, and 0.87 and $0.5 \log_{10}/\text{cm}^2$, respectively.

In clinical studies, the value of total body washing with topical antimicrobial products prior to surgery has been repeatedly demonstrated. Patients who showered with 4% Chlorhexidine prior to surgery had a lower infection rate than those who did not (Brandberg *et al.* 1981, Hayek *et al.* 1987). A reduction in clean wound infections resulted from use of a pre-operative hexachlorophene shower and from the use of Chlorhexidine skin pre-operative preparations (Cruse and Foord 1973).

Based on these data, the use of topical antimicrobial products in the bathing of patients prior to and after surgery provides a benefit to the patient and is one of a number of other applications of topical antimicrobial products that should be considered for inclusion in the regulations for topical antimicrobial products. Therefore, the development of additional product category descriptions and efficacy criteria for topical antimicrobial products containing appropriate active ingredients is necessary.

Summary

The performance criteria proposed by the SDA/CTFA Industry coalition for Surgical Hand Scrubs, Pre-operative Skin Preparations and Healthcare Personnel Hand Preparations reflect the levels of efficacy that provide benefits in the situations where

these products are used. These criteria provide an appropriate measure of efficacy that can be related to a significant incremental benefit from the use of such topical antimicrobial products.

As shown in the HCCM, the uses and benefits of Topical Antimicrobial Products are not limited to these three product categories. Additional product category descriptions and efficacy criteria for Topical Antimicrobial Products containing appropriate active ingredients are necessary for the proper regulation of claims.