

Nobac Fact Sheet

Nobac[®] Instant Foam Hand Sanitizer, based on the active ingredient Benzalkonium chloride, is a unique Patented formulation featuring exceptional skin feel, conditioning and moisturizing properties. The efficacy of this product has been confirmed to reduce *S. aureus* 99.9999% in as little as 15 seconds.

Nobac Instant Foam Hand Sanitizer is in compliance with the FDA Final Tentative Monograph for OTC Hand Sanitizer preparations (leave-on sanitizers not requiring a rinse), and registered in Canada. Nobac Instant Foaming Hand Sanitizer is available in a 10X Concentrate, prepared and shipped from our FDA Registered Establishment, for dilution, addition of fragrance, and packaging in your FDA Registered Establishment, or the FDA Registered Establishment of your choice, under your name. We are currently filling orders for Nobac 10X Concentrate.

We've received numerous questions regarding Nobac, and the marketing environment for these types of products. Summarized below are some general answers:

What are the FDA Regulatory issues relating to Leave-On Antiseptic Products?

One question that folks will have 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 antiseptics. 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 we have confirmed it with FDA). Nobac Instant Hand Sanitizer 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 Mason Chemical has generated formulation specific efficacy data confirming Nobac, and is generating additional formulation specific efficacy data to support Nobac within industry practice guidelines, we may be required to generate additional efficacy data when the Monograph becomes final.

Now, the real issue is that FDA does not feel that the 1994 TFM includes hand sanitizers (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 sanitizer 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 sanitizers 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 to us 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 Sanitizers?

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, sterilizing 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 Sanitizers have demonstrated efficacy in real-world environments. When evaluated in Elementary School environments where the importance of proper hygiene practices including hand washing is taught and emphasized, the use of non-alcohol benzalkonium chloride-based leave-on instant hand sanitizers 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 Sanitizers?

Benzalkonium chloride based Hand Sanitizers have several distinct advantages over alcohol-based hand sanitizers. 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- Nobac benzalkonium chloride-based instant Hand Sanitizer is non-flammable. An internet search for alcohol-based Hand Sanitizers 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 sanitizers are effective for occasional use, but long-term, frequent use of the alcohol products can cause skin irritation. Alcohol solubilizes and strips away sebum and lipids that guard against bacterial infections of the skin. Extensive use of alcohol-based hand sanitizers 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 sanitizers stop working the instant they dry. The leading manufacturer of alcohol-based hand sanitizers claims that their product kills 99.99% of most common germs that may cause disease in as little as 15 seconds. Alcohol-based hand sanitizers dry in 8-10 seconds, and fall below the efficacious concentration of alcohol in seconds. It has been reported that alcohol-based hand sanitizers 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⁾. Nobac benzalkonium chloride-based hand sanitizer dries fast, but 10-15 seconds slower than alcohol-based hand sanitizers allowing more than the minimum contact time for complete efficacious coverage, including under fingernails. Additionally, benzalkonium chloride-based hand sanitizers deliver 2 to 4 hours of residual protection.

Published studies report that benzalkonium chloride-based hand sanitizers demonstrated greater sustained antibacterial activity than gelled alcohol-based hand sanitizers 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, an alcohol-based and alcohol-free benzalkonium chloride-based hand sanitizer were compared. In the study, subject's hands were repeatedly inoculated with bacteria followed by application of hand sanitizer, then evaluated for antimicrobial effectiveness. The antimicrobial efficacy of the alcohol-based hand sanitizer showed a markedly decreased antimicrobial efficacy with subsequent contamination and decontamination cycles, whereas the alcohol-free benzalkonium chloride-based hand sanitizer 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 sanitizer 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⁾.

In summary:

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

(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.