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.

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

* outlier excluded from calculation
Minimum Inhibitory Concentration Study\(^1\): 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.

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Lab Strains</th>
<th>Clinical Isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>MIC Range (µg/ml)</td>
</tr>
<tr>
<td>Acinetobacter sp.</td>
<td>25</td>
<td>2 - 16</td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>23</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>25</td>
<td>0.5 - 4</td>
</tr>
<tr>
<td>Enterobacter sp.</td>
<td>25</td>
<td>2 - 16</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>25</td>
<td>2 - 8</td>
</tr>
<tr>
<td>Klebsiella sp.</td>
<td>25</td>
<td>0.5 - 16</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>25</td>
<td>2 - 16</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>25</td>
<td>4 - 32</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>25</td>
<td>4 - 32</td>
</tr>
<tr>
<td>Staphylococcus aureus including MRSA</td>
<td>25</td>
<td>2 - 4</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>24</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Staphylococcus hominis</td>
<td>9</td>
<td>0.5 - 8</td>
</tr>
<tr>
<td>Staphylococcus haemolyticus</td>
<td>7</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Staphylococcus saprophyticus</td>
<td>15</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Micrococcus luteus</td>
<td>25</td>
<td>0.5 - 8</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>25</td>
<td>&lt;0.25 - 2</td>
</tr>
<tr>
<td>Enterococcus faecalis including VRE</td>
<td>25</td>
<td>1 - 8</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>24</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>25</td>
<td>1 - 4</td>
</tr>
<tr>
<td>Candida sp.</td>
<td>24</td>
<td>1 - 16</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>25</td>
<td>4 - 16</td>
</tr>
</tbody>
</table>
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 products. 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 products. 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) conducted in 217 subjects, Avagard antiseptic hand prep displayed no evidence suggesting a sensitization potential. In a 21-Day Evaluation of the Cumulative Irritation Potential 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 ANITISEPTIC 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
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 wrists
• 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

**Drug Facts**

**Active ingredients**

- Chlorhexidine gluconate 1% w/w
- Ethanol 61% w/w

**Purpose**

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

**Precautions**

- 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: wash 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 gel and work it under the nails.

Spread the remaining gel over the hands and up to just above the elbow. Use another 2 mL of gel, repeat with the other hand.

Dispense another 2 mL of gel onto either hand and spread 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. Pay particular attention to the spaces between the fingers and under fingernails, apply the gel evenly to cover both hands up to the wrists. Allow to dry without wiping.

**Other information**

- Store at 30-70°F (88-77°F)
- Inactive ingredients: behentrimonium chloride, benzyl alcohol, C20-40 paraffins, cetyl palmitate, disodium edetate, disodium edetate, glucose, glycerin, polyethylene glycol, sorbic acid, water

**Questions?** Call 1-800-228-3957

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*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

![Primary Display Panel Label]

Back Panel Label

Cat. No. 9210
Made in U.S.A. by
3M Health Care
St. Paul, MN 55144-1000
U.S.A. 1-800-222-3957
34+7000-5830-2

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

![Outer Carton]

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

Read Drug Facts Panel before use.

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

Note: [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 microorganisms on the hands of healthcare personnel prior to surgery or patient care
• Surgical and healthcare personnel hand antiseptic: handwash to help reduce bacteria that can potentially cause disease

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.

Step 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
Benzethonium, behenyl alcohol, C20-40 parenet-24, cetyl palmitate, diisopropyl dimethylole, dimethicone, glycine, methylcellulose, glycol, quaternium, water.

Questions? Call 1-800-228-3967

US Pat. No. 6,096,395

Cat. No. 9208
Made in U.S.A. for
3M Health Care
St. Paul, MN 55144-1000

16 fl oz • 473 mL

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

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

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