SoluPrep™
Brand

Summary of Clinical Studies for Professional Healthcare Use Approval in Canada

3M™ SoluPrep™ 2% chlorhexidine gluconate (CHG) and 70% isopropyl alcohol (IPA)

Preoperative Skin Antiseptic

May 2018

Optimal protection

To help protect patients and the public, Health Canada has developed a guidance document (2009), Human-Use Antiseptic Drugs,[1] that outlines the safety and efficacy requirements manufacturers must achieve in order to meet the regulatory standards for licensure in Canada.

Human-Use Antiseptic Drugs Guidance Document

Safety and efficacy requirements

Regulatory standards for licensure in Canada

The guidance document defines

1. test methods
2. test organisms
3. data requirements
4. and labeling required for product submission/ authorization in Canada.

Skin antiseptics licensed for use in Canadian healthcare facilities must meet even more rigorous standards in order to be authorized as a professional healthcare use product. This rigour provides optimal protection for patients who are exposed to high-risk environments and organisms, and for whom the safety risk is highest. Health Canada's guidance document helps healthcare professionals comply with governing statutes and regulations, and aids them in choosing skin antiseptic products. Antiseptic products for professional healthcare use are those indicated to reduce transient and/or resident organisms on the skin in a healthcare setting such as hospitals, nursing homes, clinics, dental offices.

in vitro studies

in vivo studies

conducted for 3M by independent and different clinical research organizations

After implementation of this guidance by Health Canada, 3M Canada has performed comprehensive *in vitro* and *in vivo* studies to support the efficacy and safety of the 3M™ SoluPrep™ Brand Drug Products. All of these studies were conducted for 3M by independent and different clinical research organizations.

3M | SoluPrep™ Brand

Safety and efficacy criteria – Health Canada Human-Use Antiseptic Drugs Guidance Document[1]

The following table is a summary of the safety and efficacy requirements a product must meet to be authorized for use in Canada as a patient preoperative skin preparation.

Type of Data	Test Method and Acceptable Criteria
Safety	a) published or unpublished safety data testing local tolerance, such as • irritation and sensitization (in the presence and absence of UV exposure when this is likely to be a risk factor) and preferably conducted in human species; • photoallergenicity; and • photocarcinogenicity, etc. b) When evidence is not available to show that topically-applied medicinal ingredients are not absorbed systemically to a significant degree, toxicity data should be submitted. c) Safety tests for (a) and (b) should be performed in accordance with relevant internationally-accepted test methods (e.g. OECD, ICH) (Page 9)
Efficacy – *in vitro*	a) EN 13727 – Bactericidal activity • ≥ 5 $\log_{10}$ reduction after 60 minutes  b) EN 13624 – Fungicidal activity • ≥ 4 $\log_{10}$ reduction after 60 minutes  (Pages 33–38)

Type of Data	Test Method and Acceptable Criteria
Efficacy – *in vivo*	c) ASTM E1173 – Bactericidal activity • ≥ 2 $\log_{10}$ reduction (dry site/abdomen) and 3 $\log_{10}$ reduction (moist site/inguinal) after 30 seconds at a power of 80% and alpha of 5%; • Test product $\log_{10}$ reduction ≥ reference product (60% n-propanol); and • Persistent activity for ≥ 6 hours. d) ASTM E2613 – Fungicidal activity • ≥ 2 $\log_{10}$ reduction on dry (abdomen) and moist (inguinal) sites after 30 seconds at a power of 80% and alpha of 5%; • Test product $\log_{10}$ reduction ≥ reference product (60% n-propanol); and • Persistent activity for ≥ 6 hours. (Pages 33–38)
Efficacy – General requirements	*In vivo* tests • For non-surrogate test organisms: one independent test report, which proves the antiseptic activity of a product. • Each *in vivo* test report should include three separate lots of product. • Tests should be performed with sufficient subjects per tested product to satisfy the statistical criteria of the clinical trial design. **Test reports should include at a minimum** • identification of the standard method used to verify the product efficacy; • proof of the effectiveness of the neutralizer utilized in the tests for both the reference standard and the test product; • the relationship of each test to specific area of application; • the time differential (between application of the test product and the collection of organisms) used in the test and whether the time stated is sufficient to meet the required criteria of specific activity; • initial number of the test organisms; • information on the lot number, expiry date, and date of manufacture for each lot tested; • overview of the statistical plan and assumptions; • supporting raw data; • proof of a washout period if a cross-over study is employed, or if a subject is reused; • the minimum inhibitory concentration (MIC) for the product, when available; and • at minimum, tests must demonstrate that the lower bound of the confidence interval is at the required log reduction; and that a power of 80% and alpha of 5% is used. • based on practicality, no product will be accepted if the *in vivo* time-to-effect upon completion of application is greater than 30 seconds (for a leave-on product) (Page 7,8)

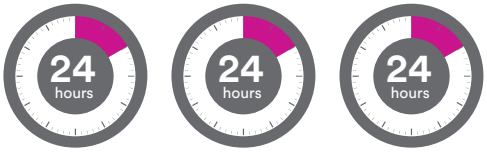
Clinical studies supporting the safety and efficacy of 3M™ SoluPrep™ 2% chlorhexidine gluconate (CHG) and 70% isopropyl alcohol (IPA) drug products.

Information is applicable to all formats of the 3M™ SoluPrep™ 2% CHG/70% IPA drug delivery formats: applicator, sponges, swabs, wipes and bulk solution.

A) Safety Studies

Even though there are many published and unpublished safety data reports that support the safety of CHG/IPA drug combination products, 3M Canada conducted three safety studies for the drug development of the 3M™ SoluPrep™ Brand product line of 2% CHG/70% IPA products.

a i) Evaluation of Primary Irritation Potential in Humans (Three 24-Hour Applications) [2]



The study tested different active concentrations of CHG (1.5%, 2.0%, 2.5%, and 3.0%), but with the same concentration of IPA (70%), for their potential to cause irritation after three 24-hour patch applications. The study consisted of three 24-hour exposures to the test materials under fully occluded and semi-occluded conditions. Each subject was also tested with aqueous 10% povidone-iodine solution, a positive control (sodium lauryl sulfate) and a negative control (saline).

Results

No visible irritation was induced by CHG/IPA under semi-occluded conditions (clinical use conditions) when tested using chlorhexidine concentrations of 1.5%, 2.0%, 2.5%, and 3.0%, while very slight irritation was induced by the aqueous 10% povidone-iodine solution.

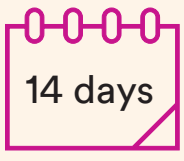
ii) 14-Day Cumulative Irritation Patch Test [3]

The study compared the following solutions in a panel of healthy human adult subjects; CHG/IPA solution, 10% aqueous povidone-iodine solution, 70% IPA, 4% aqueous CHG detergent, sodium lauryl sulfate (positive irritant control), and 0.9% aqueous sodium chloride (saline, negative irritant control).

All subjects received applications of the test materials once a day for 14 consecutive days. The test materials were first applied to patches and the patches were applied under either semi-occlusive or occlusive conditions to the backs of the subjects. For open application (no patch used), test materials were massaged directly into the skin of the upper arm for 30 seconds and left to air dry for 30 seconds. Scoring for cumulative irritation was measured every 24 hours.

Results

Under semi-occluded conditions, as would apply in clinical use, the CHG/IPA solution exhibited irritation equivalent to that of the saline solution (negative control). The CHG/IPA solution did not produce any irritation during the 14 days when used without a dressing (open application)



The study confirms that the 3M™ SoluPrep™ Brand Solution is non-irritating under clinical use conditions and when allowed to completely air dry before covering the site with a semi-permeable or gauze dressing.

iii) A Repeated Insult Patch Test for the Evaluation of Sensitization [4]

The study was conducted in a panel of healthy human adult subjects to evaluate the CHG/IPA solution for contact sensitization after repeated application. The testing method used was a repeated insult patch test (Draize Procedure) on the deltoid area of the upper arm of subjects. Each subject received applications of both CHG/IPA (test solution) and 0.9% aqueous sodium chloride (saline, negative irritant control).

The products were applied nine times during a 23-day test period (induction period) and then applied again on Day 36 (challenge period). The challenge consisted of two 48-hour patch applications—one on a naïve site and one on the original site. The sites were scored approximately 48 and 96 hours after patch application.

Results

Under the conditions of this study (semi-occluded), the CHG/IPA solution did not elicit any evidence of sensitization. Further, irritation elicited by the CHG/IPA solution was slightly less than that of the negative control.

B) Efficacy Studies *(in vitro)*

a i) EN 13727: Chemical Disinfectants and Antiseptics—Quantitative Suspension Test for the Evaluation of Bactericidal Activity of Chemical Disinfectants for Instruments Used in the Medical Area [5]

Time Kill Evaluation

The product, when diluted with hard water and tested in accordance with the test method section, under simulated clean conditions (0.3 g/L bovine albumin solution), shall demonstrate at least a 5 $\log_{10}$ reduction.

The bactericidal activity is evaluated against 21 test organisms selected by Health Canada:
Acinetobacter baumannii, Bacteroides fragilis, Enterococcus faecium, Enterococcus hirae, Escherichia coli K-12, Haemophilus influenza MDR, Klebsiella pneumoniae subspecies pneumonia and ozaenae, Micrococcus luteus, Proteus mirabilis, Pseudomonas aeruginosa ATCC 15442, Pseudomonas aeruginosa ATCC 27583, Serratia marcesens, Staphylococcus aureus ATCC 6538, Staphylococcus aureus ATCC 29213, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus saprophyticus, Streptococcus pneumonia, Streptococcus pyogenes.

Results

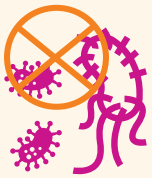
The 3M™ SoluPrep™ Brand Solution met the requirements of the EN13727 standard: the mean $\log_{10}$ reduction of each of the test strains was >5.00 $\log_{10}$.

ii) Minimum Inhibitory Concentration (MIC): Activity of 3M™ SoluPrep™ Brand Against 1104 Microbial Isolates [6]

A total of 1104 microbial isolates were tested during this phase of the investigation. Of these, 660 (59.8%) were clinical isolates. Among the stock isolates, strains with known antimicrobial resistance were represented. Specific American Type Culture Collection (ATCC) strains were also included. MICs were determined by the broth microdilution method. The test media varied with the species being tested. For statistical calculations of MIC_{50} and MIC_{90}, all values were rounded up to the next highest even log_2 dilution.

Results

The MIC_{50s} and MIC_{90s} were < 0.0064%CHG in 0.1422% IPA concentrations for the majority of species tested. There were no species (including anaerobes and yeasts) with MIC_{90s} > 0.0128% CHG in 0.2844% IPA concentrations.



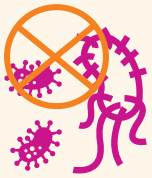
b EN 13624: Chemical disinfectants and antiseptics – Quantitative suspension test for the evaluation of fungicidal activity of chemical disinfectants for instruments used in the medical area [7]

The product, when diluted with hard water and tested in accordance with the test method section, under simulated clean conditions (0.3 g/L bovine albumin solution), shall demonstrate at least a 4 log_{10} reduction.

The fungicidal activity is evaluated using two test organisms selected by Health Canada: *Candida albicans, Aspergillus niger*

Results

The 3M™ SoluPrep™ Brand Solution met the requirements of the EN13614 standard: the mean log_{10} reduction of each of the test strains was >4.00 log_{10}.



C) Efficacy Studies *(in vivo)*

a i) ASTM E1173: Preoperative Skin Preparation Study Following ASTM E1173 to Evaluate the Antimicrobial Capabilities of One Test Product and a Reference Control [8]

The purpose of the study was to determine the immediate and persistent antimicrobial efficacy of the 2% CHG and 70% IPA solution delivered via three different applicators. The reference product was 60% 1-propanol. The test products and reference product were randomly assigned to subjects per a computer generated schedule, such that the test product was used on one side and the reference product on the opposite side. The 3M™ SoluPrep™ Brand test products were applied using repeated back and forth strokes to the desired body sites over a determined treatment area for the required time. Sampling time points of 30 seconds, 10 minutes and 72 hours were chosen to provide data for a preoperative, pre-catheter and pre-injection indication.

Health Canada requires an *in vivo* time-to-effect of 30 seconds on dry and moist sites and 6 hours for persistence. Including a 72 hour sampling time, although not required, is especially important for invasive devices. The clinical trials have shown the antimicrobial activity of the CHG/IPA solution is effective for at least 72 hours.

Results

The study results confirm both the immediate and persistent antimicrobial activity of the 3M™ SoluPrep™ 2% CHG and 70% IPA products.

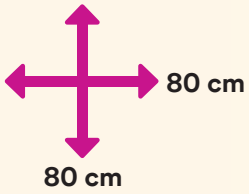
ii) ASTM E1173 (Coverage): Evaluation of Microbial Population Reductions within a Defined Product Coverage Area [9]

Two different and independent studies were performed. The purpose of these studies were to determine the relationship between the amount of antiseptic solution and the size of the treatment area that can be effectively prepared with the test solution (ratio of solution per cm^2 of skin).

In these studies, the 3M™ SoluPrep™ Brand (2% CHG and 70% IPA) product was applied using repeated back and forth strokes to the desired body site over a determined treatment (coverage) area for the required time. Log reductions of resident flora were measured at three sample sites within this treatment area (centre, mid-way and periphery). The microbial counts at these sample sites after skin preparation were found to be clinically equivalent and not statistically different.

Results

As was determined in these efficacy studies, 1 mL of 2% CHG and 70% IPA solution can cover up to 80 cm^2 of dry skin and still meet the efficacy requirement set in the Health Canada guidance. Treatment/coverage areas based on efficacy testing are listed on product labels.



iii) ASTM E1173: Preoperative Skin Preparation Study Following ASTM E1173 Methods to Evaluate the Antimicrobial Capabilities of Three Applicators Containing 2% Chlorhexidine Gluconate and 70% Isopropyl Alcohol, One Applicator Containing 2% Chlorhexidine Gluconate, and One Applicator Containing 70% Isopropyl Alcohol [10]

The objective of this clinical trial was to determine the immediate and persistent antimicrobial activity of the 3M™ SoluPrep™ Brand Product compared to its mono-components. The log reduction data of the 2% CHG and 70% IPA was compared with the log reduction data of each mono-component.

Results

The results clearly confirmed the immediate antimicrobial activity of the alcohol component and the persistent activity of the chlorhexidine component for at least 72 hours. Combining the components resulted in a formulation with superior antimicrobial activity than either component alone.

b ASTM E2613 Fungicidal Study

3M has performed a comprehensive program of *in vitro* efficacy studies that included bacteria and fungi/yeasts. In addition, a thorough literature review has been conducted of published medical reports and regulatory guidance documents pertaining to antifungal testing requirements and efficacy of 2% CHG/70% IPA solution in decreasing infections.

The justification for the antifungal testing conducted by 3M is outlined below:

- The ASTM E 2613 (Section 1.1) states that **this test method is not meant for use with preoperative skin preps**. Since the 3M™ SoluPrep™ Brand Solution is intended for preoperative skin preparation, 3M did not conduct *in vivo* efficacy studies according to ASTM E 2613 but has conducted two *in vitro* fungal tests (EN 13624 and MIC) in support of fungicidal activity of the 2% CHG/70% IPA solution as seen in points B) a) ii and b) above.
- The FDA monograph for antiseptic products requires *in vitro* testing against yeast (*Candida* species and *Candida albicans*) for preoperative skin antiseptics; however, the FDA monograph does not require *in vivo* testing to support antifungal activity.
- Furthermore, the United Kingdom (UK) regulatory agency (MHRA) and the French regulatory agency (ANSM) also do not require any *in vivo* antifungal testing.
- It is generally accepted that 70 to 92% alcohol solutions have good antifungal activity (Ali et al., 2001[12] ; Mangram et al., 1999[13]; Kampf and Kramer, 2004[14]) and that fungi and yeasts are usually sensitive to chlorhexidine (Denton, 2001[15]). Apart from the two active components, 2% CHG and 70% IPA, the 3M™ SoluPrep™ skin antiseptic solution does not contain any additional ingredients that could negatively affect the antimicrobial efficacy of the formulation.
- 3M performed the required EN 13624 *in vitro* test, which evaluates the fungicidal activity of the 2% CHG/70% IPA solution against *Aspergillus brasiliensis* and *Candida albicans*. Furthermore, the MIC study was performed against 109 yeast strains (four species: *Candida albicans*, *Candida krusei*, *Candida parapsilosis* and *Candida tropicalis*). Both tests confirmed the excellent antifungal activity of the 2% CHG /70% IPA solution in the 3M™ SoluPrep™ Skin Antiseptic Solution.
- In a recent article reviewing invasive fungal infections in intensive care units (ICUs), Shoham and Marwaha (2010)[16] found the majority of invasive fungal infections were due to *Candida* species. *Candida* species (including *Candida albicans*) are part of the normal microbial flora of skin and mucosal surfaces and can be detected in up to 71% of the healthy population. Superficial and invasive Candida infections are most frequent in immunocompromised patients. Data supporting the skin as a possible origin of Candida blood stream infections are few and incomplete. In most cases of candidemia, the gastrointestinal system is reported to be the origin of the microorganism. Penetration of the organism into tissue and capillaries from the mucosal surfaces is hypothesized (Mavor et al., 2005).[17] These episodes of candidemia therefore cannot be prevented with the application of topical skin antiseptics. The exception appears to be *Candida parapsilosis*, which occurs more frequently in patients with central venous catheters, suggesting cutaneous origin (Mavor et al., 2005)[17].

- The MIC study performed demonstrates that *Candida parapsilosis* is highly sensitive to the 2% CHG/70% IPA solution — the MIC_{90} was found to be equivalent to 0.0064% CHG/0.1422% IPA. The concentration of chlorhexidine in the 2% CHG/70% IPA solution thereby far exceeds the MIC_{90}.
- According to the CDC Guideline for Prevention of Surgical Site Infection (SSI) (Mangram et al., 1999),[13] the incidence rate of fungal SSI was 0.3 per 1000 discharges in 1995. The guideline states that fungal SSIs are caused by *Candida* species and that fungi from exogenous and endogenous sources rarely cause SSIs. Fungal SSIs are mainly found in severely ill and immunocompromised patients (Mangram et al., 1999).[13]
- For the 3M™ SoluPrep™ Brand drug products, 3M Canada has not included a fungal claim on the product label as proposed in the Health Canada Guidance document. The indication for use is [To reduce bacteria on skin to diminish the risk of surgical site infection] rather than *[To reduce bacteria and fungi on the skin to diminish the risk of surgical site infection.]*

Fungicidal Activity

It is 3M Canada's belief that the comprehensive program of *in vitro* efficacy studies (including bacteria and fungi/yeasts) and analysis of the published medical literature provides sufficient evidence of the broad-spectrum antimicrobial efficacy of the 2% CHG/70% IPA solution and that further clinical study according to ASTM E 2613 is not needed.

Overall Conclusion of the Safety & Efficacy Studies

More than 2,000 skin exposures to CHG/IPA solution occurred during the drug development and clinical safety trials for the 3M™ SoluPrep™ Brand Products. Neither the skin irritation safety studies nor the sensitization study in human subjects demonstrated skin irritation or induced sensitization when the products were applied as directed. As with any skin antiseptic, alcoholic chlorhexidine solutions should be allowed to thoroughly dry on the skin before the application of any dressing product. To minimize irritation, transparent, semi-occlusive, or gauze dressings should be used.

Neither the skin irritation safety studies nor the sensitization study in human subjects demonstrated skin irritation or induced sensitization when the products were applied as directed.

The results of the efficacy studies confirm that 3M™ SoluPrep™ 2% CHG and 70% IPA conforms to the Health Canada Guidance Document: Human-Use Antiseptic Drugs.[1]

In addition, the results demonstrate the extended persistent activity of the formulation for at least 72 hours.

The excellent persistent activity provided by CHG is of particular importance in helping prevent infections when used to prepare skin in situations where invasive devices, such as intravascular catheters, are left in place.

The studies summarized above provide the scientific evidence that has been used to develop and support the application instructions that are included with the products.

Application Time of the 3M™ Soluprep™ 2% CHG and 70% IPA Drug Products

Application time

The application times used in the efficacy studies on the 2% CHG/70% IPA solution were as follows:

i. Pre-injection, pre-catheterization (vascular) and pre-surgery use (dry site)

ii. Pre-surgery use (moist site)

Application Method

To achieve the required efficacy, the application of our 2% CHG/70% IPA skin antiseptic requires a technique that differs from traditional practice. Historically, skin antiseptics were applied using a "boxed" or "concentric circle" single-pass painting technique, working from the centre of the prepped area out toward the periphery. These practices were established using single-ingredient and less effective products and the scientific evidence to support efficacy was lacking. The superior activity of CHG/IPA solutions to these single-ingredient products has been demonstrated.[18,19] It is important to recognize that the mechanism of action and the optimal application techniques may vary with different skin antiseptic drug products.

Test Application Method

During our studies, the antiseptic products were applied using a **continuous back and forth friction motion** moving horizontally across the centre of the treatment area to the periphery and repeating the motion over the desired treatment area for 15 seconds.

After the required application time, the product was allowed to air dry completely before the sampling was obtained.

The continuous back and forth motion was then repeated over the same area moving in a vertical direction for an additional 15 seconds to achieve the required application time of 30 seconds on a dry body site.

Note: Application times must be extended if the site being prepared is considered a "moist site" (such as the groin) as these sites are more heavily colonized with organisms. Refer to package insert for additional instruction for moist site application.

Results

- Statistically equivalent log reductions obtained from the centre, mid and outer edges of the treatment area.
- An effective, evidence-based manner in which to apply the product and does not result in contamination of the treatment area.

Note: The product was repeatedly applied from the outer edges over the centre point (contrary to traditional concentric circle or boxed painting application) with no increase in bacteria observed at the centre point.

The goal is to obtain 30 seconds of application with friction by applying the antiseptic in two different directions to optimize binding of the chlorhexidine to the skin layers.

The back-and-forth application method has been developed as a result of extensive research and *in vivo* testing. This method is necessary in order to achieve the highest efficacy in terms of log reduction and persistence of the drug solution. The mechanical effect of this application method allows the drug solution to penetrate into the layers of the skin where resident bacteria are found. Disruption of the layer of sebum, sweat and organic matter found on the surface of the skin through the application of the antiseptic, combined with the mechanical back and forth action, enables the product to reach down through the layers of skin, and achieve optimum bacterial log reduction.

During our clinical studies, it was determined that using repeated back and forth strokes was the most efficient method to meet the strict requirements for professional healthcare use identified in the Health Canada Guidance Document. (Page 5 of this document)

Single application

The clinical studies performed on 3M™ SoluPrep™ 2% CHG/70% IPA drug products demonstrated the required efficacy was achieved using a single application procedure of the antiseptic solution.

Note: Applying multiple layers of the antiseptic solution to the site may increase the risk of skin irritation and the length of time required for the treatment area to dry due to additional volume of the drug product used.

Dry time

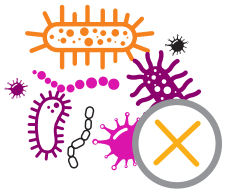
It is important that the drug solution be allowed to air dry completely for the following reasons:

a to prevent the risk of fire in an operating room environment

where ignition sources such as electrocautery and laser are present. When an ignition source is present, **a minimum of 3 minutes for drying is required** on hairless skin prior to draping or commencing procedure. Up to 1 hour may be required if hair is present;

b to minimize the risk of skin irritation

if the site will be covered with drapes or dressings;



c to achieve maximum bacterial reduction.

The longer the drug solution is in contact with the skin, the greater the bacterial log reduction achieved. Samples for efficacy testing were obtained after thorough air drying of the treatment area.

In summary, the important points related to the application of the 2% CHG/70% IPA antiseptic are

a **Apply enough antiseptic** to adequately cover the intended area. Treatment area area varies depending on the dosage form

b Apply antiseptic using a **"back and forth" motion** that provides friction

c Binding of CHG to the skin is optimized when the **product is applied in two different directions**

d Application time may vary by formulation and body site. **Apply the antiseptic for the appropriate length of time as per label instructions**

e Ensure the antiseptic is **applied to all skin surfaces that will be exposed within drape opening, handled with sterile gloves during the procedure or covered by the finished dressing**

f Ensure the antiseptic has **completely air dried prior to the application of a drape, dressing or use of an ignition source.** Dry time can be affected by volume of product, prepping dimension, body site, presence or absence of hair, humidity, etc

g **Always refer to detailed instructions for use** as provided on product labels and package inserts

Compliance to the 2009 Health Canada Guidance: Human-Use Antiseptic Drugs

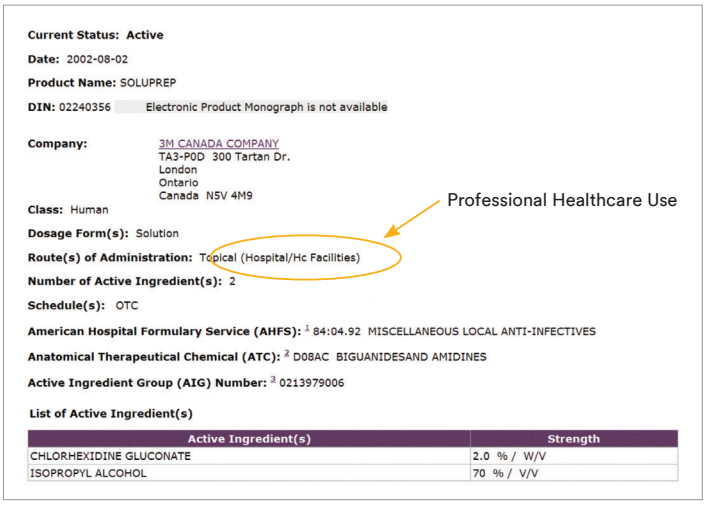
Demonstrating compliance with the Health Canada Guidance document is important because it provides evidence of tests that have been conducted in accordance with standardized test methods; and for *in vivo* studies, under the conditions of use prescribed on the label.

Because the risk of exposure to organisms that can cause healthcare associated infections is greater in healthcare settings, antiseptics intended to reduce transient or resident organisms on the skin must meet the most rigorous requirements to be authorized for professional healthcare use. This authorization provides assurance of optimum efficacy and safety for patients prior to invasive procedures. *(Health Canada Guidance Document, Page 32)*

How to Verify the Professional Use Status of an Antiseptic Drug Product

The Health Canada Drug Product Database[20] and the Licensed Natural Health Products Database[21] list those products that have been authorized for use in Canada. If approved under the new Guidance Document, the specific setting in which they should be used based upon the supportive safety and efficacy testing that has been provided to Health Canada, will be indicated by the manufacturer. Health Canada has determined these settings/categories for use to be personal domestic or commercial use, professional food premises and professional healthcare facility use. It is Health Canada's expectation that professional use products would seek this new enhanced labelling. (Health Canada Guidance Document, page 2)

Once Health Canada requirements have been met and the authorization for a professional healthcare use antiseptic drug product has been awarded, the product will be identified as "Hospital / HC Facilities" in the Drug Product Database and the Licensed Natural Health Products Database. (See Figure 1.)



Current Status: Active

Date: 2002-08-02

Product Name: SOLUPREP

DIN: 02240356 Electronic Product Monograph is not available

Company: 3M CANADA COMPANY
TA3-P0D 300 Tartan Dr.
London
Ontario
Canada N5V 4M9

Class: Human

Dosage Form(s): Solution

Route(s) of Administration: Topical (Hospital/Hc Facilities)

Number of Active Ingredient(s): 2

Schedule(s): OTC

American Hospital Formulary Service (AHFS): [1] 84:04.92 MISCELLANEOUS LOCAL ANTI-INFECTIVES

Anatomical Therapeutical Chemical (ATC): [2] D08AC BIGUANIDESAND AMIDINES

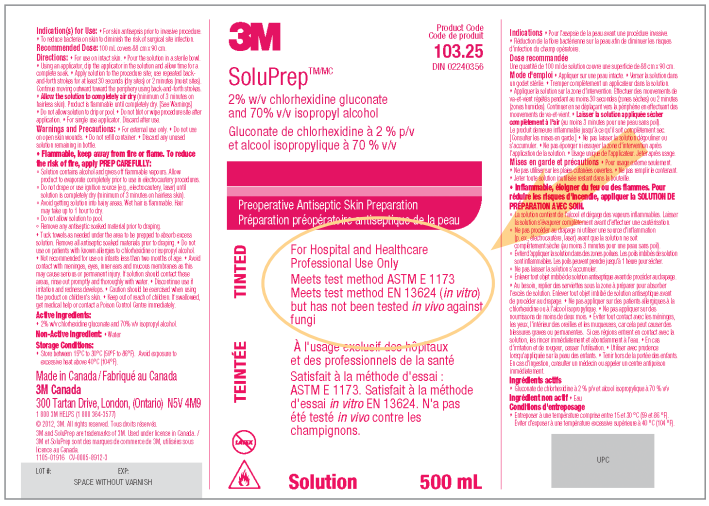
Active Ingredient Group (AIG) Number: [3] 0213979006

List of Active Ingredient(s)

Active Ingredient(s)	Strength
CHLORHEXIDINE GLUCONATE	2.0 % / W/V
ISOPROPYL ALCOHOL	70 % / V/V

Professional Healthcare Use

Figure 1



3M

SoluPrep™

2% w/v chlorhexidine gluconate and 70% v/v isopropyl alcohol

Gluconate de chlorhexidine à 2 % p/v et alcool isopropylique à 70 % v/v

Product Code / Code de produit 103.25

DIN 02240356

Preoperative Antiseptic Skin Preparation

Préparation préopératoire antiseptique de la peau

TINTED

TEINTÉE

For Hospital and Healthcare Professional Use Only

Meets test method ASTM E 1173

Meets test method EN 13624 (*in vitro*) but has not been tested *in vivo* against fungi

À l'usage exclusif des hôpitaux et des professionnels de la santé

Satisfait à la méthode d'essai : ASTM E 1173. Satisfait à la méthode d'essai *in vitro* EN 13624. N'a pas été testé *in vivo* contre les champignons.

Solution 500 mL

Figure 2

Another way to identify products that have achieved professional healthcare use approval in Canada, is through review of the product label. The *in vivo* test methods (e.g., "Meets EN 1173") must be reflected on the label. In addition, any testing limitations must be clearly indicated on the product label. (See Figure 2.)

Effective reduction of the bacterial load on the patient's skin through the use of topical antiseptics is an important part of the preparation before invasive medical and surgical procedures. Using skin antiseptics that have proven efficacy when measured against current rigorous Canadian standards for professional use products provides maximum protection and assurance of safety for patients.

[1] Health Canada Guidance Document: Human-Use Antiseptic Drugs, Ottawa, 2009/11/27. http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/prodpharma/applic-demande/guide-ld/antiseptic_guide_ld-eng.pdf

[2] Study 01-108751-76

[3] Study SLM-SC-01 (01-108088-76)

[4] Study SLM-SC-02 (01-105168-76)

[5] Study EM-05-01212 (100633-201)

[6] Study SLM:ITSSTK-01

[7] Study 100934-201

[8] Study 100611-103

[9] Studies 090934-150.01 and 120314-103.01

[10] Study 091023-103

[11] Study 090527-103

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[20] http://webprod3.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp

[21] http://webprod3.hc-sc.gc.ca/lnhpd-bdpsnh/index-eng.jsp

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