

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-074

APPROVED DRAFT LABELING

PRODUCT TITLE

Avagard™

(Chlorhexidine gluconate 1% and ethyl alcohol 61%, w/w)

Surgical and Healthcare Personnel Hand Antiseptic
with moisturizers

DESCRIPTION

Avagard Antiseptic Hand Preparation with moisturizers for surgical and healthcare disinfection, provides rapid bactericidal action and persistent antimicrobial protection against a broad spectrum of organisms. Avagard antiseptic hand prep contains 1% (w/w) chlorhexidine gluconate, and 61% (w/w) ethyl alcohol in an emollient-rich lotion base.

This product is flammable and should not be used near flame or in any situation which can cause ignition.

Avagard antiseptic hand prep does not require the use of water, or mechanical scrubbing with a surgical brush to achieve the bactericidal effect. Water should not be used in its application.

CLINICAL PHARMACOLOGY

In vitro Microbiology

The following *in vitro* data are available but their clinical significance is unknown.

Time Kill Study: In an independent Time Kill Study, the speed of the microbicidal activity of Avagard antiseptic hand prep was measured using a select battery of microorganisms. Avagard antiseptic hand prep demonstrated rapid bactericidal activity against the broad range of microorganisms tested.

Microorganism	% Microbial Kill in 15 Seconds
	Avagard™ Antiseptic hand prep
<i>Staphylococcus aureus</i> (ATCC 29213)	99.99
<i>Staphylococcus aureus</i> (ATCC 6538)	99.99
<i>Staphylococcus aureus</i> (MRSA) (ATCC 33592)	99.98
<i>Escherichia coli</i> (ATCC 11229)	99.96
<i>Escherichia coli</i> (ATCC 25922)	99.99
<i>Pseudomonas aeruginosa</i> (ATCC 15442)	99.91
<i>Pseudomonas aeruginosa</i> (ATCC 27853)	99.99
<i>Serratia marcescens</i> (ATCC 14756)	99.99
<i>Staphylococcus epidermidis</i> (ATCC 12228)	99.99*
<i>Staphylococcus epidermidis</i> (MRSE) (ATCC 51625)	99.99
<i>Micrococcus luteus</i> (ATCC 7468)	99.56
<i>Enterococcus faecalis</i> (ATCC 29212)	99.95
<i>Enterococcus faecalis</i> (VRE) (ATCC 51299)	99.48
<i>Enterococcus faecium</i> (VRE) (ATCC 51559)	99.81
<i>Candida albicans</i> (ATCC 10231)	99.98

*outlier excluded from calculation

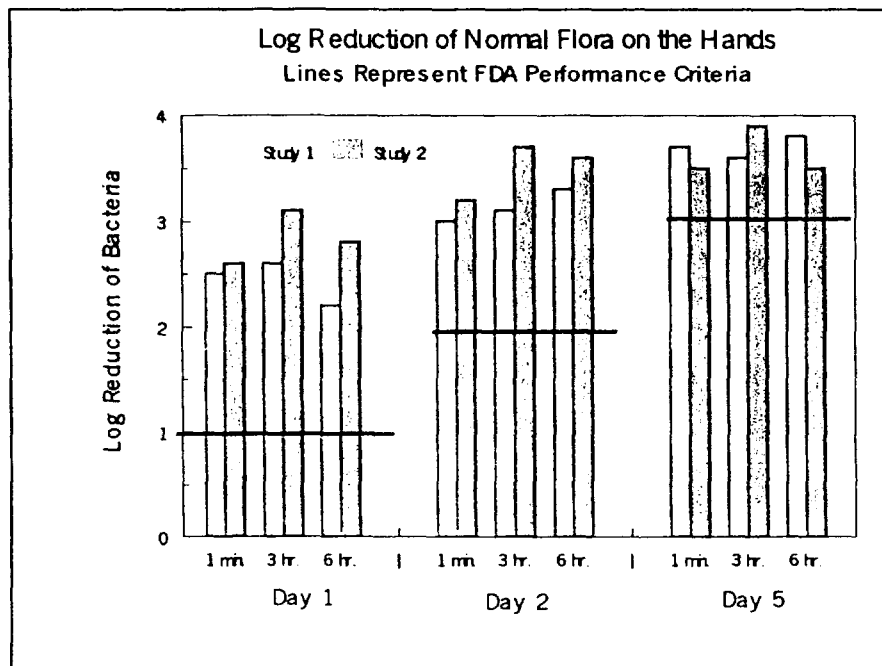
Minimum Inhibitory Concentration Study¹: In an independent study, Avagard antiseptic hand prep was tested against 1058 isolates while the vehicle control and the reference product were tested against 266 isolates of the organisms listed below. Avagard antiseptic hand prep demonstrated antiseptic activity against all organisms tested.

Microorganism	Lab Strains		Clinical Isolates	
	N	MIC Range (µg/ml)	N	MIC Range (µg/ml)
<i>Acinetobacter</i> sp.	25	2 – 16	25	2 – 32
<i>Bacteroides fragilis</i>	23	1 – 4	24	1 – 4
<i>Haemophilus influenzae</i>	25	0.5 – 4	25	0.5 – 8
<i>Enterobacter</i> sp.	25	2 – 16	25	4 – 32
<i>Escherichia coli</i>	25	2 – 8	26	2 – 8
<i>Klebsiella</i> sp.	25	0.5 – 16	25	4 – 8
<i>Pseudomonas aeruginosa</i>	25	2 – 16	29	4 – 16
<i>Proteus mirabilis</i>	25	4 – 32	25	4 – 128
<i>Serratia marcescens</i>	25	4 – 32	25	4 – 32
<i>Staphylococcus aureus</i> including MRSA	25	2 – 4	26	1 – 16
<i>Staphylococcus epidermidis</i>	24	1 – 4	28	0.5 – 4
<i>Staphylococcus hominis</i>	9	0.5 – 8	41	1 – 4
<i>Staphylococcus haemolyticus</i>	7	1 – 4	43	1 – 4
<i>Staphylococcus saprophyticus</i>	15	1 – 4	36	1 – 4
<i>Micrococcus luteus</i>	25	0.5 – 8	25	0.5 – 4
<i>Streptococcus pyogenes</i>	25	<0.25 - 2	25	0.5 – 8
<i>Enterococcus faecalis</i> including VRE	25	1 – 8	25	2 – 8
<i>Enterococcus faecium</i>	24	1 – 4	26	1 – 16
<i>Streptococcus pneumoniae</i>	25	1 – 4	27	2 – 32
<i>Candida</i> sp.	24	1 – 16	26	2 – 8
<i>Candida albicans</i>	25	4 - 16	25	4 - 16

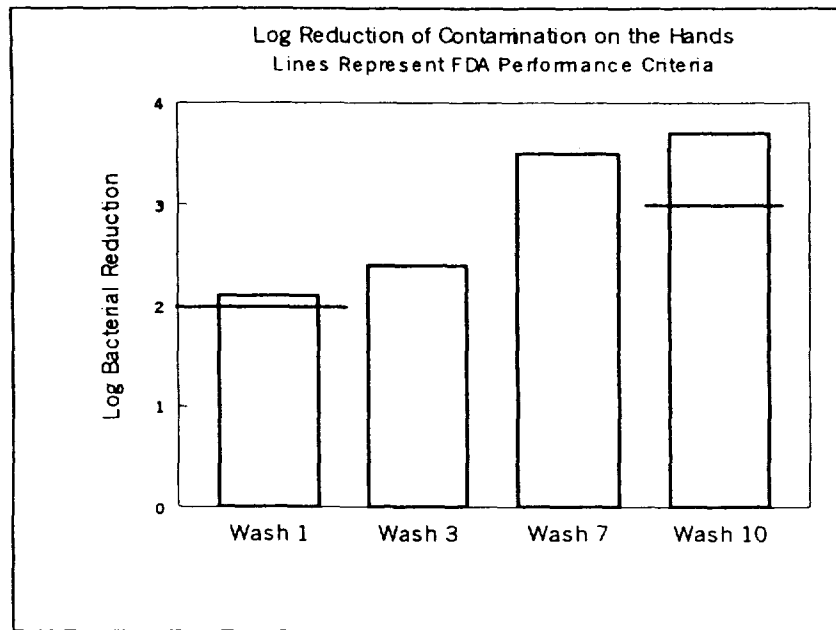
Clinical Studies

The following section details studies designed to simulate actual clinical use.

Surgical Hand Antiseptic Studies: The procedure used was the FDA specified test method for Surgical Scrub products². In two studies, the immediate bactericidal effect of Avagard antiseptic hand prep after a single application resulted in a 2.5 log reduction from a 6 log baseline (99.6%) in resident bacterial flora, with a continued 3.5 log reduction (99.96%) after the final (eleventh) scrub. Reductions on surgically gloved hands were maintained over the six-hour test period.



Health Care Personnel Antiseptic Study: The procedure used was the FDA specified test method for health care personnel handwash products². After one application, use of Avagard antiseptic hand prep demonstrated a 2.1 log reduction from a 7 log baseline (99.2%) of bacteria on artificially contaminated hands. After the final (tenth) application, the reduction increased to 3.7 logs (99.98%).



Safety Studies

In a Human Repeat Insult Patch Test (Jordan-King Modification of the Draize Sensitization Procedure)^{3,4} conducted in 217 subjects, Avagard antiseptic hand prep displayed no evidence suggesting a sensitization potential. In a 21-Day Evaluation of the Cumulative Irritation Potential⁵ of Avagard antiseptic hand prep and its vehicle, both articles were classified as mild materials, under occlusive and semi-occlusive conditions. The test products were allowed to dry on the skin for 15 minutes prior to patch application, which may have minimized irritation potential. However, available safety data indicates that repeated use of Avagard antiseptic hand prep was associated with little change in moisture, scaliness, erythema or tactile roughness when compared to baseline conditions.

In animal studies, Avagard antiseptic hand prep produced mild ocular irritation when instilled into the eyes of albino rabbits. Avagard antiseptic hand prep was not teratogenic when applied to the skin of rats. Avagard antiseptic hand prep has not been tested for mutagenicity or carcinogenicity.

PRODUCT TITLE

Avagard™.

Chlorhexidine gluconate 1% and ethyl alcohol 61%, w/w

DESCRIPTION

Avagard- Antiseptic with moisturizers for surgical and healthcare skin disinfection, provides rapid bactericidal action and persistent antimicrobial protection against a broad spectrum of organisms. Avagard antiseptic contains 1% (w/w) chlorhexidine gluconate, and 61% (w/w) ethyl alcohol in an emollient-rich lotion base.

This product is flammable and should not be used near flame or in any situation which can cause ignition.

Avagard- antiseptic does not require the use of water, or mechanical scrubbing with a surgical brush to achieve the bactericidal effect. Water should not be used in its application.

CLINICAL PHARMACOLOGY

The following in vitro data are available but their clinical significance is unknown.

INDICATIONS AND USAGE

Avagard- Antiseptic is indicated for use as a surgical hand and as a healthcare personnel hand

CONTRAINDICATIONS

Avagard- Hand should not be used by persons who are known to be hypersensitive to chlorhexidine gluconate or any of its components.

WARNINGS

FLAMMABLE. FOR EXTERNAL USE ONLY. KEEP OUT OF EYES, EARS, AND MOUTH. IF AVAGARD SHOULD CONTACT THOSE AREAS, RINSE WITH WATER. Products containing chlorhexidine gluconate have been reported to cause serious and permanent eye injury if permitted to remain in the eye.

Irritation, sensitization and generalized allergic reactions have been reported with some chlorhexidine-containing products. If adverse reactions occur, discontinue use immediately, and, if severe, contact a physician. **Keep out of reach of children.** If swallowed, get medical help or contact a Poison Control Center right away.

INDICATIONS AND USAGE

Avagard™ Antiseptic Hand Preparation is indicated for use as a surgical hand antiseptic and as a healthcare personnel hand antiseptic.

CONTRAINDICATIONS

Avagard Antiseptic Hand Preparation should not be used by persons who are known to be hypersensitive to chlorhexidine gluconate or any of its components.

WARNINGS

FLAMMABLE. FOR EXTERNAL USE ONLY. KEEP OUT OF EYES, EARS AND MOUTH. IF AVAGARD ANTISEPTIC HAND PREPARATION SHOULD CONTACT THOSE AREAS, RINSE WITH COLD WATER RIGHT AWAY. Products containing chlorhexidine gluconate have been reported to cause serious and permanent eye injury if permitted to remain in the eye. Do not use routinely if you have wounds that involve more than the superficial layers of the skin. Irritation, sensitization and generalized allergic reactions have been reported with some chlorhexidine-containing products. If adverse reactions occur, discontinue use immediately, and, if severe, contact a physician. **Keep out of reach of children.** If swallowed, get medical help or contact a Poison Control Center right away.

ADVERSE REACTIONS

There were two adverse events probably or possibly related to Avagard antiseptic hand prep use in the 85 subjects who used this product in pivotal clinical trials. One subject suffered conjunctivitis and blurred vision after he rubbed his eye with a hand that had been treated with Avagard antiseptic hand prep. The other subject developed a maculopapular rash.

DIRECTIONS FOR USE

Surgical Hand Antiseptic

1. Apply to clean, dry hands and nails. For the first use of each day, clean under nails with a nail stick.
2. Dispense one pump (2 ml) of lotion into the palm of the hand.
3. Dip the fingertips of the opposite hand into the lotion and work it under the nails. Spread the remaining lotion over the hand and up to just above the elbow.
4. Using another 2 ml of lotion, repeat above steps with the other hand.
5. Dispense another 2 ml of lotion into either hand and reapply to all aspects of both hands up to the wrists.
6. Allow to dry before donning gloves.

Healthcare Personnel Hand Antiseptic

1. Apply to clean, dry hands and nails.
2. Dispense one pump (2 ml) into the palm of one hand.
3. Paying particular attention to the spaces between the fingers and under the fingernails, apply the lotion evenly to cover both hands up to the wrists.
4. Allow to dry without wiping.

HOW SUPPLIED

500 ml (16.9 fl oz) filled plastic bottle with wall-bracket dispenser assembly (NDC #17518-051-01); and 10 ml (0.34 fl oz.) filled plastic bottle (NDC #17518 051-10).

Store at 20-25°C (68-77°F)

INFORMATION FOR THE USER

Skin Condition Studies

Two independent 5-day handwashing studies were performed in a total of 58 subjects with normal, healthy skin, who washed with Avagard antiseptic hand prep. In these studies, use of Avagard antiseptic hand prep was associated with little change in moisture, scaliness, erythema, or tactile roughness after repeated use, when compared to baseline condition.

Made in U.S.A. for
3M Health Care
St. Paul, MN 55144-1000
(U.S.A.) 1-800-228-3957

34-XXXX-XXXX-X

REFERENCES

1. National Committee for Clinical Laboratory Standards, "Methods for Dilution Antimicrobial Susceptibility Test for Bacteria that Grow Aerobically", Document M7-A2, Vol. 5, No. 22.
2. Tentative Final Monograph for Health Care Antiseptic Drug Products; Federal Register; Vol. 59, No. 116, Friday June 17, 1994.
3. Jordan WP, King SE. Delayed hypersensitivity in females. The development of allergic contact dermatitis in females during comparison of two predictive patch tests. *Contact Dermatitis* 3, 19-23, 1977.
4. Jordan WP: 24-, 48-, and 48/48 hour patch tests. *Contact Dermatitis* 6, 151-152, 1980.
5. Lanman BM, Elvers EB, and Howard CJ. The role of human patch testing in a product development program. Joint Conference on Cosmetic Sciences. The Toilets Goods Association (Currently The Cosmetic, Toiletry, and Fragrance Association), Washington, D.C., April 21-23, 1968.

3M™ Avagard™ Surgical and Healthcare Personnel Hand Antiseptic
NDA 21-074/A-017
February 20, 2001

16.9 fl. oz. (500 mL) Custom Wedge Bottle Label – Primary Display Panel

Peel-off Front Panel Label – Directions for Use as a Surgical Hand Antiseptic



Avagard™ NDC 17518-051-01
(Chlorhexidine Gluconate 1% Solution and Ethyl Alcohol 61% w/w)
*surgical and healthcare personnel hand antiseptic
with moisturizers*

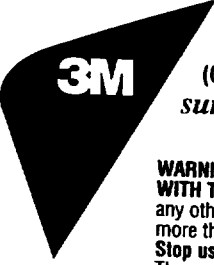
WARNING: FLAMMABLE. DO NOT TOUCH THE EYE WITH HANDS THAT HAVE BEEN TREATED WITH THIS PREPARATION. DO NOT USE • if you are allergic to chlorhexidine gluconate or any other ingredient in this preparation • routinely if you have wounds which involve more than the superficial layers of the skin.
Stop use and ask a doctor if irritation, sensitization or allergic reaction occurs. These may be signs of a serious condition.
Read Drug Facts Panel before use.

Directions: *Surgical hand antiseptic*

- apply to clean, dry hands and nails. For the first use of each day, clean under nails with a nail stick.
- dispense one pump (2 mL) into the palm of one hand
- dip the fingertips of the opposite hand into the lotion and work it under the nails
- spread the remaining lotion over the hand and up to just above the elbow
- using another 2 mL of lotion, repeat with the other hand
- dispense another 2 mL of lotion into either hand and reapply to all aspects of both hands up to the wrist
- allow to dry before donning gloves

16.9 fl oz • 500 mL

Bottom Front Panel Label – Directions for Use as a Healthcare Personnel Hand Antiseptic



Avagard™ NDC 17518-051-01
(Chlorhexidine Gluconate 1% Solution and Ethyl Alcohol 61% w/w)
*surgical and healthcare personnel hand antiseptic
with moisturizers*

WARNING: FLAMMABLE. DO NOT TOUCH THE EYE WITH HANDS THAT HAVE BEEN TREATED WITH THIS PREPARATION. DO NOT USE • if you are allergic to chlorhexidine gluconate or any other ingredient in this preparation • routinely if you have wounds which involve more than the superficial layers of the skin.
Stop use and ask a doctor if irritation, sensitization or allergic reaction occurs. These may be signs of a serious condition.
Read Drug Facts Panel before use.

Directions: *Healthcare personnel hand antiseptic*

- apply to clean, dry hands and nails
- dispense one pump (2 mL) into the palm of one hand
- paying particular attention to the spaces between the fingers and under fingernails, apply the lotion evenly to cover both hands up to the wrists
- allow to dry without wiping

16.9 fl oz • 500 mL

Note: Lot number and expiration date are ink jet printed on line during packaging the operation.

16.9 fl. oz. (500 mL) Custom Wedge Bottle Label – Back Panel, Drug Facts Box

U.S. Patent Nos. 5,897,031, 6,090,395
Cat. No. 9200 Made in USA for 3M Health Care, St. Paul, MN 55144 USA

Drug Facts	
Active ingredients	Purpose
Chlorhexidine gluconate 1% w/w Ethyl alcohol 61% w/w	Antiseptic Antiseptic
Uses · surgical hand antiseptic: significantly reduces the number of micro-organisms on the hands and forearms prior to surgery or patient care · healthcare personnel hand antiseptic: handwash to help reduce bacteria that potentially can cause disease · recommended for repeated use	
Warnings Flammable, keep away from fire or flame. For external use only Do not use · if you are allergic to chlorhexidine gluconate or any other ingredients in this preparation When using this product · do not touch the eye with hands that have been treated with this preparation · keep out of eyes, ears, and mouth. May cause serious and permanent eye injury if permitted to enter and remain in the eye. · if contact occurs, rinse with cold water right away · do not use routinely if you have wounds which involve more than the superficial layers of the skin 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.	
Directions Surgical hand antiseptic · apply to clean, dry hands and nails. For the first use of each day, clean under nails with a nail stick. · dispense one pump (2 mL) into the palm of one hand · dip the fingertips of the opposite hand into the lotion and work it under the nails · spread the remaining lotion over the hand and up to just above the elbow · using another 2 mL of lotion, repeat with the other hand · dispense another 2 mL of lotion into either hand and reapply to all aspects of both hands up to the wrists · allow to dry before donning gloves Healthcare personnel hand antiseptic · apply to clean, dry hands and nails · dispense one pump (2 mL) into the palm of one hand · paying particular attention to the spaces between the fingers and under fingernails, apply the lotion evenly to cover both hands up to the wrists · allow to dry without wiping	
Other information · store at 20-25°C (68-77°F)	
Inactive ingredients beheneth 10, behenyl alcohol, C20-40 pareth-24, cetyl palmitate, diisopropyl dimer diisoleate, dimethicone, glycerin, polyethylene glycol, squalane, water	
Questions? Call 1-800-228-3957	

Note: Lot number and expiration date are ink jet printed on line during packaging the operation.

3M™ Avagard™ Surgical and Healthcare Personnel Hand Antiseptic

NDA 21-074/A-017

February 20, 2001

0.34 fl. oz. (10 mL) Sample Bottle Labels

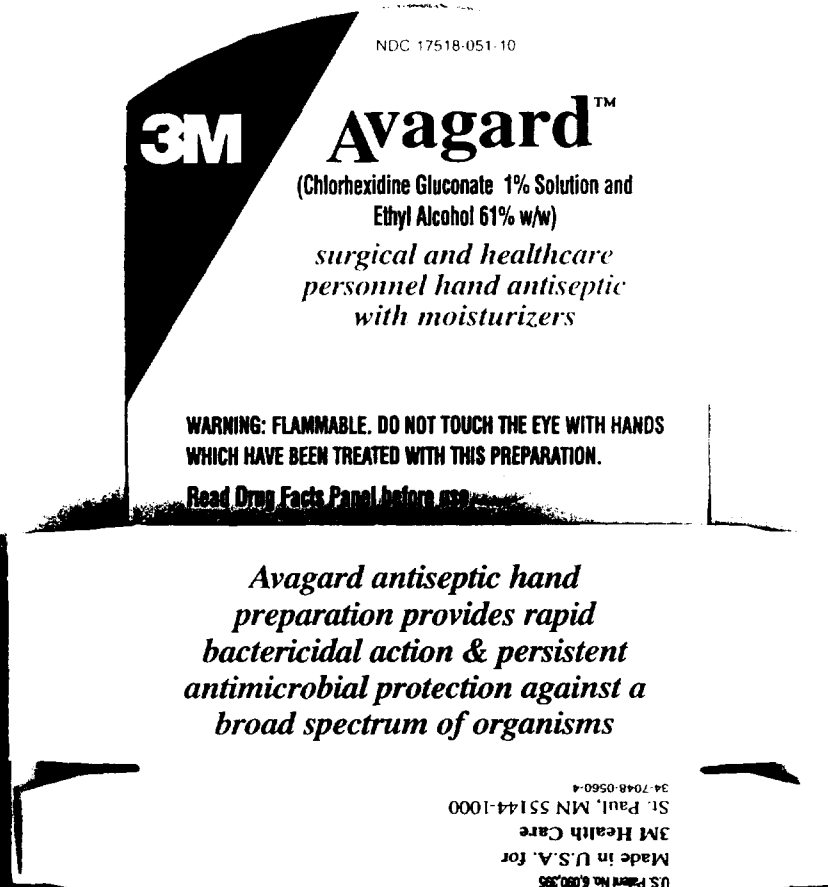
Primary Display Panel Label



Back Panel Label

Cat. No. 9210
Made in U.S.A. for
3M Health Care
St. Paul, MN 55144-1000
(U.S.A.) 1-800-228-3957
34-7050-5830-2

Outer Carton for 0.34 fl. oz. (10mL) Sample Bottle



Note: If the product is used during the packaging operation, it may be flammable during packaging the operation.

3M™ Avagard™ Surgical and Healthcare Personnel Hand Antiseptic
NDA 21-074/A-017
February 20, 2001

16 fl. oz. (473 mL) Cylinder Bottle Label

Drug Facts	
Active ingredients	Purpose
Chlorhexidine gluconate 1% w/w	Antiseptic
Ethyl alcohol 61% w/w	Antiseptic
Uses	
• surgical hand antiseptic: significantly reduces the number of micro-organisms on the hands and forearms prior to surgery or patient care	
• healthcare personnel hand antiseptic: handwash to help reduce bacteria that potentially can cause disease • recommended for repeated use	
Warnings	
Flammable, keep away from fire or flame. For external use only	
Do not use • if you are allergic to chlorhexidine gluconate or any other ingredients in this preparation	
When using this product	
• do not touch the eye with hands that have been treated with this preparation	
• keep out of eyes, ears, and mouth. May cause serious and permanent eye injury if permitted to enter and remain in the eye.	
• if contact occurs, rinse with cold water right away	
• do not use routinely if you have wounds which involve more than the superficial layers of the skin	
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.	
Directions	
Surgical hand antiseptic • apply to clean, dry hands and nails. For the first use of each day, clean under nails with a nail stick.	
• dispense one pump (2 mL) into the palm of one hand	
• dip the fingertips of the opposite hand into the lotion and work it under the nails	
• spread the remaining lotion over the hand and up to just above the elbow	
• using another 2 mL of lotion, repeat with the other hand	
• dispense another 2 mL of lotion into either hand and reapply to all aspects of both hands up to the wrists	
• allow to dry before donning gloves	
Healthcare personnel hand antiseptic • apply to clean, dry hands and nails	
• dispense one pump (2 mL) into the palm of one hand	
• paying particular attention to the spaces between the fingers and under fingernails, apply the lotion evenly to cover both hands up to the wrists	
• allow to dry without wiping	
Other information • store at 20-25°C (68-77°F)	
Inactive ingredients beheneth 10, behenyl alcohol, C20-40 pareth-24, cetyl palmitate, diisopropyl dimer dilinoleate, dimethicone, glycerin, polyethylene glycol, squalane, water	
Questions? Call 1-800-228-3957	

U.S. Patent No. 6,090,395

Cat. No. 9208

Made in U.S.A. for

3M Health Care

St. Paul, MN 55144-1000



(01) 0 07 07387 47252 8

NDC 17518-051-08

3M **Avagard™**
(Chlorhexidine Gluconate 1% Solution and Ethyl Alcohol 61% w/w)
*surgical and healthcare personnel
hand antiseptic
with moisturizers*

WARNING: FLAMMABLE.
DO NOT TOUCH THE EYE WITH HANDS THAT HAVE BEEN TREATED WITH THIS PREPARATION.

*Avagard antiseptic hand
preparation provides rapid
bactericidal action & persistent
antimicrobial protection against a
broad spectrum of organisms*

16 fl oz • 473 mL

Note: Lot number and expiration date are ink jet printed on line during packaging the operation.