



Chlorascrub™

PATIENT PREOPERATIVE & PREINJECTION* SKIN PREPARATION

Chlorhexidine Gluconate (3.15% w/v) and Isopropyl Alcohol (70% v/v)

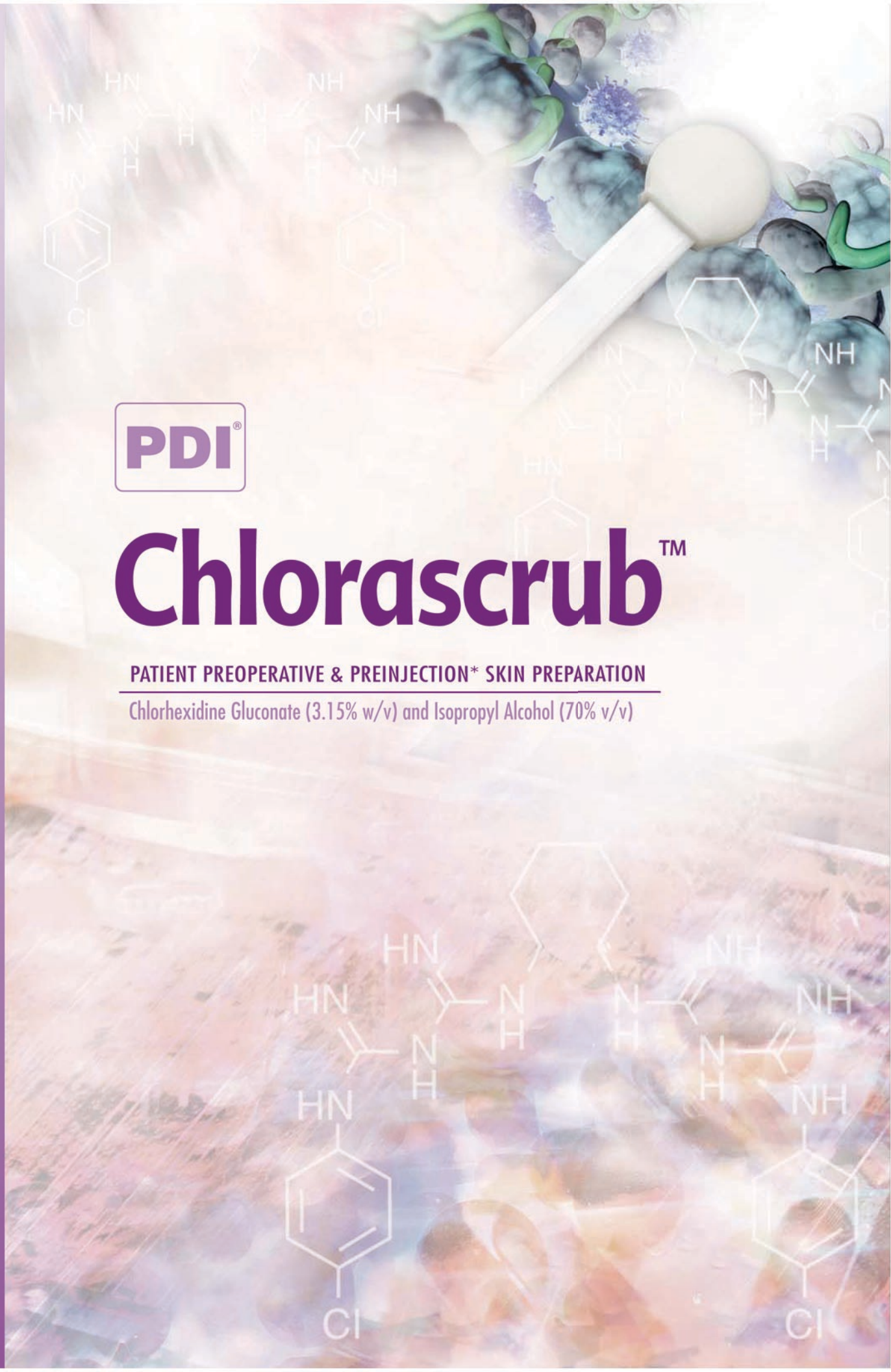


Table of Contents

Introduction	1
Chlorhexidine Gluconate Usage for Skin Antisepsis	1
Chlorascrub™ Skin Antiseptic Features	2
Properties and Comparison of Antiseptic Agents	3
Properties of 3.15% Chlorhexidine Gluconate and 70% Isopropyl Alcohol	3
Comparison of Antiseptic Agents	4
Chlorascrub™ Studies	5
In Vitro Studies	5
Time Kill Study	5
Minimum Inhibitory Concentration (MIC) study	5
List of Organisms Tested Susceptible to Chlorascrub™	6
Resistance Development	7
Summary of In Vitro Clinical Study Results	8
In Vivo Clinical Studies	9
Efficacy and Safety Study Comparison to IPA and 4% CHG	9
Maxi Swabstick Efficacy Study: Comparison to IPA and 4% CHG	12
Efficacy Study: Evaluation of Post-Application Wait Time	14
7-Day Persistence Study	16
Irritation Safety Study: Evaluation of a 14-Day Cumulative Irritation Patch Test	17
Sensitization Safety Study: Evaluation of a Repeated Insult Patch Test	18
Safety of Chlorascrub™	19

INTRODUCTION

CHLORHEXIDINE GLUCONATE USAGE FOR SKIN ANTISEPSIS

Chlorhexidine Gluconate (CHG) was first introduced in the United States in the 1970s as a handwashing agent for healthcare workers. Since that time, aqueous CHG agents have been widely used as an effective antiseptic handwashing and surgical scrub. The use of CHG for antiseptic skin prepping was studied by Maki et. al. in the early 1990s.¹ Dr. Maki compared the use of 2% aqueous CHG, 70% Alcohol, and 10% Povidone-Iodine (the most common iodophor) for skin prepping prior to surgical procedures. The results of this study showed that use of an aqueous 2% CHG substantially reduced the incidence of procedure-related infections. Another study by Mimoz et. al, showed Chlorhexidine was more efficacious than Povidone-Iodine skin preparation in reducing contamination of blood cultures.² In 2000, the first Chlorhexidine Gluconate [CHG] and 70% Isopropyl Alcohol [IPA] skin antiseptic was approved by the FDA in the United States. Since that time, antiseptic skin prepping agents that contain a combination of two antiseptics, CHG/IPA, are favored by clinicians.

*Many evidence-based studies
have been published showing that
CHG/IPA skin antiseptics
are effective in reducing infections.*

References:

¹Maki DG, Ringer M, Alvarado CJ. Prospective randomized trial of Povidone-Iodine, alcohol, and Chlorhexidine for prevention of infection associated with central venous and arterial catheters. *The Lancet* 1991; Vol. 338: 339-343.

²Mimoz O, Karim A, et al. Chlorhexidine compared with Povidone-Iodine as skin preparation before blood culture. *Annals of Internal Medicine* 1999; Vol.131; No. 11; 834-837.

CHLORASCRUB™ - SKIN ANTISEPTIC FEATURES

The unique formulation of Chlorascrub™ features a combination of two active ingredients: 3.15% Chlorhexidine Gluconate (w/v) and 70% Isopropyl Alcohol (v/v). Together, these ingredients kill most pathogens including bacteria, fungi/yeast and viruses. Chlorascrub™ was approved by the FDA on June 3, 2005 as a topical antiseptic for the preparation of skin prior to surgery (Swabstick and Maxi Swabstick) or injection (Swab, Swabstick and Maxi Swabstick).

User friendly delivery systems.

Chlorascrub™ is the only FDA approved 3.15% w/v CHG/70% v/v IPA and is available in three delivery systems: Swab, Swabstick and Maxi Swabstick. The Chlorascrub™ Swab is the only FDA approved CHG/IPA swab on the market and is available in individual packets for bedside applications and for inclusion in prepackaged kits. The Chlorascrub™ Swabstick and Maxi Swabstick are available in an easy to open peel apart package or tear open package for kits. Each Chlorascrub™ applicator is pre-saturated with the right amount of solution for delivery to the site. No activation is necessary. After application, the area prepped can be visualized by the appearance of a clear sheen marking the area prepped. The Chlorascrub™ Swab contains 1.0 mL of solution which provides coverage for a 2.5" x 2.5" area - (6.25 sq. in.). The Chlorascrub™ Swabstick contains 1.6 mL of solution. This provides coverage for a 4" x 4" area (16 sq. in.) for dry sites or 3" x 5" (15 sq. in.) for moist sites. The Maxi Swabstick contains 5.1 mL of solution. This provides coverage for a 7" x 7" area (49 sq. in.) for dry sites or 3" x 7.5" area (22.5 sq. in.) for moist sites. The foam tip applicators of the Swabstick and Maxi Swabstick design makes it easy to use and provides enough friction for scrubbing.

PROPERTIES AND COMPARISON OF ANTISEPTIC AGENTS

PROPERTIES OF 3.15% CHLORHEXIDINE GLUCONATE AND 70% ISOPROPYL ALCOHOL

The 3.15% Chlorhexidine Gluconate (CHG) and 70% Isopropyl Alcohol (IPA) formulation of Chlorascrub™ provides a fast kill time after application, long persistence, and broad spectrum antiseptis. Below is a summary of the main characteristics of Chlorascrub™.

Clinical studies have demonstrated that 60 seconds after application Chlorascrub™ Swabstick and Maxi Swabstick achieve a greater than 3 log₁₀ reduction, exceeding the FDA log reduction requirements for preoperative skin antiseptics. The Chlorascrub™ Swab achieve a greater than 2 log₁₀ reduction 30 seconds after application, thus exceeding the FDA requirements for preinjection. A 2% CHG and 70% IPA skin antiseptic achieved FDA requirements for preoperative skin antiseptics 10 minutes after application. Unlike 2% CHG and 70% IPA, there is no difference in prepping time for dry sites and moist (wet) sites using Chlorascrub™.

Combined prepping and drying time with Chlorascrub's™ unique formulation provides fast microbial kill thus greater log reduction.

The 3.15% CHG and 70% IPA solution of Chlorascrub™ is the first skin antiseptic product with a clinically proven persistent activity of 7 days. The persistent properties of 3.15% Chlorhexidine Gluconate and 70% IPA prevented the re-growth of microorganisms after a single application. This exceeds previous claims for persistence.

The risk of skin irritation with Chlorascrub™ is minimal. Clinical studies have determined that 3.15% CHG and 70% IPA solution is no more irritating than 2% CHG and 70% IPA. Clinical studies with both 2% CHG and 3.15% CHG and 70% IPA skin antiseptics show irritancy when used with an occlusive patch. An occlusive patch is a dressing that does not permit air and moisture vapor to permeate through the dressing material. Therefore use of non-occlusive, semi-permeable (transparent) dressing is recommended.

COMPARISON OF ANTISEPTIC AGENTS

Chlorascrub™ is a broad spectrum antiseptic that kills pathogens including most bacteria, fungi/yeast and viruses. The solution in a 1:10 dilution killed 99.9% of pathogenic microorganisms.

Table 1 below provides an overview of the properties and antimicrobial activity of several skin antiseptics that are utilized for patient prepping before surgery or other medical procedures.

TABLE 1

Properties and Antimicrobial Activity of Antiseptic Agents^{1,2}

Antiseptic	Mode of Action	Spectrum of Activity	Safety and Toxicity	Antimicrobial Activity		
				Kill Time	Residual, Persistent Activity	Inactivation by Blood or Body Fluids
Chlorascrub™ 3.15%CHG/ 70%IPA	Denatures proteins and disrupts cell membranes	GM+, GM-* bacteria, fungi, viruses	Minimal risk of skin irritation or sensitization. Minimal absorption.	Rapid	Excellent	No
2%CHG/70%IPA	Denatures proteins and disrupts cell membranes	GM+, GM- bacteria, fungi, viruses	Minimal risk of skin irritation or sensitization. Minimal absorption.	Rapid	Excellent	No
70% Alcohol	Denatures proteins	GM+, GM- bacteria, fungi, viruses	Minimal risk of skin irritation or sensitization. Skin dryness.	Rapid	None	No data
Chlorhexidine 2-4% Aqueous	Disrupts cell membranes	GM+, <GM- bacteria, <fungi, viruses	Minimal risk of skin irritation or sensitization. Minimal absorption.	Intermediate	Excellent	No
Iodine and Iodophors 10% PVP-I	Oxidizes cell membranes and cytoplasm	GM+, GM- bacteria, fungi, viruses	Moderate skin irritation or sensitization. Absorption with possible toxicity.	Intermediate	Minimal	Moderate to Inactive

Reference:

* GM + is gram positive bacteria, GM- is gram negative bacteria

^{1.} Denton GW. Chlorhexidine. In: Block SS, ed. *Disinfection, Sterilization, and Preservation*; 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2001:321-336.

^{2.} Larson, E. Guideline for use of topical antimicrobial agents. *Am J Infect Control*. 1988;16(6):253-266.

Chlorascrub™ STUDIES

IN VITRO STUDIES

Chlorascrub™ meets the requirements of the FDA's Tentative Final Monograph for Healthcare Antiseptic Drug Products. The following in vitro studies were performed to assess the antimicrobial activity of Chlorascrub™.

Time Kill Study

A time kill study was conducted to evaluate the efficacy of Chlorascrub™ against the following strains of bacteria:

Microorganism	Classification	ATCC#
Staphylococcus aureus	Gram positive	6538
Staphylococcus aureus	Gram positive	29213
Staphylococcus epidermidis	Gram positive	12228
Micrococcus luteus	Gram positive	7468
Enterococcus faecalis	Gram positive	29212
Escherichia coli	Gram negative	11229
Escherichia coli	Gram negative	25922
Pseudomonas aeruginosa	Gram negative	15442
Pseudomonas aeruginosa	Gram negative	27853
Serratia marcescens	Gram negative	14756

At a 1:10 dilution, Chlorascrub™ reduced the bacterial count by more than 99.9% in less than 3 minutes. The majority of the strains were killed immediately upon exposure to Chlorascrub™.¹

Minimum Inhibitory Concentration (MIC) Study

A MIC study was conducted to assess the in vitro efficacy of Chlorascrub™ against 1104 microorganisms. 1083 (98.1%) of the 1104 organisms tested, were inhibited by ≤50 µg/mL of Chlorascrub™ solution. A concentration of 50 µg/mL represents a 1:630 dilution of the 3.15% (w/v) topical solution. Therefore, Chlorascrub™ was effective against all the microorganisms listed in Table 2, including antibiotic resistant strains. Results are presented in Table 2.

References

¹. Data on file. Les Entreprises Solumed, Inc. Laval, Quebec, Canada.

TABLE 2

List of Organisms Tested Susceptible to Chlorascrub™

Species	Number of Strains	Minimum (µg/ml)	Maximum (µg/ml)	MIC50* (µg/ml)	MIC90* (µg/ml)
All Aerobic Strains Combined	896	0.20	200	16	64
All Gram-Negative Aerobic Strains Combined	448	0.78	200	32	64
All Gram-Positive Aerobic Strains Combined	448	0.20	100	8	16
A. ANITRATUS	17	6.25	50	16	32
A. BAUMANNII	28	6.25	50	32	64
A. LWOFFII	4	6.25	25	N.A.	N.A.
B. CEPACIA	21	12.50	200	64	128
E. AEROGENES	26	25	50	32	64
E. CLOACAE	26	0.78	50	32	64
E. COLI	51	0.78	13	4	4
E. COLI ESBL+	6	1.56	25	N.A.	N.A.
E. FAECALIS, VANCO RESISTANT	23	6.25	25	16	32
E. FAECALIS, VANCO SENSITIVE	31	3.13	25	16	16
E. FAECIUM, VANCO RESISTANT	26	3.13	13	8	8
E. FAECIUM, VANCO SENSITIVE	26	0.78	13	8	16
E. HIRAE	1	6.25	6	N.A.	N.A.
H. INFLUENZAE B-LACTAMASE NEGATIVE	28	6.25	25	16	32
H. INFLUENZAE B-LACTAMASE POSITIVE	28	6.25	50	16	32
K. OXYTOCA	11	12.50	50	32	64
K. OXYTOCA-ESBL+	5	6.25	50	N.A.	N.A.
K. PNEUMONIAE	16	6.25	50	32	64
K. PNEUMONIAE-ESBL+	5	6.25	25	N.A.	N.A.
M. LUTEUS	3	0.78	2	N.A.	N.A.
P. AERUGINOSA	36	6.25	50	32	32
P. AERUGINOSA, Cipro-R	15	25	50	32	64
P. MIRABILIS	36	6.25	100	32	64
P. VULGARIS	16	12.50	50	32	64
S. AGALACTIAE	53	1.56	13	8	8
S. AUREUS, METHICILLIN RESISTANT	53	0.78	6	4	8
S. AUREUS, METHICILLIN SUSCEPTIBLE	53	0.78	6	4	4
S. EPIDERMIDIS, METHICILLIN RESISTANT	13	1.56	6	4	8
S. EPIDERMIDIS, METHICILLIN SUSCEPTIBLE	16	1.56	6	4	4
S. HAEMOLYTICUS, METHICILLIN RESISTANT	21	0.78	6	4	8
S. HAEMOLYTICUS, METHICILLIN SENSITIVE	7	0.78	3	N.A.	N.A.
S. HOMINIS	5	0.78	2	N.A.	N.A.
S. MALTOPHILIA	21	0.78	100	64	64
S. MARCESCENS	51	3.13	100	64	64
S. PNEUMONIAE PEN INTERMEDIATE	17	12.50	100	32	128
S. PNEUMONIAE PEN RESISTANT	17	12.50	100	64	64
S. PNEUMONIAE PEN SENSITIVE	22	1.56	50	16	64
S. PYOGENES	51	0.20	6	4	8
S. SAPROPHYTICUS	11	0.20	2	1	1
Anaerobic Species					
All Anaerobic Strains Combined	99	0.78	200	16	32
B. FRAGILIS	55	6.25	200	16	32
B. THETAIOAOMICRON	19	6.25	200	16	>35
BACTEROIDES SPP.	13	6.25	100	16	32
P. BIVIA	11	0.78	13	8	8
E. LENTUM	1	25	25	N.A.	N.A.
Yeast Species					
All Yeast Strains Combined	109	3.13	50	16	32
C. ALBICANS	57	3.13	25	32	32
C. KRUSEI	17	6.25	50	16	32
C. PARAPSILOSIS	19	6.25	50	16	64
C. TROPICALIS	16	6.25	13	16	16
Total Number of Strains	1104				

*Actual MICs were rounded up to nearest 2 log¹⁰ dilution for calculating MIC50 and MIC90.

RESISTANCE DEVELOPMENT

The Chlorascrub™ MIC study shows that 98.1% of the 1104 organisms tested,¹ were inhibited by ≤ 50 $\mu\text{g/mL}$ of Chlorascrub™ solution. The tested pathogens included several antibiotic resistant strains.¹ The concentration of Chlorhexidine in Chlorascrub™ is 31,500 $\mu\text{g/mL}$, thereby far exceeding the 50 $\mu\text{g/mL}$ concentration.

Acquired resistance to Chlorhexidine is rare and has only been found when dilute aqueous solutions have been used for disinfection.² When used undiluted and as directed, Chlorascrub™ with its 3.15% (w/v) CHG and 70% (v/v) IPA concentrations is expected to be highly effective against most pathogens, including antibiotic resistant microorganisms.

Literature reports indicate that there is no evidence of increased resistance development after prolonged and extensive use of Chlorhexidine in clinical use concentrations.³

References

- ¹. Data on file. Les Entreprises Solumed, Inc. Laval, Quebec, Canada.
- ². Maki DG, Ringer M, Alvarado CJ. Prospective randomized trial of Povidone-Iodine, alcohol, and Chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet*. 1991;338:339-343.
- ³. Denton GW. Chlorhexidine. In: Block SS, ed. *Disinfection, Sterilization, and Preservation*; 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2001:321-336.

SUMMARY OF CLINICAL STUDY RESULTS

This brief summary explains the key results of the Chlorascrub™ clinical studies.

Chlorascrub™ Swabs reduce the microbial count on the forearm by greater than 2 log₁₀ 30 seconds after application. The greater than 2 log₁₀ reduction is maintained for at least 24 hours.

Chlorascrub™ Swabsticks and Maxi Swabsticks reduce the microbial count on the abdomen by greater than 2 log₁₀ 30 seconds after application. After 24 hours the microbial count reduction has increased to greater than 3 log₁₀. These results confirm the rapid-acting, effective and persistent antimicrobial activity of Chlorascrub™ on a dry site.

Chlorascrub™ Swabsticks and Maxi Swabsticks reduce the microbial count on the groin by greater than 3 log₁₀ 1 minute after application. The greater than 3 log₁₀ reduction is maintained for at least 24 hours. These results confirm the rapid-acting, effective and persistent antimicrobial activity of Chlorascrub™ on a wet site.

Chlorascrub™ Swabsticks and Maxi Swabsticks when applied to the forearm, abdomen and groin, maintain low bacterial count for 7 days.

IN VIVO CLINICAL STUDIES

Efficacy and Safety Study: Comparison to IPA and 4% CHG

A study was conducted to evaluate and compare the immediate and persistent antimicrobial activity of Chlorascrub™ 3.15% (w/v) Chlorhexidine Gluconate with 70% (v/v) Isopropyl Alcohol, 70% (v/v) Isopropyl Alcohol (active vehicle) and Hibiclens® (4% Chlorhexidine Gluconate, reference product) when used as an antimicrobial skin preparation prior to surgery or injection.¹ In addition, this randomized, parallel-group study evaluated and compared the safety of the products.

Methods

Healthy subjects of mixed age, gender, and race between 18 and 70 years of age, and with no evidence of dermatoses, inflammation or injury to the treatment areas were enrolled in the study. The skin preparations were tested on the forearm, on the abdomen, and in the groin (inguinal region). A minimum of 81 volunteers for the inguinal and 60 volunteers for the forearm and abdominal portions were employed, using bilateral applications. Bacterial counts of the subjects in the various treatment groups did not differ significantly at baseline.

Chlorascrub™ Swabsticks and Maxi Swabsticks were tested on the abdomen and in the groin to evaluate their efficacy for preoperative patient skin prepping. The abdominal and inguinal sites were prepped for 2 minutes, allowed to air dry for 1.5 minutes, and then evaluated at 30 seconds, 10 minutes, 6 hours, and 24 hours after skin prepping.

Chlorascrub™ Swabs were tested on the forearm to evaluate their efficacy for patient skin preparation prior to injection. The forearm sites were prepped for 15 seconds, allowed to air dry for 30 seconds and then evaluated at 30 seconds and 24 hours after prepping.

The CHG reference product was applied twice for 2 minutes followed by drying with a sterile towel for all three treatment sites (manufacturer's recommendation). Application of the active vehicle (IPA) was performed identically to the Chlorascrub™ products.

The *FDA Tentative Final Monograph for Health-Care Antiseptic Drug Products: Proposed Rule* published in the *Federal Register* of June 17, 1994 requires a:

- 2 log₁₀ reduction in CFU/cm² of skin on the abdomen and
- 3 log₁₀ reduction in CFU/cm² of skin on groin sites

Ten (10) minutes after drug application to approve a material as a preoperative skin preparation antiseptic. In addition, the microbial count (CFUs) from both sites must remain below the baseline CFU count for 6 hours.

The monograph also requires a 1 log₁₀ reduction in CFU/cm² of skin on a dry site (forearm or abdomen) thirty (30) seconds after application to approve an antiseptic for preinjection skin preparation.

Results

Chlorascrub™ Swabs produced a 2.70 log₁₀ reduction on the forearm 30 seconds after application, therefore, exceeding the monograph requirement of 1 log₁₀ reduction for preinjection skin preparation. At 24 hours after application the log₁₀ reduction was still at 2.55, confirming the persistent activity of Chlorascrub™ Swabs.

Chlorascrub™ Swabsticks and Maxi Swabsticks achieved the following microbial count reductions from average baseline on the abdomen:

- 2.79 log₁₀ reduction at 30 seconds post-application
- 2.86 log₁₀ reduction at 10 minutes post-application
- 2.83 log₁₀ reduction at 6 hours post-application
- 3.09 log₁₀ reduction at 24 hours post-application

Chlorascrub™ Swabsticks and Maxi Swabsticks exceeded the FDA requirements of a 1 log₁₀ reduction at 30 seconds for preinjection skin preparation and of a 2 log₁₀ reduction at 10 minutes for preoperative skin preparation on the abdomen. Chlorascrub™ reached a >2 log₁₀ reduction on the abdomen 30 seconds after application. After 24 hours microbial counts had further decreased to a >3 log₁₀ reduction, attesting to the persistent activity of Chlorascrub™.

On the groin, Chlorascrub™ Swabsticks and Maxi Swabsticks were the only products tested that achieved a >3 log₁₀ reduction at 10 minutes, 6 hours, and 24 hours post-prepping, therefore exceeding the FDA criteria. A post-application wait time of 30 seconds resulted in a 2.92 log₁₀ reduction that was just below the 3 log₁₀ requirement for patient preoperative skin preparation.

Chlorascrub™ was more efficacious than Isopropyl Alcohol alone. At 24 hours after initial prepping, a significant difference in microbial count was detected in the inguinal and abdominal test sites (p≤0.05).

Chlorascrub™ reduced microbial populations at a significantly lower level than did IPA. On the IPA-prepped sites, the populations were beginning to recover to baseline levels at 24 hours after prepping, while Chlorascrub™ continued to maintain a greater than 3 log₁₀ reduction.

No adverse events were reported during the study. Chlorascrub™ did not demonstrate any significant skin irritating properties.

A graphic representation of the study results can be seen in the charts below:

FIGURE 1

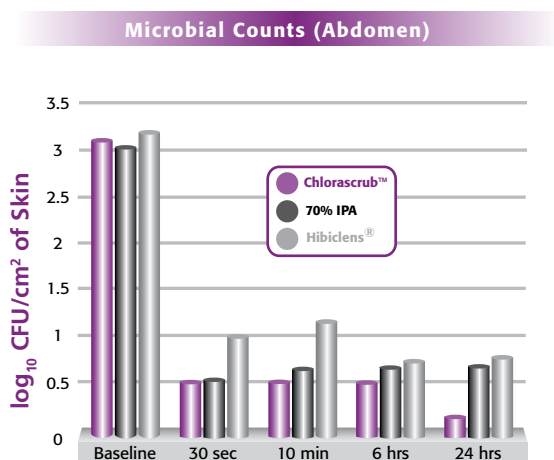
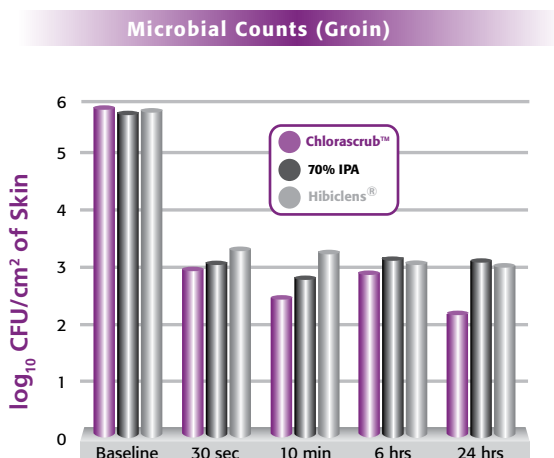


FIGURE 2



Conclusion

Chlorascrub™ was found to be safe and effective as a patient skin antimicrobial preparation for use prior to surgery and injection. Chlorascrub™ exceeds the FDA requirements in terms of wait time for full efficacy, microbial count reduction, and duration of antimicrobial activity. A microbial count reduction of 3.5 log₁₀ on the inguinal site after 24 hours verifies the product's excellent persistent activity. The >2 log₁₀ reduction on the abdomen and forearm 30 seconds after application attests to the fast and effective antimicrobial activity of Chlorascrub™.

Maxi Swabstick Efficacy Study: Comparison to IPA and 4% CHG

A study was conducted to evaluate and compare the immediate and persistent antimicrobial activity of Chlorascrub™ Maxi Swabsticks, Maxi Swabsticks Vehicle (70% (v/v) Isopropyl Alcohol), and Hibiclens® (4% (w/v) Chlorhexidine Gluconate, reference product) and to evaluate and compare the safety of all three test articles.¹

Methods

Healthy subjects of mixed age, gender, and race between 18 and 64 years of age, and with no evidence of dermatoses, inflammation or injury to the treatment areas were enrolled in the study. Bacterial counts of the subjects in the various treatment groups did not differ significantly at baseline. All skin preparations were tested in the groin (inguinal region). The subjects were randomized and 41 inguinal areas were treated and analyzed with each test preparation. Chlorascrub™ Maxi Swabstick (3.15% (w/v) CHG with 70% (v/v) IPA) was applied topically for 2 minutes over a 3 x 7.5 inch area on the groin and allowed to air dry for 1.5 minutes.

A Maxi Swabstick saturated with 5.1 mL of the 70% v/v IPA was applied topically for 2 minutes over a 3 x 7.5 inch area on the groin and allowed to air dry for 1.5 minutes. The CHG reference product was applied topically for 2 minutes over a 3 x 7.5 inch area on the groin and dried with a sterile towel and applied for another 2 minutes and dried with another sterile towel (per manufacturer's recommendation).

References

¹. Data on file. Les Entreprises Solumed, Inc. Laval, Quebec, Canada.

Results

For a Healthcare Antiseptic to be approved by the FDA for the indication of preoperative skin preparation, it must achieve a 3 log₁₀ reduction in microbial count (CFU)/cm² in the groin within 10 minutes of initial drug application. In addition, the microbial count must remain below the baseline CFU count for 6 hours.

Chlorascrub™ Maxi Swabsticks demonstrated significantly better antimicrobial activity than Maxi Swabsticks Vehicle (IPA) and the CHG reference product after antiseptic application at ten (10) minutes, six (6) hours and twenty four (24) hours (p≤0.05).

Treatment with Chlorascrub™ Maxi Swabsticks resulted in a 3.77 log₁₀ reduction at 10 minutes, increasing to a reduction in microbial count of 4.24 log₁₀ after 24 hours. The Maxi Swabsticks Vehicle (IPA) achieved the 3 log₁₀ reduction at 10 minutes however, the microbial load started rising and the product was not able to maintain the 3 log₁₀ reduction after 6 or 24 hours.

Only Chlorascrub™ Maxi Swabsticks and Maxi Swabsticks Vehicle (IPA) achieved the required 3 log₁₀ reduction at 10 minutes. For all products, the microbial counts remained below baseline at 6 hours.

TABLE 3

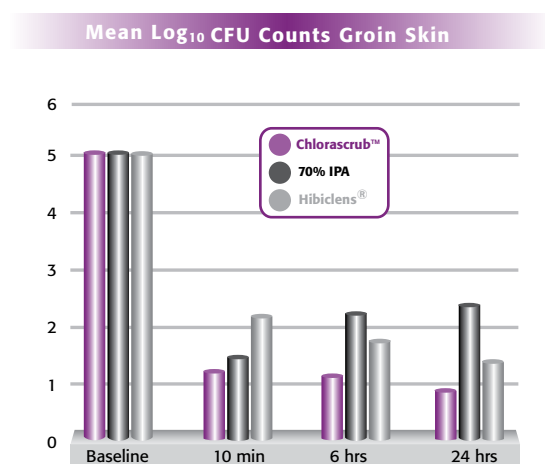
Summary of the log₁₀ Reductions Achieved on the Groin Sites

Product	Mean log ₁₀ Reductions from Baseline			
	N	10 Minutes	6 Hours	24 Hours
Chlorascrub™ Maxi Swabsticks	41	3.77	4.01	4.24
Maxi Swabsticks Vehicle (IPA)	41	3.48	2.78	2.57
CHG Reference Product	41	2.89	3.34	3.68

Conclusion

Chlorascrub™ Maxi Swabsticks exceeded the FDA criteria in the groin region for patient preoperative skin preparation. Chlorascrub™ Maxi Swabsticks demonstrated significantly greater antimicrobial activity than 70% (v/v) IPA; Maxi Swabsticks and the CHG reference product after antiseptic application at 10 minutes, 6 hours and 24 hours. Microbial counts decreased over the 24-hour period, confirming the highly persistent activity of Chlorascrub™.

FIGURE 3



No adverse events were reported during the course of the study.

Efficacy Study: Evaluation of Post-Application Wait Time

The FDA *Tentative Final Monograph for Healthcare Antiseptic Drug Products: Proposed Rule* published in the *Federal Register* of June 17, 1994 requires a 3 log₁₀ reduction in microbial count on groin sites ten (10) minutes after drug application to approve an antiseptic solution with the indication of preoperative skin antiseptics. In addition, the microbial counts (CFUs) must remain below the baseline CFU count for 6 hours.

In the clinical setting it is often not desired or even possible to wait the additional 10 minutes to assure that the product reaches the required 3 log₁₀ reduction. Therefore, this study was designed and conducted to determine the maximum wait time after application of Chlorascrub™ Maxi Swabsticks until the 3 log₁₀ reduction is achieved on the groin skin (inguinal area).¹

Methods

Healthy subjects of mixed age, gender, and race between 18 and 64 years of age, and with no evidence of dermatoses, inflammation or injury to the treatment areas were enrolled in the study.

Chlorascrub™ Maxi Swabstick (5.1 mL of 3.15% (w/v) CHG and 70% (v/v) IPA) was applied topically for two minutes over a 3 x 7.5 inch area on the groin using the following technique. The Chlorascrub™ Maxi Swabstick, a flat two-sided device with a foam tip was removed from the package with sterile gloves. One of the flat sides of the foam tip of Chlorascrub™ Maxi Swabstick was placed in the center of the 3 x 7.5 inch prep area. The skin was held taut and prepped vigorously in a rapid back and forth technique for one minute. The Swabstick was turned over and the unused side of the foam tip was used to prep the same area. The skin was held taut and prepped vigorously in a rapid back and forth technique for one minute. The area was again air dried for 1.5 minutes prior to beginning the contact time.

The inguinal sites were randomly sampled after the following post-application wait times: thirty (30) seconds, one (1) minute, three (3) minutes, and ten (10) minutes. The technicians responsible for plating and data collection were blinded as to the post-application sample time assignment.

References

¹. Data on file. Les Entreprises Solumed, Inc. Laval, Quebec, Canada.

Results

Chlorascrub™ Maxi Swabsticks significantly reduced the microbial count (CFU) in the groin at all time points.

Chlorascrub™ achieved a $>3 \log_{10}$ reduction after a wait time of one minute post-application. The mean \log_{10} reductions in CFU/cm² of groin skin are listed in Table 4 below.

TABLE 4

Microbial Count Reductions at Various Time Intervals After Chlorascrub™ Application in the Groin

	Wait Time After Application					
	30 sec.	1 min.	3 min.	5 min.	10 min. (left) a	10 min. (right) b
Mean \log_{10} Reduction	2.85	3.22	3.18	3.10	3.08	3.24

^A - left inguinal site; ^B - right inguinal site

Conclusion

Chlorascrub™ reduces the microbial count on the groin by more than $3 \log_{10}$ one minute after application, thus exceeding the ten (10) minute FDA required wait time in the groin region for approval as a patient preoperative skin preparation drug product.

References

¹. Data on file, Les Enterprise Solumed, Inc. Laval, Quebec Canada.

Chlorascrub™ 7-Day Persistence Data

Chlorascrub™ products combine the immediate antimicrobial activity of 70% (v/v) Isopropyl Alcohol with the persistent properties of 3.15% (w/v) Chlorhexidine Gluconate. This formulation results in a broad-spectrum skin antiseptic that is both fast acting and demonstrates a significant persistent log reduction. Chlorascrub™ kills transient and resident skin microorganisms rapidly and then prevents the recolonization of microorganisms.

A clinical study was performed to effectively evaluate the persistent properties of Chlorascrub™ Swabsticks and Maxi Swabsticks. The study was performed using a cross-over design that allows for exchangeability of the study results between the applicators. The treatment sites were covered with a semi-permeable dressing for the duration of the study to simulate actual clinical practice. The results are listed in Table 5 below:

TABLE 5

Mean log₁₀ Reductions After Skin Preparation with Chlorascrub™ Products

Treatment Site	Mean log ₁₀ Reductions from Baseline			
	30 seconds	10 minutes	48 hours	7 days
Abdomen	N/A	2.01 (N=24)	N/A	1.76 (N=23)
Inguen	N/A	3.29 (N=38)	3.07 (N=35)	1.51 (N=28)
Forearm	1.80 (N=33)	N/A	N/A	1.70 (N=28)

Conclusion

The study results confirm the long-lasting antimicrobial activity of Chlorascrub™ products. A single application of the Chlorascrub™ Swabstick or Maxi Swabstick is sufficient enough to produce a persistent log reduction for up to 7 days. Chlorascrub™ is the first skin antiseptic product with clinically proven persistent activity of 7 days.

Irritation Safety Study: Evaluation of a 14-Day Cumulative Irritation Patch Test

A skin irritation study was conducted to evaluate Chlorascrub™ for induction of skin irritation under occlusive dressing, semi-occlusive dressing, and open conditions (under no dressing).¹ Thirty-one subjects completed this single-center, blinded, randomized study.

Methods

The subjects received applications of test solutions consecutively for 14 days, every day for 14 days. The test solutions applied were:

- 3.15% (w/v) Chlorhexidine Gluconate in 70% (v/v) Isopropyl Alcohol (Chlorascrub™)
- 10% aqueous Povidone-Iodine solution (Betadine®)
- 70% (v/v) Isopropyl Alcohol
- 4% (w/v) aqueous Chlorhexidine Gluconate (Hibiclens®)
- Sodium Lauryl Sulfate (positive irritant control)
- 0.9% Sodium Chloride (saline, negative irritant control)

All tested solutions were applied under semi-occlusive and occlusive conditions. The solutions were applied to a patch pad and allowed to dry for a maximum of thirty (30) minutes prior to patch application to the subject. In addition, Chlorascrub™ was tested under open skin not covered by a dressing with the solution applied and massaged into the skin for thirty (30) seconds and allowed to air dry for thirty (30) seconds.

Results

Under semi-occlusive dressing, Chlorascrub™, 70% (v/v) Isopropyl Alcohol and 4% w/v CHG produced irritation equivalent to saline solution (negative irritant control) and equivalent to each other. Povidone-Iodine, however, produced significantly greater irritation.

Under total occlusion, both Chlorascrub™ and Povidone-Iodine were significantly more irritating than 70% (v/v) Isopropyl Alcohol, 4% (w/v) CHG and saline.

When Chlorascrub™ was applied without a dressing, it did not produce any irritation during the 14-day testing period.

In general, all test solutions, except Povidone-Iodine, produced more irritation under occlusive conditions than under semi occlusive conditions.

Conclusion

Chlorascrub™ has an irritation potential equivalent to saline solution when it is used under semi-occlusive conditions (clinical use conditions) for 14 days.

References

¹. Data on file. Les Entreprises Solumed, Inc. Laval, Quebec, Canada.

Sensitization Safety Study: Evaluation of a Repeated Insult Patch Test

A study was conducted with 210 volunteers to evaluate Chlorascrub™ for induction of contact sensitization.¹

Methods

Each subject received applications of both, Chlorascrub™ (3.15% (w/v) Chlorhexidine Gluconate in 70% (v/v) Isopropyl Alcohol) and saline solution (0.9% Sodium Chloride). Saline served as the negative control. Chlorascrub™ was tested under semi-occlusive and saline under occlusive conditions.

The products were applied ten (10) times during a twenty three (23) day period (induction period), followed by a rest period, and then were applied again at day thirty six (36), thirty eight (38) and forty (40) (challenge period).

Results

Under the semi-occlusive conditions of this study, Chlorascrub™ did not induce any sensitization. In addition, irritation elicited by Chlorascrub™ (under semi-occlusive conditions) was slightly less than that of saline under occlusive conditions.

Conclusion

Chlorascrub™ does not elicit evidence of sensitization when used under semi-occlusive conditions (clinical use conditions).

References

¹. Data on file. Les Entreprises Solumed, Inc. Laval, Quebec, Canada.

SAFETY OF Chlorascrub™

Chlorascrub™ clinical studies have demonstrated that there is only minimal risk of skin irritation under clinical use conditions (semi-occlusive).¹ To prevent irritation and achieve satisfactory clinical use conditions, it is important to:

- Let the treatment area dry completely before applying the dressing
- Use transparent, semi-permeable or gauze dressings (semi-permeable dressings are considered similar to a plain gauze dressing or a highly permeable dressing)

Like other products containing Chlorhexidine Gluconate, Chlorascrub™ should not be used in the following situations:

- Under occlusive dressings (which completely prevent air penetration through dressing material) because this can cause irritation.
- On premature or low birth weight infants or children less than two (2) months of age because of the potential for excessive skin irritation and increased drug absorption.¹ The permeable nature of a newborn's skin may increase the risk of absorption of Chlorhexidine Gluconate as compared to the skin of older children and adults. Chlorhexidine Gluconate is only minimally absorbed through mature skin.
- For lumbar puncture or in contact with the meninges.¹
- On patients with known allergies to Chlorhexidine Gluconate or Isopropyl Alcohol.² Chlorhexidine has an extremely low potential for sensitization reactions. Isolated cases of generalized allergic reactions have been reported in the literature.²
- On open wounds or as a general cleanser.
- Chlorascrub™ is for external use only. Keep it out of eyes, ears, mouth and mucous membranes, where it may cause serious or permanent injury if permitted to enter and remain. If such contact occurs, rinse immediately with cold water and call a doctor.

Like other alcohol containing topical antiseptics, Chlorascrub™ is a flammable solution and should be kept away from fire and flames. This product should not be used with electrocautery procedures.²

For external use only.²

Keep out of reach of children. If swallowed seek medical help or contact Poison Control Center right away.²

References

¹ Data on file, Les Entreprises Solumed, Inc., Laval, Quebec, Canada.

² Denton GW. Chlorhexidine. In: Block SS, ed. *Disinfection, Sterilization, and Preservation*; 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2001:321-336.



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*Chlorascrub swab is approved for preinjection use.