Target Product Information

3M™ SoluPrep™
Film-Forming Sterile Surgical Solution

August 1, 2018

1 Indications and Usage

3M™ SoluPrep™ Film-Forming Sterile Surgical Solution (3M CHG/IPA Prep) is indicated for use as a patient preoperative skin preparation, for preparation of the skin prior to surgery, and to help reduce bacteria that can potentially cause skin infection.

2 Dosage and Administration

Single use topical application:

10.5 mL applicator (Clear/Tint)

- For head, neck and small prep areas
- Sterile solution
- Applicator is sterile if package is intact
- Solution volume 10.5 mL / 0.36 fl. oz.
- Maximal treatment area for one applicator is approximately 13 in x 13 in. (178.8 in^2)

26 mL applicator (Tint)

- For large prep areas below the neck
- Sterile solution
- Applicator is sterile if package is intact
- Solution volume 26 mL / 0.9 fl. oz.
- Maximal treatment area for one applicator is approximately 19.5 in x 19.5 in. (387.5 in^2)

Directions (follow all directions for use)

- Discard the applicator after a single use along with any portion of the solution not required to cover the prepped area. It is not necessary to use the entire amount available.

Getting patient ready for solution:

- Use in well-ventilated area.
- Do not microwave or heat the solution applicator.
- Apply to clean, completely dry, residue-free, intact skin.
- When hair removal is necessary, use a surgical clipper on the morning of surgery. If a wet shave is used, thoroughly remove all soap residues.

Activating the applicator:

- Remove applicator from package; do not touch sponge.

For 26 mL Applicator:

- With sponge face parallel to the floor, press the cap end of the applicator. Solution will begin to flow into the sponge.
- Wait for fluid level to reach indicator line of applicator barrel.

For 10.5 mL Applicator:

- Grasp product by wrapping hand and fingers around the labeled portion of the applicator. Place thumb on the lever.
- With sponge face parallel to the floor, snap lever. Allow all fluid to flow into sponge.

When applying solution:

- Completely wet the treatment area with antiseptic.
- Dry surgical sites (e.g., abdomen or arm): Use repeated back-and-forth strokes for 30 seconds.
- Moist surgical sites (e.g., inguinal fold): Use repeated back-and-forth strokes for 2 minutes.
- Maximal treatment area for one 26 mL applicator is approximately 19.5 in x 19.5 in.
- Maximal treatment area for one 10.5 mL applicator is approximately 13 in x 13 in.
- Do not allow solution to pool; tuck prep towels to absorb solution, and then remove.
- Clean umbilicus with enclosed swabs when applicable. (Moisten swabs by pressing against solution-soaked sponge applicator.) (26 mL applicator only).
- Avoid getting solution into hairy areas. Wet hair is flammable. Hair may take up to 1 hour to dry.
- When prepping skin folds, toes, or fingers, use a sterile-gloved hand to hold skin apart until completely dry. Otherwise, skin may adhere to itself.

After applying solution:

- To reduce the risk of fire, wait until solution is completely dry (minimum of 3 minutes on hairless skin; up to 1 hour in hair).

While waiting for solution to completely dry:

- Do not drape or use ignition source (e.g., cautery, laser).
- Check for pooled solution. Use sterile gauze to soak up pooled solution. Do not blot because it may remove solution from skin.
- Remove wet materials from prep area. Replace if necessary.

After solution is completely dry:

- To reduce risk of fire, begin draping and/or using cautery only after solution is completely dry and all wet materials are removed.
- If incise drapes are used, apply directly to dry prep.
- Apply dressing following standard practices.

Other information for product with tint:

- The tint will slowly fade from the skin over time postoperatively. Alcohol may be used to remove the tint if desired.

3 Dosage Forms and Strengths

Antiseptic solution for topical delivery.

Active ingredients:
Chlorhexidine gluconate (CHG) 2% w/v
Isopropyl alcohol (IPA) 70% v/v

4 Contraindications

Do not use:

- on patients with known allergies to chlorhexidine gluconate or any other ingredient in this product.
- for lumbar puncture or in contact with the meninges.
- on open skin wounds or as a general skin cleanser.

5 Warnings and Precautions

FOR EXTERNAL USE ONLY. FLAMMABLE, KEEP AWAY FROM FIRE OR FLAME.

To reduce risk of fire; PREP CAREFULLY:

- Do not use 26 mL applicator for head and neck surgery.
- Do not use 26 mL applicator on an area smaller than 13 in x 13 in. Use a smaller applicator instead.
- Solution contains alcohol and gives off flammable vapors.
- Avoid getting solution into hairy areas. Wet hair is flammable. Hair may take up to 1 hour to dry.
- Do not drape or use ignition source (e.g., cautery, laser) until solution is completely dry (minimum of 3 minutes on hairless skin; up to 1 hour in hair).
- Do not allow solution to pool.
- Remove wet materials from prep area.

When using this product

- Keep out of eyes, ears, and mouth. May cause serious or permanent injury if permitted to enter and remain. If contact occurs, rinse with cold water right away and contact a doctor.
- Use with care in premature infants or infants under 2 months of age. These products may cause irritation and chemical burns. See Clinical Pharmacology section 12 regarding possible cutaneous absorption.

Stop use and ask a doctor if irritation, sensitization, or allergic reaction occurs. These may be signs of a serious condition.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

6 Adverse Reactions

A total of 1544 subjects received at least one treatment in the studies supporting approval: pivotal studies (one of the studies, a study of 169 subjects, was discontinued early due to technical and quality issues), the persistence study, the two coverage area and dry time studies, the two drape adhesion clinical studies and the three safety challenge studies. Exclusion criteria in trials included known hypersensitivity. Thirty-one (31) AEs (2%) were reported. Adverse events reported in the development program were typically related to the skin, mild to moderate in severity and similar to typical adverse events associated with this type of product. Nine moderate adverse events occurred in studies designed to evaluate safety under exaggerated conditions (see section 14, Human Safety Studies). Seven discontinuations occurred secondary to adverse events in the Human Safety Studies. A few (12) adverse events required treatment. All adverse results resolved or stabilized.

Skin irritation scores of 0 to 3 for categories of erythema, edema, rash and dryness were collected for many of the clinical studies. A skin irritation rating of 3 represented significant irritation and qualified as an adverse event. There was no skin irritation rating of 3 in any clinical study. Under wet conditions in one of the studies of drape adhesion, moderate reactions of erythema were seen with all surgical preparations including this NDA product.

7 Drug Interactions

Not applicable.

8 Use in Specific Populations

Pediatric Use:

Use with care in premature infants or infants under 2 months of age. These products may cause irritation or chemical burns or be detectable in the blood of infants. See section 12.

9 Drug Abuse and Dependence

Not applicable.

10 Overdosage

Not applicable.

11 Description

3M™ SoluPrep™ Film-Forming Sterile Surgical Solution is an antimicrobial skin preparation containing two active ingredients, 2% weight/volume (w/v) chlorhexidine gluconate (CHG) and 70% volume/volume (v/v) isopropyl alcohol (IPA), in combination with an acetyltri-n-butyl citrate, acrylate copolymer and purified water. The tinted solution also contains FD&C Blue #1 and FD&C Yellow #5.

3M™ SoluPrep™ Surgical Solution provides fast acting, broad-spectrum antimicrobial activity, and persistence up to 6-hours post-prep.

3M™ SoluPrep™ Surgical Solution is a film-forming, sterile patient preoperative skin preparation. Each 7130 unit dose applicator contains 0.9 fl oz (26 mL) of solution which covers 19.5 in x 19.5 in area (approximately from shoulder to groin in an average full size adult).

For procedures requiring less coverage, a smaller applicator is available (7133-Tinted or 7134-Clear). The smaller applicator size contains 0.36 fl oz (10.5 mL) of solution which covers an approximate 13 in x 13 in area.

12 Clinical Pharmacology

Chlorhexidine is a cationic biguanide that exhibits broad-spectrum antimicrobial activity, which is thought to be related to its ability to disrupt cell membranes of bacterial cells. Isopropyl alcohol is a secondary aliphatic alcohol that, at the proposed concentration of 70%, also exhibits antiseptic properties, most likely resulting from protein denaturation.

No clinical pharmacokinetic or pharmacodynamic studies have been conducted with the drug product formulation.

It is generally recognized that chlorhexidine is not or is only minimally absorbed through mature intact adult skin. Literature publications, generally of small numbers of subjects and generally of neonates, have demonstrated detectable CHG blood levels after topical exposure to CHG containing products for either bathing or catheter antisepsis[1,2,3,4]. The clinical significance is not known.

The systemic absorption of chlorhexidine after topical application of 3M CHG/IPA Prep was evaluated following a single application to 24 female and male adult subjects. Plasma concentrations of chlorhexidine were all below the level of quantitation (<1 ng/mL) following a topical application of four 26 mL 3M CHG/IPA Prep applicators to approximately 1550 in^2 (10,000 cm^2) surface area of intact skin.

The systemic absorption of isopropyl alcohol after topical application of 3M CHG/IPA Prep was not studied. Isopropyl alcohol is slightly absorbed, approximately 1% of the amount applied to the intact skin. In a published study[5], a different product containing 49.8% (w/w) isopropyl alcohol was applied to subjects aged 1 month to 23 years for a preoperative skin preparation resulting in detectable blood concentration of isopropyl alcohol ranging from 0.83 to 12.25 mg/L 1 hour after application.

13 Nonclinical Toxicology

Chlorhexidine gluconate and isopropyl alcohol both have long histories of use. No studies addressing the mutagenicity, carcinogenicity, or development/reproductive toxicity of the drug product formulation or its active ingredients were conducted in support of marketing of this drug product.

14 Clinical Studies

Pivotal Studies:

Three pivotal studies were conducted to evaluate the safety and antimicrobial efficacy of 3M CHG/IPA Prep on the abdominal and inguinal regions. One of these studies was discontinued prematurely due to technical and data quality issues; efficacy data were not evaluated.

In the pivotal randomized, third-party blind studies, efficacy was assessed from analyses of bacterial counts of cultures obtained from test sites on the abdominal and inguinal regions. The results from two pivotal studies are summarized in the table below.

Study 1

	3M CHG/IPA Prep, 10.5 mL, tinted	3M CHG/IPA Prep, 26 mL, tinted	Saline
Abdominal Region			
N	205	201	62
Responder rate*, % (95% CI)	81.5 (76.1, 86.8)	87.1 (82.4, 91.7)	0
Bacterial Count Reduction Mean (SD)**	2.66 (0.71)	2.74 (0.64)	0.64 (0.49)
Difference in Mean Compared to Saline***	1.96 (1.8, 2.12)	2.07 (1.91, 2.23)	
Inguinal Region			
N	204	203	59
Responder rate*, % (95% CI)	82.4 (77.1, 87.6)	79.8 (74.3, 85.3)	6.8 (0.4, 13.2)
Bacterial Count Reduction Mean (SD)**	3.98 (1.03)	3.89 (0.93)	1.34 (1.10)
Difference in Mean Compared to Saline***	2.64 (2.35, 2.93)	2.55 (2.27, 2.94)	

* Responder defined as a subject with 2-$\log_{10}/cm^2$ (abdominal region) and 3-$\log_{10}/cm^2$ (inguinal region) bacterial reduction at 10 minutes and for whom the skin flora did not return to baseline at 6 hours
** $\log_{10}/cm^2$ scale
*** This is the average treatment effect of test drug compared to saline. It is estimated from a linear regression of final bacterial count on treatment and baseline bacterial count

Study 2

	3M CHG/IPA Prep, 10.5 mL, clear	3M CHG/IPA Prep,10.5 mL with HEDTA, clear	Saline
Abdominal Region			
N	196	202	59
Responder rate*, % (95% CI)	81.1 (75.6, 86.6)	81.7 (76.3, 87.0)	8.5 NA
Bacterial Count Reduction Mean (SD)**	2.78 (0.94)	2.73 (1.00)	0.76 (0.81)
Difference in Mean Compared to Saline***	1.99 (1.73, 2.26)	2.03 (1.76,2.29)	
Inguinal Region			
N	208	209	61
Responder rate*, % (95% CI)	38.9 (32.3, 45.6)	46.9 (40.1, 53.7)	1.6 (NA)
Bacterial Count Reduction Mean (SD)**	2.84 (1.19)	2.99 (1.13)	1.01 (0.67)
Difference in Mean Compared to Saline***	1.9 (1.59, 2.2)	1.72 (1.42, 2.03)	

* Responder defined as a subject with 2-$\log_{10}/cm^2$ (abdominal region) and 3-$\log_{10}/cm^2$ (inguinal region) bacterial reduction at 10 minutes and for whom the skin flora did not return to baseline at 6 hours
** $\log_{10}/cm^2$ scale
*** This is the average treatment effect of test drug compared to saline. It is estimated from a linear regression of final bacterial count on treatment and baseline bacterial count

In the two pivotal studies to support safety and efficacy, no adverse events were reported in one study. In the other study, AEs reported were related to the skin, mild to moderate in severity and similar to typical adverse events associated with this type of product. All AEs resolved without sequelae though one subject required treatment.

Skin irritation scores for 0 to 3 for categories of erythema, edema, rash and dryness were collected prior to collection of the baseline, 10-minute and 6-hour post prep samples for the three pivotal studies. A skin irritation rating of 3 represented significant irritation and qualified as an adverse event. There was no skin irritation rating of 3 in any of the pivotal studies. Under wet conditions in one of the studies of drape adhesion, moderate reactions of erythema were seen with all surgical preparations including this NDA product.

Coverage Area and Dry Time Studies:
Two open-label clinical studies, one using the tinted 3M CHG/IPA Prep 10.5mL applicator and the other using the tinted 3M CHG/IPA Prep 26mL applicator, evaluated the treatment area coverage, dry time, IPA vapor dissipation (in the 3M CHG/IPA Prep 26mL applicator study only), ease of removability, and safety of tinted 3M CHG/IPA Prep when applied to areas of the back, arms and legs of healthy subjects. Each study included 16-20 subjects.

For both applicators sizes, the mean coverage per gram of product was similar, approximately 50 in^2/g. The mean dry time for both applicator sizes was under 2 minutes. Removability of 3M CHG/IPA Prep was considered moderate for 25 (73.5%) subjects and difficult for 9 (26.5%) subjects.

- The mean coverage area with the 26 mL applicator was 387.5 (31.96) in^2 or 2499.8 (206.2) cm^2. The mean dry time was 1.54 (0.79) minutes.
- The mean (SD) coverage area with the 10.5 mL applicator was 178.8 (16.8) in^2 or 1153.7 (108.7) cm^2. The mean (SD) dry time was 1.80 (0.48) minutes.

Collection of IPA vapor in the 3M CHG/IPA Prep 26 mL study yielded a mean maximum alcohol concentration of 18.6 ppm; all individual values were well below the lower flammability limit (LFL) of 23,000 ppm.

A laboratory study was performed to determine the dry time of 3M CHG/IPA Prep (from 10.5 mL and 26 mL applicators) on human hair (using mannequins), as well as vapor dissipation values and ignition potential. Twelve human hair mannequins were used in this study that was performed under surgical suite conditions.

The mean weight of prep delivered was:
- 2.95 g for the 10.5 mL applicator
- 9.16 g for the 26 mL applicator

The mean dry time of prep was:
- 29.17 minutes for the 10.5 mL applicator
- 40.83 minutes for the 26 mL applicator

Collection of IPA vapor yielded a mean maximum IPA concentration of:

- 1097.8 ppm for the 10.5 mL applicator
- 4117.3 ppm for the 26 mL applicator

All individual maximum values for both applicator size was well below the LFL of 23,000 ppm.

For each applicator size, a mannequin head with dried prep was tested for ignition capability; on each of these heads, the hair did not ignite with multiple attempts using a sparking device.

In vitro studies:
Two in vitro studies using a modified time-kill procedure were conducted to examine microbial activity with and without the presence of serum, and one in vitro study was conducted to examine the potential of antimicrobial resistance.

In the first **time-kill study** (Table 1), both tinted and colorless 3M CHG/IPA Prep products (at full strength and at 50% strength) showed >5 $\log_{10}$ reductions at both the 3-minute and 5-minute time points for all microorganisms tested, thus meeting the efficacy criterion of a 3 $\log_{10}$ or greater reduction required by the FDA.

In the second **time-kill study** (Table 2), **in the presence of a serum challenge**, both tinted and colorless 3M CHG/IPA Prep products showed >5 $\log_{10}$ reductions at both the 3-minute and 5-minute timepoints for all microorganisms tested, again meeting the efficacy criterion of a 3 $\log_{10}$ or greater reduction.

The development of antimicrobial resistance study (Table 3) was designed to detect the potential for development of resistance to the test product (tinted 3M CHG/IPA Prep) and a control product (2% aqueous CHG) by the sequential passage of several clinically relevant microorganisms (42 isolates) through increasing concentrations of the antimicrobial included in the culture media. If the microorganisms were able to acclimate to at least a 4-fold increase in the initial MIC of the test product or control product and maintain that increase after 3 serial passages on media that did not contain the antimicrobial, resistance to the product was to have been established. The MIC did not increase for any of the strains evaluated for emergence of resistance; therefore, tinted 3M CHG/IPA Prep and the control 2% aqueous CHG were not considered to have the potential for the development of resistance. In addition, an evaluation of the potential for antibiotic cross-resistance was done by comparing the MICs of several antibiotics before and after extended exposure to sublethal levels of each antiseptic. There was no indication of a change in MIC related to cross-resistance observed for any of the organism/antibiotic combinations tested.

Note: The clinical significance of in vitro data is unknown.

Table 1. Microbial Kill for 3M CHG/IPA Prep Solution

Full-strength Test Product and Active Control Product Average Bacterial Counts and Reductions at Specific Contact Times

Microorganism	Contact Time	3M CHG/IPA Prep, Tint			3M CHG/IPA Prep, Colorless		
		Average CFU/mL	Percent Reduction	Log Reduction	Average CFU/mL	Percent Reduction	Log Reduction
Burkholderia cepacia	3 min	1.0E+01	99.99986	5.87	1.0E+01	99.99986	5.87
	5 min	1.0E+01	99.99984	5.84	1.0E+01	99.99984	5.84
Drug-resistant *Burkholderia cepacia*	3 min	1.0E+01	99.99978	5.67	1.0E+01	99.99978	5.67
	5 min	1.0E+01	99.99981	5.74	1.0E+01	99.99981	5.74
Candida albicans	3 min	1.0E+01	99.99978	5.75	1.0E+01	99.99978	5.75
	5 min	1.0E+01	99.99977	5.75	1.0E+01	99.99977	5.75
Drug-resistant *Candida albicans*	3 min	1.0E+01	99.99941	5.27	1.0E+01	99.99941	5.27
	5 min	1.0E+01	99.99938	5.25	1.0E+01	99.99938	5.25
Enterococcus faecalis	3 min	1.0E+01	99.99980	5.70	1.0E+01	99.99980	5.70
	5 min	1.0E+01	99.99979	5.69	1.0E+01	99.99979	5.69
Drug-resistant *Enterococcus faecalis*	3 min	1.0E+01	99.99974	5.70	1.0E+01	99.99974	5.70
	5 min	1.0E+01	99.99976	5.73	1.0E+01	99.99976	5.73
Enterococcus faecium	3 min	1.0E+01	99.99983	5.83	1.0E+01	99.99983	5.83
	5 min	1.0E+01	99.99982	5.82	1.0E+01	99.99982	5.82
Drug-resistant *Enterococcus faecium*	3 min	1.0E+01	99.99976	5.68	1.0E+01	99.99976	5.68
	5 min	1.0E+01	99.99973	5.65	1.0E+01	99.99973	5.65
Escherichia coli	3 min	1.0E+01	3M 99.99984	5.93	1.0E+01	99.99984	5.93
	5 min	1.0E+01	99.99984	5.93	1.0E+01	99.99984	5.93
Drug-resistant *Escherichia coli*	3 min	1.0E+01	99.99974	5.64	1.0E+01	99.99974	5.64
	5 min	1.0E+01	99.99975	5.67	1.0E+01	99.99975	5.67
Klebsiella pneumoniae	3 min	1.0E+01	99.99983	5.84	1.0E+01	99.99983	5.84
	5 min	1.0E+01	99.99978	5.78	1.0E+01	99.99978	5.78
Drug-resistant *Klebsiella*	3 min	1.0E+01	99.99983	5.78	1.0E+01	99.99983	5.78
	5 min	1.0E+01	99.99983	5.78	1.0E+01	99.99983	5.78

pneumoniae							
Pseudomonas aeruginosa	3 min	1.0E+01	99.99978	5.81	1.0E+01	99.99978	5.81
	5 min	1.0E+01	99.99977	5.79	1.0E+01	99.99977	5.79
Drug-resistant *Pseudomonas aeruginosa*	3 min	1.0E+01	99.99987	5.92	1.0E+01	99.99987	5.92
	5 min	1.0E+01	99.99987	5.92	1.0E+01	99.99987	5.92
Serratia marcescens	3 min	1.0E+01	99.99969	5.69	1.0E+01	99.99969	5.69
	5 min	1.0E+01	99.99971	5.69	1.0E+01	99.99971	5.69
Drug-resistant *Serratia marcescens*	3 min	1.0E+01	99.99977	5.73	1.0E+01	99.99977	5.73
	5 min	1.0E+01	99.99978	5.75	1.0E+01	99.99978	5.75
Staphylococcus aureus	3 min	1.0E+01	99.99974	5.59	1.0E+01	99.99974	5.59
	5 min	1.0E+01	99.99974	5.58	1.0E+01	99.99974	5.58
Drug-resistant *Staphylococcus aureus*	3 min	1.0E+01	99.99973	5.59	1.0E+01	99.99973	5.59
	5 min	1.0E+01	99.99974	5.62	1.0E+01	99.99974	5.62
Staphylococcus epidermidis	3 min	1.0E+01	99.99988	5.97	1.0E+01	99.99988	5.97
	5 min	1.0E+01	99.99988	5.96	1.0E+01	99.99988	5.96
Drug-resistant *Staphylococcus epidermidis*	3 min	1.0E+01	99.99980	5.73	1.0E+01	99.99980	5.73
	5 min	1.0E+01	99.99978	5.67	1.0E+01	99.99978	5.67
Streptococcus pneumoniae	3 min	1.0E+01	99.99944	5.30	1.0E+01	99.99944	5.30
	5 min	1.0E+01	99.99944	5.30	1.0E+01	99.99944	5.30
Drug-resistant *Streptococcus pneumoniae*	3 min	1.0E+01	99.99968	5.57	1.0E+01	99.99968	5.57
	5 min	1.0E+01	99.99970	5.60	1.0E+01	99.99970	5.60
Streptococcus pyogenes	3 min	1.0E+01	99.99983	5.81	1.0E+01	99.99983	5.81
	5 min	1.0E+01	99.99984	5.83	1.0E+01	99.99984	5.83
Drug-resistant *Streptococcus pyogenes*	3 min	1.0E+01	99.99957	5.39	1.0E+01	99.99957	5.39
	5 min	1.0E+01	99.99953	5.34	1.0E+01	99.99953	5.34

Abbreviations: CFU=colony-forming units; E=x10 with an exponent of; min=minute

Table 2. Microbial Kill with Serum Challenge for SoluPrep Solution

Average Control Bacterial Counts and Test Product Bacterial Counts and Reductions at Specific Contact Times

Microorganism	ATCC No.	Contact Time	Control (Initial) Count	Tinted 3M CHG/IPA Prep			Colorless 3M CHG/IPA Prep		
			Average CFU/mL	Average CFU/mL	Percent Reduction	Log Reduction	Average CFU/mL	Percent Reduction	Log Reduction
Multidrug-resistant *Escherichia coli*	BAA-197	3 min	7.8E+06	<1.0E+01	>99.99987	>5.89	<1.0E+01	>99.99987	>5.89
		5 min	7.8E+06	<1.0E+01	>99.99987	>5.89	<1.0E+01	>99.99987	>5.89
Multidrug-resistant *Escherichia coli*	BAA-200	3 min	1.4E+07	<1.0E+01	>99.99993	>6.13	<1.0E+01	>99.99993	>6.13
		5 min	1.2E+07	<1.0E+01	>99.99992	>6.08	<1.0E+01	>99.99992	>6.08
Methicillin-resistant *Staphylococcus aureus*	33591	3 min	4.6E+06	<1.0E+01	>99.99978	>5.66	<1.0E+01	>99.99978	>5.66
		5 min	4.8E+06	<1.0E+01	>99.99979	>5.68	<1.0E+01	>99.99979	>5.68
Methicillin-resistant *Staphylococcus aureus*	33592	3 min	9.0E+06	<1.0E+01	>99.99989	>5.95	<1.0E+01	>99.99989	>5.95
		5 min	1.3E+07	<1.0E+01	>99.99992	>6.10	<1.0E+01	>99.99992	>6.10
Methicillin-resistant *Staphylococcus epidermidis*	51625	3 min	8.5E+06	<1.0E+01	>99.99988	>5.93	<1.0E+01	>99.99988	>5.93
		5 min	1.3E+07	<1.0E+01	>99.99992	>6.10	<1.0E+01	>99.99992	>6.10
Multidrug-resistant *Staphylococcus epidermidis*	700563	3 min	7.1E+06	<1.0E+01	>99.99986	>5.85	<1.0E+01	>99.99986	>5.85
		5 min	6.6E+06	<1.0E+01	>99.99985	>5.82	<1.0E+01	>99.99985	>5.82

Abbreviations: ATCC No.=the identification number of the official bacterial strain; CFU=colony-forming units; E=x10 with an exponent of; min=minute

Note: Control (initial) count was the count in the dilution blanks that were inoculated, plated, and incubated along with the test products at each time point. The log10 reduction was calculated by subtracting the log10 recovery of each test product from the log10 recovery of the control (initial) count at each time point.

Table 3. Antimicrobial Resistance and Cross-resistance

A total of 42 isolates were evaluated.

ATCC Challenge microorganisms:
Ten repository isolates from eight species were evaluated:
• Methicillin-resistant *Staphylococcus aureus* (MRSA), ATCC 33591 • Methicillin-sensitive *Staphylococcus aureus* (MSSA), ATCC 25923 • Methicillin-resistant *Staphylococcus epidermidis* (MRSE), ATCC 51625 • Vancomycin-resistant *Enterococcus faecalis* (VRE), ATCC 51299 • *Acinetobacter baumannii*, ATCC 17904 • *Burkholderia cepacia*, ATCC 25608 • *Escherichia coli*, ATCC 11229 • *Pseudomonas aeruginosa*, ATCC 15442 • *Serratia marcescens*, ATCC 14756 • Multi-Drug Resistant (MDR) *Serratia marcescens*, ATCC 43297
Clinical Challenge microorganisms:
Eight clinical isolate species, 2 resistant and 2 nonresistant, per species were evaluated:
• *Staphylococcus aureus* • *Staphylococcus epidermidis* • *Enterococcus faecalis* • *Acinetobacter baumannii* • *Burkholderia cepacia* • *Escherichia coli* • *Pseudomonas aeruginosa* • *Serratia marcescens*

Human Safety Studies:

Three clinical safety studies were performed under exaggerated but controlled conditions to assess the cumulative irritation potential, allergic contact sensitization potential, phototoxic potential, photoallergic potential, and photoirritant potential of 3M CHG/IPA Prep compared to positive and negative controls.

The objective of the **cumulative irritation patch (21-day) with challenge trial** is to determine by repetitive epidermal contact the primary or cumulative irritation potential of the test materials compared to the positive control and a marketed active control.

For the 205 evaluable subjects over all product test sites, the individual observed erythema scores ranged from 0 (no visible erythema) to 3 (marked erythema). Individual cumulative irritation test (CIT) scores for evaluable subjects ranged from 0 to 34.5 for colorless 3M CHG/IPA Prep and 0 to 36 for tinted 3M CHG/IPA Prep. An overall CIT score was generated for each study product by adding up the erythema scores on the product test sites for all evaluable subjects during the cumulative irritation induction phase. For evaluable subjects, colorless 3M CHG/IPA Prep and tinted 3M CHG/IPA Prep had overall CIT scores (1716.5 and

1937.0, respectively) that categorized them as products that would be probably mild in normal use.

There were 14 adverse events in 9 subjects and no serious adverse events during the clinical trial. Five adverse events in one subject were judged to be related and the other 7 adverse events in 7 subjects to be unlikely related to the investigational products or marketed active control. Of the 14 adverse events, 9 were moderate, and 5 were mild in severity. All of the events resolved. In this clinical trial, both investigational products appeared safe and well tolerated.

The objective of the clinical evaluation to assess **phototoxicity potential trial** was to determine the phototoxicity potential in human subjects of two investigational products, 3M CHG/IPA Prep colorless and tint, and a marketed active control product.

Evaluation scores remained within normal limits for the investigational products and the marketed active control throughout the clinical trial. Because observations remained within normal limits throughout the trial, there was no indication of phototoxic contact dermatitis observed at any time during the course of the trial. During the course of this study there were no adverse events and there were no clinically significant changes in vital signs. The investigational products were safe and well tolerated.

The primary objective of the clinical evaluation of **photoallergy potential trial** was to determine by repetitive epidermal contact and UV radiation, the photoallergic potential of a test material when applied to human subjects. The secondary objective of this trial is to determine by repetitive epidermal contact and UV radiation, the photo irritant potential of a test material when applied to human subjects.

The observations remained within normal limits throughout the Induction Phase and the Challenge Phase for both investigational products and for the marketed active control. The evaluation scores during the Induction Phase are consistent with the twice the minimum erythema dose (MED) of UV full spectrum irradiation. Similarly, the evaluation scores during the Challenge Phase are lower, consistent with half the MED of full spectrum irradiation and 16 Joules.cm^2 of UVA radiation.

Under the conditions of this trial, the investigational products 3M CHG/IPA Prep colorless and tint, did not induce a response indicative of irritant contact dermatitis, allergic contact dermatitis, photoallergic contact dermatitis, or phototoxic contact dermatitis.

15 References

1. Garland JS, Alex CP, Uhing MR, Peterside IE, Rentz A, and Harris MC. Pilot trial to compare tolerance of chlorhexidine gluconate to povidone-iodine antisepsis for central venous catheter placement in neonates. J Perinatol. 2009;29(12):808–813.

2. Chapman, AK, Aucott SW, Gilmore MM, et al. Absorption and tolerability of aqueous chlorhexidine gluconate used for skin antisepsis prior to catheter insertion in preterm neonates. J Perinatol. 2013;33:768-771.

3. Chapman AK, Aucott SW, and Milstone AM. Safety of chlorhexidine gluconate for skin antisepsis in the preterm infant. J Perinatol. 2012;32(1):4-9.

4. Lee A, Harlan R, Bread AR, et al. Blood concentrations of chlorhexidine in hospitalized children undergoing daily chlorhexidine bathing. Infect Control Hosp Epidemiol. 2011;32(4):395-397.

5. Wittmann S, Gilg T, Dietz HG, et al. Isopropanol and acetone serum levels after presurgical disinfection with isopropanol containing antiseptics. Blutalkohol. 1992;291:326-335.

16 How Supplied/Storage and Handling

Single Use Applicator

10.5 mL applicator (Clear/Tint)

- Solution volume 10.5 ml / 0.36 fl.oz.

26 mL applicator (Tint)

- Solution volume 26 mL / 0.9 fl.oz.

Active ingredients:
Chlorhexidine gluconate (CHG) 2% w/v
Isopropyl alcohol (IPA) 70% v/v

Inactive ingredients (Tinted):
acetyltri-n-butyl citrate, acrylate copolymer, FD&C blue #1, FD&C yellow #5, purified water USP, Trisodium HEDTA

Inactive ingredients (Clear):
acetyltri-n-butyl citrate, acrylate copolymer, purified water USP, Trisodium HEDTA

Storage and Handling:

- Store between 15-30ºC (59-86ºF)
- Avoid freezing and excessive heat above 40ºC (104ºF)

17 Patient Counseling Information

3M recommends all users participate in product in-service training prior to use.
In-servicing is available on video, from your 3M sales representative, or at the 3M website (www.3M.com).