HAND SANITIZER TECHNOLOGY AND PROGRESS TOWARDS A MORE FUNCTIONAL CONCEPT (NIMBUDERM™)

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Introduction

It is well-known that the primary vector of transmission for disease causing pathogens is hand contact. Even when rigorous protocols for hand washing and hygiene are followed, pathogens present on any contact surface can easily recolonize recently sanitized hands. Health care settings in particular increasingly demonstrate the problems of pathogen transmission leading to nosocomial infections due to the number of the highly susceptible populations in health care facilities. Other problems associated with regulatory pressures are also demonstrated by the fact that Medicare is planning to no longer reimburse for hospital-acquired infections– particularly **MRSA**.

•USA Today reported in May 2006 that some hospitals are experiencing an increase of **MRSA** infections from 33% of all *Staphylococcus aureus* tested in 2000 to 75% in 2006.

•The CDC reports that nearly 4 per 1000 hospital discharges have acquired an **MRSA** infection, demonstrating a growing problem within the community from a community health perspective as well as a financial perspective.

•The Washington Post reports that a Pennsylvania hospital study indicated that 180 hospitals reporting nosocomial infections showed an additional billing of $2.3 billion of which only $614 million was collected from insurance.

Hand Sanitizer Technologies Available to Consumers and Health Care Providers

Sanitizer Type	Mechanism of Kill	Disadvantages
•Antibacterial Soaps (Triclosan)	Molecule attacks multiple targets within the bacterial cellular membrane and also inhibits the fatty acid synthesis during bacterial metabolism.	•Soap formulations with **Triclosan** as the active agent have shown high toxicity index ratings against infant dermal fibroblasts.
•Alcohol Based Gels	Denatures bacterial cellular components essential to function by fracturing the physical structure of the proteins that make up the major framework of the bacterial cell.	•Solutions with **alcohol** as the active agent do not persist and can leave the sanitized skin both dry and flaky.
•Iodine Solutions	Acts as an oxidizing agent by capturing electrons from all essential bacterial cellular components rendering said components non-operational.	•**Povidone-Iodine** solutions have been proven to show contact dermatitis in as little as 2% Iodine in solution in both allergy sensitive and non-allergy sensitive subjects and have been shown to inhibit human fibroblast growth.
•Hydrogen peroxide solutions	Acts as an oxidizing agent through free radical oxidation (super-oxide radical) by capturing electrons from all essential bacterial cellular components.	•**Hydrogen peroxide** solutions have shown a high toxicity index rating against keratinocytes.
•Quaternary ammonium compounds (quats)	Positively charged molecules disrupt layers of negatively charged bacterial membranes rendering cellular collapse due to intercellular osmotic pressure.	•Smaller molecularly chained **quats** (mono-quats) can sometimes be less effective than larger molecularly chained quats (poly-quats) against Gram – bacteria and fungal species.

•(References available upon request)

Competitive Advantages and Benefits of NimbuDerm™ Leave-On Skin Sanitizer

•**Effectiveness**-initial kill is greater than or equal to that of current alcohol based sanitizers on the market and is effective against a wide range of organisms including some viruses.

•**Persistence with a breathable layer**-provides a breathable bacterial barrier for at least 6 hours while being easily removed with common soaps and water.

A novel and useful improvement on existing hand sanitization technology is a leave-on skin sanitizer that continues to protect skin from bacterial colonization for hours after application. Continuing persistent protection of hands from colonization can interrupt pathogen transmission between caregiver and patient, between contaminated objects or surfaces and a person, and can prevent the contamination of a surface from a person that is not effectively sanitized. Quick-Med Technologies, Inc. (QMT) has developed an advanced "leave-on" skin sanitizer formulation by combining the immediate disinfection power of an alcohol-based product with the long-lasting antimicrobial persistence of an advanced bio-active polymer. Performance at the time of application matches that of common alcohol-based hand sanitizers; however, the **NimbuDerm** advanced antimicrobial polymer formulation also provides continuous persistent efficacy against microbial contamination for a prolonged period against a wide range pathogenic bacteria associated with nosocomial infections including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, as well as antibiotic-resistant organisms such as **MRSA** and **VRE** (up to 6 hours in laboratory testing, even after repeated rinsing with water).

The advanced **NimbuDerm** polymer is suitable for incorporation into various formulations and is compatible with common additives such as emollients (to help keep skin soft and hydrated), therapeutic nutrients, and other active ingredients. Antimicrobial skin care products formulated with **NimbuDerm** technology are the perfect choice for everyday use by both patients and health-care professionals seeking to reduce the spread of bacteria.

Initial Effectiveness of NimbuDerm™ Skin Sanitizer

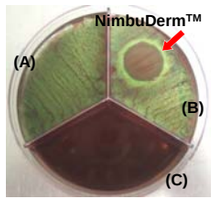


Figure 1

Figures 1 and 2. Left **(A)** and right **(B)** sections of agar plates display bacterial lawn of *E. coli*. Right **(B)** sections were inoculated with ~50 ul **NimbuDerm**, left sections **(A)** were left as negative controls, and the bottom sections **(C)** displayed the growth agar in its original state. The clear lack of growth on the **NimbuDerm** applied areas for both the EMB agar (left) and the WL nutrient agar (right) demonstrate both instantaneous kill and sustained microbicidal properties.

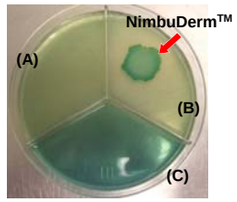


Figure 2

Bactericidal Persistence Efficacy of NimbuDerm™ Skin Sanitizer Versus a Leading Alcohol Based Hand Sanitizer After 4 Hours

Kill levels for:	% killed **NimbuDerm**	% killed alcohol based sanitizer
Staphylococcus aureus[1,2] (ATCC #6538)	>99.9999%	<0.0%
Escherichia coli[1,2] (ATCC #15597)	>99.9999%	<0.0%
Pseudomonas aeruginosa[1,2] (ATCC #15442)	>99.9999%	<0.0%
Serratia marcescens[1,2] (ATCC #13880)	>99.9999%	
MRSA[2] (ATCC #BAA-44)	>99.9999%	
Vancomycin Resistant Enterococcus (VRE)[2] (ATCC #700221)	>99.9999%	

Test method used was modified AOAC Use-Dilution Test (Reference 5) on [1]glass slide and/or [2]pig skin carriers at a 4 hour exposure - drying time for sanitizer ranged from 1 hour to 3 hours.

How NimbuDerm™ Works

NimbuDerm utilizes polymeric quaternary cationic microbicides and achieves its bactericidal activity by destabilization of the cell wall structures and by inducing cellular collapse without requiring entry of the antimicrobial agent into the cell itself.

NimbuDerm is unlikely to stimulate resistance in microbes based on their cell wall disruption mechanism and the ultimate large size of the molecule. Safety of these agents has been tested and was found to fall within acceptable irritation levels per ISO 10993 method.

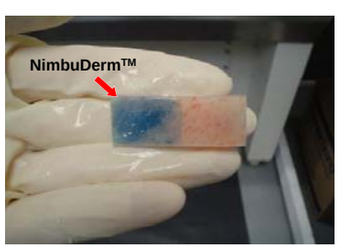


Figure 3 (left). Section of pig skin partially treated with **NimbuDerm** (left half). The skin section was rinsed after treatment, then had Bromothymol blue indicator dye applied and was rinsed again. Blue area represents coverage of the treatment due to the electrostatic interactions between the dye and **NimbuDerm**.

NimbuDerm™ Instant Effectiveness Versus a Leading Alcohol Based Hand Sanitizer

Contact Time vs. *P. aeruginosa* (ATCC #15442)	Average Log reduction, **NimbuDerm**	Average Log reduction, Alcohol Based Sanitizer
~1 second	2.16	0.88
~15 seconds	3.40	1.52
30 seconds	5.25*	2.24
1 minute	5.25*	2.20
3 minutes	5.25*	2.38
4 minutes	5.25*	4.43

*indicates full kill
Reference test methods 4, 5, and 6

Efficacy Results Using Human Subjects Demonstrating Rinsing** Persistence

% kill levels for *S. marcescens* (ATCC #14756)	Efficacy after 0 rinses	Efficacy after 1 rinse
NimbuDerm™ applied to subject 1	>99.9987%*	>99.9987%*
NimbuDerm™ applied to subject 2	>99.973%	>99.72%
NimbuDerm™ applied to subject 3	>99.9993%*	>99.9993%*

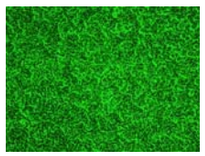
***indicates full kill**
****** Rinsing step includes 20X applications (~1 ml each) to sanitizer applied area from standard spray bottle.**

Antiviral Efficacy of NimbuDerm™ Skin Sanitizer

NimbuDerm Drying Time: Contact Time with MS-2 Bacteriophage	Inactivation efficacy
Drying time 0 minutes: 5 minute contact time	**99.93% Inactivation**

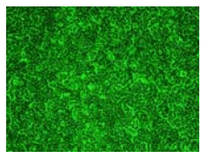
NimbuDerm Drying Time: Contact Time with Herpes Virus	Inactivation efficacy
Drying time 30 minutes: 5 minute contact time	**99.78% Inactivation**

NimbuDerm Drying Time: Contact Time with Poliovirus	Inactivation efficacy
Drying time 4 minutes: 5 minute contact time	**68.40% Inactivation**



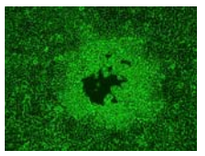
Cells before viral contact

Figure 4: Confluent monolayer of the Buffallo Green Monkey Cells (BGM) as positive control.



Viral protection by NimbuDerm

Figure 5: Undamaged cellular monolayer protected by the antiviral action of **NimbuDerm™**.



Viral infection without NimbuDerm

Figure 6: Plaque in BGM cell monolayer formed due to the Herpes virus infection.

Safety Testing

NimbuDerm™ formulation has been tested for skin irritation and was found to fall within acceptable irritation levels per ISO 10993 method. Other materials from the NIMBUS technological family have been extensively tested for a full suite of ISO 10993 and FDA biocompatibility assessments, and were found to be non irritating (skin irritation and eye irritation testing), as well as non-sensitizing, and not eliciting any systemic toxic response.

Referenced Test Methods

1. ASTM E 1874-97, "Standard Test Method for Evaluation of Antibacterial Washes by Cup Scrub Technique."
2. ASTM E 2315-03, "Standard Guide for Assessment of Antimicrobial Activity Using a Time-Kill Procedure."
3. ASTM E 1053-97, "Standard Test Method for Efficacy of Virucidal Agents Intended for Inanimate Environmental Surfaces."
4. ASTM 1153-03, "Standard Test Method for Efficacy of Sanitizers Recommended for Non-Food Contact Surfaces."
5. AOAC, Use-Dilution Test, (955.14, 955.15, and 964.02).
6. AATCC 100-2004, "Antibacterial Finsihes on Textile Materials: Assessment of."

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