AGT -1 Liquid Glove (AGT)

HEALTH TECHNOLOGY ASSESSMENT SECTION
MEDICAL DEVELOPMENT DIVISION
MINISTRY OF HEALTH MALAYSIA
001/09

DISCLAIMER

Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. It is not subjected to an external review process. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.

Please contact: htamalaysia@moh.gov.my, if you would like further information.

Health Technology Assessment Section (MaHTAS),
Medical Development Division
Ministry of Health Malaysia
Level 4, Block E1, Precinct 1
Government Office Complex
62590 Putrajaya

Tel: 603 88831246

Fax: 603 8883 1230

Available at the following website: http://www.moh.gov.my

Prepared by:

Ms Mariammah Krishnasamy
Assistant Director
Health Technology Assessment Section
Ministry of Health Malaysia

Reviewed by:
Datin Dr Rugayah Bakri
Deputy Director
Health Technology Assessment Section
Ministry of Health Malaysia

DISCLOSURE

The author of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia

EXECUTIVE SUMMARY

Introduction

AGT-1 liquid glove (AGT) is a disinfectant that has been claimed to be effective against nosocomial infections including bacteria, viruses and other pathogens. Besides that this solution was also claimed as having good dermal tolerance and skin rejuvenation properties. Currently almost all the health care settings throughout the world are recommending good hand hygiene practices. Hand hygiene is considered to be the most important tool in Nosocomial infections control.

Technical features

The manufacturer claims that AGT-1 liquid is used in Europe (private hospitals), University of Los Angeles California, UK National Health Service, Western Africa (14 members of western African countries) and Nigeria.

AGT- 1 liquid solution can be classified as alcohol-based disinfectant. It contains among other chemicals, Robicus Extract in Propanol 1-ol (78%), n- propanol (3.3 %). It claims to contain a proprietary formulation for skin rejuvenation.

In 1994, the FDA classified ethanol (60 % to 95 %) as a Category I agent as generally safe and effective for use in antiseptic hand wash by healthcare workers.

Methodology

Electronic databases were searched, which included Pubmed, Medline, CINAHL, and Cochrane database of systematic reviews, HTA Databases, Horizon scanning databases (CADTH, ASERNIP-S, Defra, Euroscan), FDA website and Google for relevant articles. Search engines used was OVID and Google

The search strategy used the following terms, which are either used singly or in various combinations namely AGT-1, hand rub, hand disinfectant , alcohol based hand rub, safety, efficacy, seaweed, effectiveness and skin rejuvenator. Relevant articles were appraised and graded according to U.S. Preventive Services Task Force (USPTF).

Results and conclusion

AGT-1 Liquid Glove (Medical Device Class 1) has been registered through the Voluntary Registration for Medical Devices Establishment (MeDVER), Ministry of Health Malaysia with the registration number A00645. However this product has yet to obtain CE mark or a US Food and Drug Administration (FDA) approval.

This review was based on 3 published laboratory experiments, 5 research notes on laboratory experiment (unpublished), 1 laboratory experiment on animal, and 3 narrative reviews. There was fair, low level evidence to show the efficacy and safety of AGT -1 liquid but no evidence to show the effectiveness of this liquid. The cost per ml of this liquid is RM 0.58.

Recommendation

Based on the above review, clinical trial to show the effectiveness of AGT-1 Liquid Glove is required. However, there was low level evidence to support the efficacy of AGT-1 Liquid Glove as shown in the laboratory experiments. Therefore, it can be recommended only for research purposes. With regards to cost issues, the cost implications of using AGT-1 Liquid Glove must be considered against the currently used alcohol-based disinfectants in Ministry of Health hospitals as it is comparatively more expensive.

1. INTRODUCTION

Currently almost all the health care settings throughout the world are recommending good hand hygiene practices. Hand hygiene is considered to be the most important tool in nosocomial infection control. [1]

Pathogens that could be found in health care workers are usually the causative organisms responsible for nosocomial infections (NIs) such as *Methicillin-resistant Staphylococcus aureus* (MRSA) which is increasing worldwide especially at the surgical–site infections. The colonization of *Staph.aureus* in the health care workers hands has been described to range between 10.5 and 78.3%. Up to 24,000,000 cells can be found per hand. The colonization rate with *Staph.aureus* was higher among doctors (36%) than amongst nurses (18%). The carrier rate may rise higher if a health care worker contacts patients with an atopic dermatitis, colonized by *Staph. aureus.*[2] MRSA has been isolated from the hands of up to 16.9 % of health care workers. [2] Vancomycin resistant *Enterococci* (VRE) can be found on the hands up to 41 % of health care workers.[2] The survival rate on hands and surfaces were also investigated. For *Staph. aureus* it can survive on hands for at least 150 minutes; VRE survives on hands or gloves for up to 60 min. [3] On inanimate surfaces, *Staph. aureus* and MRSA may survive for 7 months, with wild strains surviving longer than laboratory strains. VRE may survive on surfaces for four months. [3]

The Gram negative bacteria that is commonly found in NIs is the *Escherichia coli* which mainly causes urinary tract infections. *Pseudomonas aeruginosa* is also very common. It causes lower respiratory infections. The study by McFarland et al, reported that the frequency of colonization on the hands of health care workers for gram negative bacteria was about 21-86.1 %, the highest rate being found in ICUs (Intensive Care Unit).[4] Spore-forming bacteria which mainly cause NIs is *Clostridium difficile.* It was estimated between 15 – 55 % that causes diarrhea. The frequency of colonization of *Clostridium difficile* on hands was found mainly in the sub lingual area (43%), on the fingertips (37%), on the palm (37%) and under rings (20%). [4]

Fungi are less found as the causative organisms of NIs but their frequency and importance are increasing. The most common fungi that cause NIs is *Candida albicans*. [3]

Viruses cause approximately 5% of NIs. Five main group of viruses have been identified with respect to their nosocomial transmission:

- Blood-borne viruses such as hepatitis B, hepatitis C and Human Immunodeficiency virus (HIV)
- Respiratory route viruses such as respiratory syncytial virus (RSV)
- Influenza virus, rhinovirus, corona virus and adenovirus
- Fecal-oral route viruses such as rotaviruses, small round structured viruses [noroviruses], enteroviruses and hepatitis A virus [HAV]
- Herpes viruses obtained from direct contact with skin, mucous membranes, or wounds such as herpes simplex viruses, varicella zoster virus, cytomegalovirus, Epstein Barr viruses and exotic viruses (Ebola virus, Marburg virus, and etc).

The fingers, especially the pads and tips, are the most likely areas to come into contact with viruses. [5]

In general, it must be assumed that a health care worker wears a protective glove. However, there are still clinical situations in which contaminations with blood is unexpected. Health care workers, in invasive radiology have blood contact in 3% of clinical activities, surgeons have blood contacts in 50%, and midwives have blood contact in 71%. [6]

The study by Thomas *et al*, indicated that surgical gloves are believed to give protection against direct contact to blood. However, there are situations that perforation of the gloves happens. The perforations of gloves found on average were 17%, which correlates with the detection of blood under surgical gloves in 13 % of surgeons. Perforations in most gloves (83%) remain undetected by the surgeon.[6] Therefore gloves alone does not seem to be sufficient to give maximum protection against pathogens. [6] Other techniques such as surgical scrub and double gloving may give added protection to the health care workers in high risk procedures.[6]

There are three main types of preparations that can be used for the different procedures of hand hygiene.

(i) The first is plain, non medicated soap (social hand wash).

(ii) The second is medicated soap (antiseptic) such as chlorhexidine, Triclosan, Hexachlorophene and etc. The FDA (Food and Drug Administration) classifies these agents as not being generally recognized as safe and effective for use as an antiseptic hand wash.[7]

(iii) The final type is the alcohol- based hand rub.[2] It is applied to the skin without the use of water.

The WHO Guidelines on Hand hygiene in Health care (2005-2006), revealed that most alcohol based antiseptics contain either ethanol, isopropanol or n-propanol, or a combination of two of these products.

Concentration are given as either percentage of volume (ml/100ml), abbreviated % *V/V;* percentage of weight (g/100g), abbreviation % m/m; or percentage of weight/volume (g/100 ml), abbreviation % m/V. The antimicrobial activity of alcohols results from their ability to denature proteins. Alcohol solutions containing 60- 80 % alcohol are most effective, with higher concentration being less potent.

In 1994, FDA TFM classified ethanol 60-95% as generally safe and effective active agents for use in antiseptic hand hygiene or health care workers hand-wash products.[8]

This technology review was conducted following a request from the Deputy Director General of Health (Medical). This liquid was proposed by the manufacturing company to be used as disinfectant to kill NIs pathogens such as MRSA, HIV, Hepatitis B, Hepatitis C and others.

2. OBJECTIVE

The objective of this systematic review was to determine the safety, efficacy, effectiveness and cost of AGT-1 Liquid Glove as a disinfectant against microorganisms that cause nosocomial infections at hospitals.

3. TECHNICAL FEATURES

(Volume: 5ml, 50 ml, 1000ml and 5000ml)

AGT-1 Liquid Glove (AGT) is a disinfectant that is claimed to be effective against nosocomial infection pathogens including including bacteria, viruses and other

pathogens. In addition, this solution was claimed as having good dermal tolerance and skin rejuvenation properties.

AGT-1 Liquid Glove, as claimed by the manufacturer, is used in Europe (private hospitals), University of Los Angeles California, NHS (National Health Service, Britain), Western Africa (14 members of western African countries) and Nigeria.

3.1 AGT-1 Liquid Glove consists of:

a) Phytoserum (Proprietary formulation)
Synthesized from Brown Seaweed Extracts: Hydrocalathrus clathratus, and Lobophora variegate.

b) Other components: C. zeylanicum bark extracts, palm Stearic Acid and Citric acid.

c) Robicus Extract in Propanol 1-ol (78%), n- propanol (3.3 %) and Polyethylene Glycol -200 (PEG).

3.2 AGT-1 Liquid Glove (Medical Device Class 1) has been registered by Voluntary Registration for Medical Devices Establishments (MeDVER), Ministry of Health Malaysia with the registration number **A00645.**

However this product has yet to obtain CE mark or US Food and Drug Administration (FDA) approval.

AGT -1 liquid Glove was tested for its efficacy at:
a) NHS trust ,University College London Hospitals
b) Specialty Medical Laboratories U.S.A
c) University Malaya Medical Centre , Malaysia

3.3 Method of applying the AGT-1 Liquid Glove

This AGT-1 Liquid Glove is applied on both hands with the volume of 1.5–2.5ml before donning the surgical gloves for operating any task. It was also claimed that the protective coating of the AGT-1 Liquid Glove will remain for 9.5 hours while skin rejuvenation effects will last for 4.5 hours.

3.4 Physical appearance
The solution appears light green liquid, smooth to apply on hands and any surface area such as bench top or equipments.

3.5 Physical properties:
Boiling Point: 96 ^{o} C
pH: 6.9 at 25 ^{o} C

4. METHODOLOGY

4.1. Searching

Electronic databases were searched. This included Pubmed, Medline, CINAHL, and Cochrane database of systematic reviews, HTA Databases, Horizon scanning databases (CADTH, ASERNIP-S, Defra, Euroscan), FDA website for relevant articles. Search engine used was OVID and Google.

The search strategy used the terms, which are either used singly or in various combinations: AGT-1, hand rub, hand disinfectant, alcohol based hand rub, safety, efficacy, seaweed, effectiveness and skin rejuvenator.

4.2. Selection

All articles published and unpublished related to safety, efficacy and effectiveness of AGT-1 Liquid Glove were selected. Critical appraisal of relevant literature was performed and evidence graded according to US/Canadian Preventive Services Task Force (Appendix 1)

5. RESULTS AND DISCUSSION

This review was based on 3 published laboratory experiment design, 5 research notes on laboratory experiment (unpublished), 1 laboratory experiment on animal (unpublished), and 3 narrative reviews.

5.1. SAFETY

There was one study by the AGIT, Clinical Centre European Union, [9 Level II-3,] which conducted an acute and corrosive patch test on 30 human subjects. Human 2-D patch test was performed using 0.2 ml of AGT-1 liquid which was placed against the upper arm for 15-30 minutes through 1,2, 3 and 4th hour. The findings of this study showed that AGT-1 liquid did not show any irritation compared to the positive control Sodium Dodecyl Sulfate (SDS) a known irritant. AGT-1 liquid showed negative results for cytotoxicity assay [3-(4, 5)-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT)] and irritancy polyethylene glycol (PEG 2) towards skin and mucous membrane test. [9, level II-3]

Similarly, another study by Slotosch, 2007 investigated the biological response of regular human skin to alcohol-based disinfectants and detergents in a repetitive test design. Using non-invasive diagnostic tools such as transepidermal water loss, laser-Doppler flowmetry and corneometry, they quantified the irritative effects of a propanol-based hand disinfectant (Sterillium), its propanol mixture (2-propanol 45% w/w and 1-propanol 30% w/w), sodium lauryl sulfate (SLS) 0.5% and distilled water. The substances were applied in a 2-D patch test in a repetitive occlusive test design on health care workers. Additionally, they performed a wash test on the forearms that was supposed to mimic the skin affection in the normal daily routine of health care workers. The detergent SLS produced stronger barrier disruption, erythema and dryness as compared to the alcohol-based preparations. The findings showed a less irritant effect of alcohol-based disinfectants on the skin than detergents.[10, level II-3]

In a study conducted by Loffler *et al*, 2007 which investigated skin irritation caused by alcohols alone and in combinations with detergents washing, single and repetitive patch testing with 60-100% alcohols [ethanol, 1-propanol, 2- propanol (synonyms: isoprophl alcohol, isopropanol], a positive control [0.5% sodium lauryl sulphate and negative controls (empty chamber and water) were investigated. Wash tests were performed with 80% ethanol and 0.5% SLS on the forearms with each agent alone and with both agents in a tandem design. Skin hydration, erythema and barrier disruption measured as transepidermal water loss (TEWL) were evaluated in 15 volunteers. The findings showed significant change in skin barrier or erythema induced by the alcohols in the patch tests, whereas skin hydration decreased significantly. Application of alcohols to previously irritated skin did not show a stronger skin barrier disruption than application of SLS alone. Wash tests demonstrated that alcohol application caused significantly less skin irritation than washing with a detergent (TEWL, $P < 0.001$; skin hydration, $P < 0.05$; erythema, $P < 0.05$). A protective effect of ethanol used after skin washing was observed (TEWL, $P < 0.05$; skin hydration, $P < 0.05$; erythema, $P < 0.05$). Alcohol-based hand rubs cause less skin irritation than hand washing and alcohol-based hand rub may even decrease rather than increase skin irritation. [11, level II-3]

Similarly a narrative review by Kampf *et al*, indicated irritant contact dermatitis is commonly found on hands of healthcare employees and is often explained by contact to water and detergents. Studies on the dermal tolerance clearly show that the degree of skin irritation was significantly lower after application of alcohol in comparison to detergents. The irritant potential of commonly used alcohols in hand antiseptics is very low. It is reported that if the skin is pre-irritated, e.g. by detergents or water, alcohols can cause a burning sensation which is, not an allergic reaction and does not further harm the skin. True allergic reactions to alcohols have so far not been confirmed. From the dermatological point of view the use of alcohols for hand hygiene has clear advantages over washing with water and detergents.[12, level III]

5.2 EFFICACY

Alcohol based disinfectant

There was an experiment conducted to test the efficacy of three standard alcohol disinfectants. The effect of 1 minute hand wash on skin hydration and the efficacy of consecutive hand rubbing with three standard alcohols (60% propanol-1-ol, 60 % propanol-2-ol, and 80% ethanol) were tested on the hand flora of 20 volunteers in paired group. Three types of treatment were conducted. First, a minute pre wash before alcohol hand rub disinfectant, second no pre wash before applying alcohol hand rub disinfectant (hand rub) and no pre wash but use brush for 1 minute during disinfectant procedure. The efficacy of the alcohols was determined according to European reference method (prEN 12791). The results of the study showed that Propanol-1-ol (60%) was effective with mean log reduction of 2.11, followed by ethanol (80%) with a mean log 10 reduction of 1.75 and propanol-2-ol (60%) with a mean log 10 reduction of 0.57 (all immediate effect without hand wash). **13,** level II-3

Efficacy study on AGT-1 Liquid Glove was conducted by the AGIT Clinical centre in France, 2000. The **laboratory experiment** was performed using AGT-1 Liquid Glove and incubated various types of microorganisms namely HIV virus, MRSA , Human Papiloma Virus (HPV), Chlamydia , Hepatitis A, Hepatitis C, *Gonococcus* and *Mycobacterium Tuberculosis.* The test result showed that HIV virus was destroyed to undetectable level upon contact with AGT-1 Liquid Glove. Similarly the AGT-1 Liquid Glove was also proven to destroy MRSA, HPV, Chlamydia, Hepatitis A, Hepatitis B, and Hepatitis C., *Gonococcus*, and *Mycobacterium Tuberculosis* pathogens.[14, level II-3]

Virus

Another laboratory experiment was conducted by Speciality Medical Laboratories of U.S.A. This laboratory experiment was conducted on AGT-1 Liquid Glove and incubated it at various time intervals with plasma containing HIV virus (Human Immunodeficiency Virus). The HIV viral load was effectively reduced from 210,000 cycles /min to undetectable levels at the end of the test.[13, level II-3].

Similarly another laboratory test was conducted on clinical sample of HIV virus. Plasma samples with confirmed viral load (PCR) of 256,000 copies/ml were sprayed with 3 doses (approximately 5ml) of AGT-1 Liquid Glove. The viral load decreased to undetectable levels after the treatment of 1.5 ml AGT-1 Liquid Glove solution.[15, level II-3]

Bacteria

AGT-1 Liquid Glove was tested against two strains of Methicilin Resistant *Staphylococcus aureus*, (MRSA 27625 and 27228). These strains were obtained from infected patients admitted at the University Malaya Medical Centre (UMMC). In this experiment, AGT-1 Liquid Glove was compared with two other disinfectants that were commonly used at the hospital (labelled as Disinfectant ST and Disinfectant SF). The bacterial loads of two strains of MRSA were significantly reduced as compared to the other two commonly used disinfectants. In addition this test also assessed the effects of AGT-1 Liquid Glove with two other types of disinfectant using electron microscopy. AGT-1 Liquid Glove could be seen acting at the ultra structural levels of MRSA bacteria. The AGT-1 Liquid Glove was proven to be able to rupture the bacterial wall thus causing the contents to leak. This was confirmed by electron microscopy examination. Partial or complete structural alteration including loss of portion of electron dense core as well as irregular condensation and clumping of electron dense core materials was also discovered. However, the disinfectant SF did not show any changes and the disinfectant ST showed some effect on small number of bacteria and the affected bacteria were noticed had intact cell wall. Using transmission electron microscopy to study the bactericidal effects of disinfectants is an effective method and has been used previously by others for the same purpose. A research paper on this study has been submitted for publication in a peer reviewed journal. (personal communication with the investigator)[16] level II-3

Six strains of *Staphylococcus aureus* together with 2 MRSA strains, *Enterococcus fecalis, Escherichia coli, Pasteurella multocida* and *Pseudomonas aeruginosa* were tested against three disinfectants. In the same study AGT-1 Liquid Glove was compared with disinfectant A (Dettol based), Disinfectant C ([Sodium Dodecyl Sulfate (SDS)] and other common ingredients) which were commonly used in local hospitals. This study was conducted at the Department of Molecular Medicine, UMMC, Malaysia. The result showed that AGT-1 Liquid Glove significantly reduced Colony Forming Units counts (CFU) compared to the controls and other two disinfectants. The MRSA strains, *S. aureus 27625 and 27228* showed reduction in the colony count to $530.7^3 \times 10^3$ and 858×10^3 respectively. The remaining 4 bacterial strains showed 0 counts. The study result for the other disinfectants showed positive growth for all the bacterial strains, such as *E. coli* and *P. Multocida,* which showed higher CFU than the controls. [17] , Level II-3,

This study also indicated that the AGT-1 Liquid Glove uses a plant extract base called phytoserum as the base and is devoid of cations. Studies have shown that the involvement of plasmids in resistance to some disinfectants, such as heavy metals and formaldehyde could contribute to cross resistance between quaternary ammonium compounds (QACs) and aminoglycosides codified by plasmids. This has been reported in MRSA strains implying the extensive use of cationic agents in the hospital environment could contribute to the emergence of resistant strains to antibiotic agents.[17] , Level II-3, 17Level ,II-3

In the same study, AGT-1 Liquid Glove was found to be able to reduce the CFU of *Pseudomonas aeruginosa*, which is common cause of the most hospital acquired

infection at the medical or surgical instruments and respiratory apparatus. It is also known to be highly resistant to antibiotic agents, antiseptics and disinfectant. However, using the AGT-1 Liquid Glove, the CFU of these bacteria was significantly reduced. This study indicated that the plant based phytoserum in AGT-1 Liquid Glove appeared to be an advantage over the other two disinfectant as it probably posses a barrier protection through epidermis generating ability.[17, level II-3]

Skin rejuvenation

There was a laboratory experiment conducted by Suresh K, *et al* 2000 in Department of Molecular Medicine and department of Parasitology Faculty of Medicine, University Malaya, on AGT-1 Liquid Glove which has phytoserum. This ingredient was claimed not to cause irritation on hands and confers a healthy barrier, at the same time prevent microbial contamination and generates another layer of epidermis skin. Animal experimentation was conducted on 12 Spraque Dawley rats, four groups of three rats each were treated with the 3 disinfectants (AGT-1, ST and SF) and the control was treated with distilled water. Five hundred micro-litre of the respective disinfectant was applied on the clean shaven skin of the rats and examined at 1hr, 3hr and 5hr respectively. Tissues were trimmed, embedded, sectioned and stained with Harris' haematoxylin & eosin (H& E) stain for 10 minutes. The results of the test showed that disinfectant SF and ST have increased the thickness of epidermis almost 2½ times when compared to the controls whereas the skin treated with AGT-1 Liquid Glove at 5 hr showed no significant increase in thickness of the epidermis. The findings of this animal study showed AGT-1 Liquid Glove was better than the other two disinfectants because it did not cause any reaction to the skin**.** [18 level II-3] However, the period of exposure of the 3 disinfectants was short and questionable to provide such outcomes.

Acceptance

A prospective, randomised double blind study with intra–individual comparison of the results was undertaken with 20 volunteers to assess the influence of cosmetic additive on the acceptability of mixture of n-propanol (50% v/v) and isopropanol (30% v/v) for hand disinfectant. Three to 5 ml of antiseptic was rubbed into the hands until dry, 15 times a day, 5 days a week and for 2 weeks per preparation. The study assessed the parameters such as 'appearance', 'intactness', 'turgor' and sensation of the disinfectant. The result of this study indicated that antimicrobial efficacy of the alcoholic mixture was equivalent to or better than the standard (isopropanol 60% v/v, 1 min). The frequent application of these antiseptic preparations caused a slight but significant deterioration of the skin condition as judged by both self-assessment and dermatologist. However, this was significantly less when the antiseptic contained cosmetic additives. The addition of suitable emollients can significantly increase the acceptability of alcohol based disinfectants. [19, level 1]

5.3. COST

The cost of 1.5 ml AGT-1 Liquid Glove is estimated about **RM 0.58**. Comparatively, other alcohol based hand solution such as Desmanol costs EUR 19.20/1000 ml (approximately **RM 0.09** per ml) and Strerillium costs £ 9.30 /475 ml (approximately **RM 0.10** per ml).

6. CONCLUSION

6.1 Safety

Fair evidence on the safety aspect of AGT-1 Liquid Glove was described by laboratory experimental studies.

6.2 Efficacy

Sufficient amount of efficacy studies were conducted on AGT-1 Liquid Glove but the level of evidence is low as they were mainly laboratory experiments.

6.3 Effectivenesss

No evidence retrieved to support the effectiveness of AGT-1 Liquid Glove.

7. RECOMMENDATION

Based on the above review, clinical trial to show the effectiveness of AGT-1 Liquid Glove is required. However, there was low level evidence to support the efficacy of AGT-1 Liquid Glove as shown in the laboratory experiments. Therefore, it can be recommended only for research purposes. With regards to cost issues, the cost implications of using AGT-1 Liquid Glove must be considered against the currently used alcohol based disinfectants in Ministry of Health hospitals as it is comparatively more expensive.

8. REFERENCES

1. Nystrom, B. Impact of handwashing on mortality in intensive care: examination of the evidence. *Infect Control Hos. Epidemiol*. 1994;15: 435-436.
2. Gunter Kampf and Axel Kramer. Epidemiology Background of Hand hygiene and evaluation of the most important agents scrubs and rubs. *Clinical microbiology reviews*. Oct .2004; 863-893.
3. Williams,J.V. Vowels, P.Honig and J.J. Leyden. Staphylococcus areus isolation from the lesions, the hands, and anterior nares of patients with atopic dermatitis. *J Emerg Med*. 1999; 17: 207-211.
4. McFarland, L.V., M.E Mulligan, R.Y.Y. Kwok, and W.E. Stamm Nosocomial acquisition of Clostridium difficile infections. *N Engl J Med.* 1999; 320:204-210.
5. Sattar,S.A. V. S. Springthore J. Tetro, R. Vashon and B. Keswick. Hygienic hand antiseptics: should they not have activity and label claims against viruses? *Am J Infect Control*. 2002; 30: 355 – 372.
6. Agarwal and G. Metha (Interoperative glove perforation – single versus double gloving protection against skin contamination. *Postgrad Med J.* 2001; 77: 458-460.
7. Anonymous. Tentative final monograph for health care antiseptic products: proposed rule. *Fed Regist*. 1994; 59:31401-31452.
8. World Alliance For Patients Safety.WHO Guidelines On Hand Hyegine In Health Care (Advanced Draft). Global patient safety challenge 2005-2006.
9. Hubner No, Kampf G, lofflers H, Kramer A, Effect of a min hand wash on the bactericidal efficacy of consecutive surgical hand disinfectant with standard alcohols and on skin hydration. *Br J Dermatol.* 2003; 148:65–69.
10. Slotosch CM, Kampf G, Lofflers H. Effects of disinfectants and detergents on skin. *Contact dermatitis.* 2007; 57(4): 235-241.
11. Loffler H, Kampf G, Schmermund D, Maibach HI. How irritant is alcohol? *Br J Dermatol*. 2007 ; 157 (1) :1-3
12. Kampf G, Loffler H. Prevention of irritant contact dermatitis among health care workers by using evidence based hand hygiene products: a review. *Cad Healh.* 2007; 45 (5): 645-652.
13. Kampf G, Hubner H, Lofflers H, Kramer A. Surgical hand antisepsis to reduce surgical site infection. *Infection Control and Hospital. Epidemiology*. 2001; 22(10):635–640.
14. AGIT, Clinical Centre France. AGT-1 tested by PCR**. (unpublished).**
15. Agila Padmanathan. AGT-1 Liquid gloves & AGT-1 Latex Surface Coating Clinical Trial Application report. January 2000, Speciality Laboratories U.S.A Subsidisry Affiliated with Pharmaniaga Group. **(unpublished)**

16. Salmah S, Suresh K, Christopher A and Ralph D. Aaride AGT-1 Liquid Glove an anti- MRSA disinfectant. Department of Molecular Medicine and Department of Parasitology, Faculty of Medicine, University of Malaya, University College London Hospitals NHS Foundation Trust. **(unpublished)**
17. Salmah S and Suresh K. AGT-1 liquid glove – an effective disinfectant against bacteria. Department of Molecular Medicine and Department of Parasitology, Faculty of Medicine, University of Malaya. **(unpublished)**
18. Suresh K, Salmah S, Christopher A. Effect of disinfectant on rat skin. Department of Molecular Medicine and Department of Parasitology, Faculty of Medicine, University Malaya Malaysia. **(unpublished)**
19 Rotter ML, Koller W, Neumann R. The influence of cosmetic additives on the acceptability of alcohol – based hand disinfectants. *J Hosp Infect*. 1991 Jun; 18 Suppl B: 57-63.

9. APPENDIX

9.1 Appendix 1

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)