TECcare® Antimicrobial Technologies

TECcare® PROTECT Foam Hand Sanitiser

TECcare PROTECT

- Effective against MRSA, and Community Associated CA-MRSA

Overview

TECcare PROTECT Foam Hand Sanitiser is based on the active ingredient benzalkonium chloride in a unique non-drying, moisturising and conditioning formulation. TECcare PROTECT kills 99.9-99.9999% of most common germs that may cause illness, including E. Coli and MRSA in just 15 seconds.

Benzalkonium chloride, which is listed in the Antiseptic monograph as Category III for safety and efficacy. This category allows benzalkonium chloride based products to be marketed in use patterns that fall within the monograph as long as the formulations conform to the percentage ranges in the monograph, which is 0.1-0.13% for benzalkonium chloride. As in the case of ethanol based instant hand sanitisers, benzalkonium chloride based products qualify for monograph "grandfathering" with a demonstrated use pattern established for a material time and extent prior to December, 1975.

Typical Properties

	TECcare PROTECT RTU
Physical form	Light amber liquid
Benzalkonium chloride, active %	0.1
Assay (Epton), meq/kg	6.1-7.1
pH	4.5-6.5
Specific Gravity @25°C	1.00±0.02
Flash point (PMCC)	>200°F (>93°C)
Biorenewable Carbon, %	76 (Coconut Oil, Palm Kernel Oil)

Handling Information

Note - Manufacturing, Packaging and Marketing of this product may be subject to regulation by the Food and Drug Administration and may be subject to Enforcement Action.

Refer to and follow the guidelines in the Material Safety Data Sheet (MSDS) available from Talley Environmental Care Ltd for information on the safe use, handling and disposal of this product.

TECcare PROTECT Foam Hand Sanitiser, based on the active ingredient benzalkonium chloride, is a unique formulation featuring exceptional skin feel, conditioning and moisturising properties. The efficacy of this product has been confirmed to reduce S. aureus 99.9999% in as little as 15 seconds.

TECcare PROTECT Foam Hand Sanitiser is in compliance with the FDA Final Tentative Monograph for OTC Hand Sanitiser preparations (leave-on sanitisers not requiring a rinse).

TECcare PROTECT Foam Hand Sanitiser produces a fast drying, non-sticky foam that contains unique non-drying, conditioning and moisturising ingredients, leaves the skin with a soft, refreshing and silky after feel, and does not contain polymer thickeners or silicones.

There are numerous questions regarding TECcare PROTECT and the marketing environment for these types of products. Summarised below are some general answers:

What are the FDA regulatory issues relating to leave-on antiseptic products?

One question relates to the choice of quat active ingredient, either benzalkonium chloride or benzethonium chloride, and recent issues relating to them. With regard to benzalkonium chloride or benzethonium chloride and the Agency, note that both quats are listed in the Antiseptic monograph as Category III for safety and efficacy. Category III for safety and efficacy means FDA did not have sufficient efficacy and safety information to list them as Category I for hand antisepsis. However, this category allows them to be marketed in products that fall within the monograph as long as the formulations conform to the percentage ranges in the monograph (benzethonium = 0.1-0.2%; benzalkonium = 0.1-0.13% - note this is hard to track in the monograph but has been confirmed by FDA). TECcare PROTECT Foam Hand Sanitiser is in compliance with 0.1% benzalkonium chloride.

Even though the monograph is tentative, products must follow FDA labeling and manufacturing requirements, but due to case law, the types and extent of efficacy testing is not being enforced. While Talley Environmental Care has generated formulation specific efficacy data confirming TECcare PROTECT Foam Hand Sanitiser and is generating additional formulation specific efficacy data to support TECcare PROTECT within industry practice guidelines, there may be a requirement to generate additional efficacy data when the Monograph becomes final.

The real issue is that FDA does not feel that the 1994 TFM includes hand sanitisers (e.g. waterless or leave-on products). Though there are many paragraphs within the monograph that suggest otherwise, this is the stance of the Office of Enforcement. So, today, you can market a quat wash-off product within the above ranges and complying with the above regulations without concern. However, since the hand sanitiser use pattern is not part of the monograph in the eyes of Office of Enforcement, the product may

only be on the monograph with an NDA or if it qualifies for what is called "grandfathering". A product may be grandfathered, if records can be shown that it was in the market for a material time and extent prior to December, 1975. Enforcement did the research to prove that this was true for ethanol hand sanitisers thus they are "grandfathered". Recently, FDA enforcement staff shared with us that they have been shown information to allow grandfathering of IPA, IPA and ethanol combinations, and benzalkonium chloride. Benzalkonium chloride "grandfathering" has been confirmed, and FDA enforcement staff verbally stated that thus they plan no further regulatory action against waterless benzalkonium products that comply with the other items listed above.

Why benzalkonium chloride based hand sanitisers?

History - Benzalkonium chloride is an alcohol-free antimicrobial compound that has been widely used in the health care industry for more than 60 years in formulas for preservatives, surface cleaners, sterilising agents, and leave-on, FDA Monograph anti-bacterial skin treatment products. The chemical properties of benzalkonium chloride make it a good candidate for persistent antimicrobial activity in mammalian tissue.

EJ Singer, "Biological evaluation," in *Cationic Surfactants: Analytical and Biological Evaluation*, ed. J Cross, EJ singer (New York: Marcel Dekker, 1994) 29;

RS Boethling, "Environmental aspects of cationic surfactants," in *Cationic Surfactants: Analytical and Biological Evaluation*, ed. J Cross, EJ Singer (New York: Marcel Dekker, 1994) 95-135;

J Cross, "Introduction to cationic surfactants," in *Cationic Surfactants: Analytical and Biological Evaluation*, ed. J Cross, EJ Singer (New York: Marcel Dekker, 1994) 4-28.

Effectiveness - Benzalkonium chloride-based leave-on hand sanitisers have demonstrated efficacy in real-world environments. When evaluated in school environments where the importance of proper hygiene practices including hand washing is taught and emphasised, the use of non-alcohol benzalkonium chloride-based leave-on instant hand sanitisers reduced illness absenteeism 30-40% in double-blind, placebo-controlled studies versus hand washing alone.

DL Dyer, AL Shinder & FS Shinder (2000). Alcohol-free instant hand sanitizer reduces illness absenteeism. *Family Medicine*, 32(9), 633-638;

CG White, FS Shinder, AL Shinder & DL Dyer (2001). Reduction of Illness Absenteeism in Elementary Schools Using an Alcohol-free Instant Hand Sanitizer. *The Journal of School Nursing*, 17(5), 258-265.

What are the advantages of benzalkonium chloride-based over alcohol-based hand sanitisers?

Benzalkonium chloride based hand sanitisers have several distinct advantages over alcohol-based hand sanitisers. While both product forms are FDA Monograph for leave-on products, fast acting and allow for use without water or towels, benzalkonium chloride based products are non-flammable, non-damaging to skin, are persistent, and will not stain clothing or flooring.

Safety - TECcare PROTECT benzalkonium chloride-based instant Foam Hand Sanitiser is non-flammable. An internet search for alcohol-based hand sanitisers and fire will produce multiple hits. Flash fires associated with use of alcohol-based hand hygiene products can have potentially severe consequences for health care workers and their patients. A published example reported an incidence of flash fire associated with the use of an alcohol-based hand antiseptic agent. The fire occurred when a spark of static electricity ignited the alcohol-based hand gel on the hand of a health care worker who had just removed a 100% polyester gown. The health care worker put the pre-measured amount of alcohol-based hand gel in the palm of her hand from a wall-mounted dispenser. She then removed the 100% polyester gown, placed it on a metal surface, and began rubbing the gel onto both hands. While her hands were damp, she pulled open a metal sliding door, heard an audible static spark, saw a flash of light, and experienced spontaneous flames on the palm of one hand. After the incident, the palm showed redness but no blisters. Flames singed the hair on her arm.

KA Bryant, J Pearce & B Stover (2002). Flash fire associated with the use of alcohol-based antiseptic agent. *American Journal of Infection Control*, 30 (June 2002), 256-257.

Skin irritation - Alcohol-based hand sanitisers are effective for occasional use, but long-term, frequent use of the alcohol products can cause skin irritation. Alcohol solubilises and strips away sebum and lipids that guard against bacterial infections of the skin. Extensive use of alcohol-based hand sanitisers actually increases the skin's susceptibility to infection by transient disease-causing bacteria. This situation can increase the chances of spreading disease-causing microorganisms among patients.

SC Harvey, "Antiseptics and disinfectants; fungicides; ectoparasiticides," in *Goodman and Gilman's The Pharmacological Basis of Therapeutics, sixth ed.*, AG Gilman, LS Goodman, A Gilman eds. (New York: Macmillan Publishing, 1980) 964-987;

GL Grove, CR Zerweck, JM Heilman (2000). Comparison of skin condition in a 5-day healthcare personnel hand washing using a new ethanol-emollient waterless antiseptic versus Purell or water. Atlanta, GA. Paper presented at the Centers of Disease Control 4th Decennial International Conference on Nosocomial and Healthcare-associated Infections. Abstracts P-S1-62.

Effectiveness and residual activity - Alcohol-based hand sanitisers stop working the instant they dry. The leading manufacturer of alcohol-based hand sanitisers claims that their product kills 99.99% of most common germs that may cause disease in as little as 15 seconds. Alcohol-based hand sanitisers dry in 8-10 seconds, and fall below the efficacious concentration of alcohol in seconds. It has been reported that alcohol-based hand sanitisers offer no residual protection, and that if your hands feel dry after rubbing them together for 15 seconds, an insufficient volume of alcohol gel was likely applied [1]. TECcare PROTECT benzalkonium chloride-based Foam Hand Sanitiser dries fast, but 10-15 seconds slower than alcohol-based hand sanitisers allowing more than the minimum contact time for complete efficacious coverage, including under fingernails. Additionally, benzalkonium chloride-based hand sanitisers deliver 2 to 4 hours of residual protection.

Published studies report that benzalkonium chloride-based hand sanitisers demonstrated greater sustained antibacterial activity than gelled alcohol-based hand sanitisers that actually became less effective with repeated use and made the skin dirtier, not cleaner due to removal of protective natural skin oils and entrapment of dead skin cells by the polymer thickeners used in the gelled alcohol-based products.

In the referenced study to simulate repeated usage, alcohol-based and alcohol-free benzalkonium chloride-based hand sanitisers were compared. In the study, subject's hands were repeatedly inoculated with bacteria followed by application of hand sanitiser, then evaluated for antimicrobial effectiveness. The antimicrobial efficacy of the alcohol-based hand sanitiser showed a markedly decreased antimicrobial efficacy with subsequent contamination and decontamination cycles, whereas the alcohol-free benzalkonium chloride-based hand sanitiser showed a steady increase in antibacterial efficacy.

In addition to these objective results, subjects were asked to subjectively evaluate the condition of their hands after the completion of the test protocol. 47% of the subjects who had completed the test protocol with the alcohol-based hand sanitiser reported palmar pain or discomfort, and tended to indicate some discomfort in palmar surfaces for one to several days after the test. In contrast, none of the subjects that used the alcohol-free benzalkonium chloride-based formula reported any pain or discomfort of their hands after completing the test protocol. [2]

(1) Marples, RR, & Towers, AG (1979). A laboratory model for the investigation of contact transfer of microorganisms. *The Journal of Hygiene*, 82(2), 237-248.

(2) Dyer, DL, Gerenraich, KB, & Wadhams, PS (1998). Testing a new, alcohol-free sanitizer to combat infection. *Association of Operating Room Nurses Journal*, 68(2), 239-251.

In summary:

- Benzalkonium chloride-based hand sanitisers had a greater sustained antibacterial activity than alcohol-based hand sanitisers.
- Alcohol-based hand sanitisers became less effective with repeated use and irritated the hands of subjects.
- Benzalkonium chloride-based hand sanitisers became more effective without irritation after repeated use.

Virucidal Efficacy (Influenza A H1N1, Swine Flu, Mexican Flu)

The infectious agent for Swine flu (H1N1, Mexican flu) is an Influenza A virus (H1N1). The allowed FDA OTC claim for TECcare PROTECT benzalkonium chloride-based Foam Hand Sanitiser and for alcohol-based hand sanitisers is "reduces bacteria on the skin." However, it is known that benzalkonium chloride is effective at inactivating Influenza A virus, based on hard surface disinfectant data, at concentrations of 0.03-0.05% benzalkonium chloride. By comparison, TECcare PROTECT contains 0.10% benzalkonium chloride: 2 to 3 times higher than what is required for disinfectant activity against Influenza virus. Typically, enveloped viruses such as Influenza A are easily inactivated by benzalkonium chloride. Note that for the same FDA claim of "reduces bacteria on the skin," alcohol-based products require 62% alcohol, where benzalkonium chloride requires only 0.1%. However, as mentioned above, FDA does not allow for virucidal claims under the Topical Antimicrobials Monograph, for either benzalkonium or alcohol-based hand sanitiser products.

While the belief is that virus claims cannot be made on the product label, product literature can make reference to studies that indicate virucidal effectiveness, just as organisations such as CDC make recommendations based on literature references.

Is TECcare PROTECT Effective?

TECcare PROTECT Foam Hand Sanitiser is very efficient at reducing bacteria on the skin, effective against a broad range of pathogenic bacteria in as little as 15 seconds as data in the following Chlorine Equivalency Test and the Time Kill Study illustrate (Table 1 and Table 2 respectively).

Chlorine Equivalency Test

The object of this test is to determine the available chlorine germicidal equivalent concentration of the product as compared to 200, 100 and 50 ppm available chlorine in the NaOCl standard controls.

Initial Suspension Population

Staphylococcus aureus ATCC 6538	7.6 X 10^8 CFU/ml*
Salmonella typhi ATCC 6539	1.2 X 10^8 CFU/ml

*Colony Forming Units per ml of test mixture

Test Organism		*S. aureus*				*S. typhi*			
Test Substance		NaOCl Control			TECcare PROTECT	NaOCl Control			TECcare PROTECT
Concentration		200 ppm	100 ppm	50 ppm	RTU	200 ppm	100 ppm	50 ppm	RTU
Subculture Series	1	0	0	0	0	0	0	0	0
	2	0	0	+	0	0	0	0	0
	3	0	+	+	0	0	0	+	0
	4	0	+	+	0	0	+	+	0
	5	0	+	+	0	0	+	+	0
	6	+	+	+	0	0	+	+	0
	7	+	+	+	0	+	+	+	0
	8	+	+	+	0	+	+	+	0
	9	+	+	+	0	+	+	+	0
	10	+	+	+	0	+	+	+	0

TABLE 1.
Chlorine Equivalency Test

+ = Growth of organism
0 = No growth of organism

The subcultures of positive broths (tubes showing growth) demonstrated pure cultures of test organism.

Efficacy Result - TECcare PROTECT Foam Hand Sanitiser demonstrated an available chlorine equivalent to greater than the 200 ppm NaOCl standard control when tested against *Staphylococcus aureus* and *Salmonella typhi*.

Time Kill Study

This study is designed to examine the rate of kill of a test substance after inoculation with a test organism. Results are expressed in percent reduction and log reduction of the test organism. Exposure time is 15 seconds.

TABLE 2.
Time Kill Study

Organism	Test Population Control (CFU/ml)	Number of Survivors (CFU/ml)	% Reduction	Log Reduction
Campylobacter jejuni ATCC 29428	1.02×10^7	$<1 \times 10^2$	>99.999	>5.00 Log_{10}
Candida albicans ATCC 10231	1.60×10^5	6.0×10^3	96.3	1.42 Log_{10}
Clostridium difficile ATCC 9689	3.40×10^6	<2	>99.9999	>6.20 Log_{10}
Enterococcus faecalis Vancomycin Resistant (VRE) ATCC 51575	1.12×10^6	3.2×10^1	99.99	4.54 Log_{10}
Escherichia coli ATCC 11229	3.80×10^6	4	99.999	6.00 Log_{10}
Escherichia coli O157:H7 ATCC 35150	1.26×10^6	<2	>99.999	>5.80 Log_{10}
Klebsiella pneumoniae ATCC 4352	1.10×10^6	2	99.999	5.70 Log_{10}
Listeria monocytogenes ATCC 19117	4.7×10^6	1.9×10^3	99.9	3.39 Log_{10}
Pseudomonas aeruginosa ATCC 15442	3.5×10^6	<2	99.9999	>6.20 Log_{10}
Salmonella choleraesuis serotype enteritidis ATCC 4931	6.8×10^5	2	>99.999	5.50 Log_{10}
Salmonella choleraesuis serotype paratyphi ATCC 8759	5.6×10^5	<2	>99.999	>5.50 Log_{10}
Salmonella choleraesuis serotype pullorum ATCC 19945	8.9×10^5	<2	>99.999	>5.70 Log_{10}
Salmonella choleraesuis serotype typhimurium ATCC 23564	7.7×10^5	6	>99.999	>5.10 Log_{10}
Salmonella typhi ATCC 6539	1.27×10^6	2	99.999	5.80 Log_{10}
Shigella dysenteriae ATCC 13313	1.3×10^6	<2	>99.999	>5.80 Log_{10}
Shigella flexneri ATCC 12022	1.39×10^6	2.8×10^1	99.99	4.69 Log_{10}
Shigella sonnei ATCC 25931	2.43×10^7	2.0×10^1	99.9999	6.09 Log_{10}
Staphylococcus aureus ATCC 6538	6.7×10^6	<2	>99.9999	>6.53 Log_{10}
Staphylococcus aureus Methicillin Resistant (MRSA) ATCC 33592	1.23×10^7	3.8×10^3	>99.9	3.51 Log_{10}
Staphylococcus aureus Community Associated Methicillin Resistant (MRSA) NARSA NRS 123, Genotype USA400	1.18×10^6	5.8×10^2	>99.9	>3.30 Log_{10}
Staphylococcus epidermidis ATCC 12228	7.2×10^5	<2	99.999	5.56 Log_{10}
Streptococcus pneumonia ATCC 6305	6.4×10^5	<2	>99.999	>5.51 Log_{10}
Streptococcus pyogenes ATCC 19615	1.77×10^6	<2	>99.999	>5.90 Log_{10}
Vibrio cholera ATCC 11623	4.7×10^5	<2	>99.999	>5.40 Log_{10}
Xanthomonas axonopodis (Citrus Canker) ATCC 49118	1.28×10^6	3.6×10^1	>99.99	4.55 Log_{10}
Yersinia enterocolitica ATCC 23715	2.23×10^6	3.8×10^1	99.99	4.77 Log_{10}

Is TECcare PROTECT Safe for Use?

TECcare PROTECT Foam Hand Sanitiser is very effective at reducing bacteria on the skin, yet very gentle on the skin and eyes as the Toxicity Profile (Table 3) indicates.

TABLE 3.
Toxicity Profile

Toxicity Profile - TECcare PROTECT Hand Foam Sanitiser	
Acute Oral LD_{50}	>5.0 g/kg, Category IV
Acute Dermal LD_{50}	>2.0 g/kg, Category III
Eye Irritation	Category III
Skin Irritation	Category IV
Sensitisation	Not a Skin Sensitiser

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