ANTIMICROBIAL GLOVES **FAQ**

ABENA

1. What is AMG Antimicrobial glove?

AMG is the world's first non-leaching antimicrobial gloves, designed to kill microorganisms on the external side of the glove quickly upon contact.

2. What is the purpose of AMG antimicrobial glove?

Though conventional gloves provide a barrier between healthcare worker and patient, it does not tackle the problem of transient transmission, where microbes get transmitted from one surface to another. AMG glove is designed to help reduce the spread of HAI, as it is proven to kill up to 99.999% of selected microbes.

3. Why does AMG gloves provide Active Protection Against HAIs?

The use of medical gloves is intended to prevent cross contamination between the patient, the user and its environment.

However, conventional gloves can only provide passive protection as contaminated gloves caused by inappropriate storage, inappropriate use and techniques for donning and removing, may in turn become a vehicle for transmission of microbes.

Conversely, AMG gloves provide an active approach in HAI prevention as the gloves can continuously and effectively reduce or inhibit microbial colonisation on the glove surface within a short amount of time, thus further reducing the risk of cross contamination.

4. Does AMG antimicrobial glove replace the need for hand hygiene?

Although AMG glove has been found effective against a wide range or microbes, it does not replace the need for hand hygiene. AMG serves as an extra precaution or tool to help mitigate the spread of HAI. Protocols for hand rubbing or hand washing should still be performed before donning and after removing gloves.

5. What does it mean by non-leaching? Is it safe?

We designed the antimicrobial gloves to be non-leaching to ensure the active ingredient does not transfer to the patient. To further ensure the safety of the active ingredient, the gloves were tested for biocompatibility. Below illustrates the tests carried out:

i. Tested at Intertek UK, the gloves were extracted using water, artificial saliva, artificial sweat and alcohol at room and body temperature. The extracts were analysed by validated analytical techniques to detect the active. No active could be found extracted from the gloves' inner or outer surface.

ii. ISO 10993 biocompatibility testing has been conducted on the inside and external surface of the gloves. Results confirm that the gloves are non-sensitising, non-irritating, non-toxic (oral) and non-cytotoxic.

iii. The Modified Draize-95 test was also conducted where both the inner and outer surfaces of the gloves were tested on human skin. The gloves provided no clinical evidence of inducing allergic reactions. With this test result, U.S. FDA allows a "Low Dermatitis Potential" claim for the gloves.

6. What materials are in contact with my skin when using AMG Antimicrobial gloves?

AMG's technology is introduced on the external side of the glove. The glove user is exposed to the donning side of the glove, which is similar to a standard examination glove. The skin of the glove user is not exposed to this technology.

7. How does singlet oxygen work?

In this technology a special dye is used. The dye absorbs visible light. The dye is thus raised from a ground state to an excited quantum state, in which an elevation in energy takes place. The energy then transfers to a proximal oxygen molecule found in the air, causing the oxygen molecule to also rise to an excited quantum state. The ground state of oxygen present in air, is a triplet electronic configuration, written as $^3O_2$. Upon sensitisation by the dye molecule, the electronic configuration changes and enters the singlet state, $^1O_2$.

This singlet oxygen state is reactive and more oxidative compared to ground state oxygen and therefore, is able to kill microbes such as bacteria by oxidising the cells' protein and lipid. Using the dye as a catalyst, singlet oxygen can be generated continuously as it absorbs light and air.

8. What are the advantages of using singlet oxygen antimicrobial system?

Singlet oxygen is a non-selective system that can react rapidly against many microbial components. There is not one single protection mechanism that bacteria can protect itself from singlet oxygen.[4] This is in contrast to antibiotics, which needs very specific mechanism to treat a patient. As singlet oxygen is transient, it does not lead to the release of persistent biocides into the environment.

AMG will as such transform the standard examination glove from a passive medical device to a medical device with active protection which will actively reduce or inhibit microbial colonisation.

9. Has singlet oxygen technology been used before commercially?

Whilst it has not received as much attention as traditional biocides, singlet oxygen has been researched for a wide range of uses for many years and a number of important commercial applications are known.[5,6,7,8,9]

In humans, singlet oxygen generating dyes are used for cancer treatment, known as photodynamic therapy, PDT.

It is also used in dental disinfection prior to procedures like root canal treatments, in which the dye is rinsed into the patients' mouths, a light applied and disinfection occurs safely and rapidly.

However, probably the most ubiquitous use is in laundry powders, where a singlet oxygen generating dye is washed onto clothing, and subsequently acts as a photobleach. Many readers of this will therefore be unwitting users of singlet oxygen and will be wearing some singlet oxygen generating dye.

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10. Are there literature to show potential of resistance using singlet oxygen antimicrobial system?

Experimental studies have been done and reported in the literature about singlet oxygen efficacy and resistance.[10,11] In these, bacteria were killed to a high extent with singlet oxygen, typically 99.9% or 99.99%, leaving only the most robust bacteria. These were then re-cultivated and re-exposed to singlet oxygen. This cycle is repeated 10 or 20 times, and the efficacy of killing is measured. In all cases, it was found that there is no decrease in efficacy and no development in resistance.

Many of the mechanisms bacteria use to confer resistance involve processes internal to the cell. In AMG system however, the singlet oxygen is generated purely exogenously to the cell – the dye is separated from the bacteria, it does not leach, and it cannot enter the cells. Other authors in the literature have noted[4,10] that this makes development of resistance especially difficult, because singlet oxygen is short lived and with a short length of diffusion – nothing the bacterial cell does internally will affect the process of oxidation by singlet oxygen.

Furthermore, a review of the potential for resistance to biocidal materials was done by the EU expert scientific committee. The report puts biocidal materials into three categories: low risk of resistance developing, medium risk and high risk. These authors put oxidative systems as low risk, some traditional biocide materials such as chlorhexidine and PHMB as medium risk, and silver as high risk.[3]

11. What is the amount of light needed to activate the AMG Antimicrobial Gloves?

Testing of AMG glove has been conducted at general lighting condition at hospitals of 1000 lux and 500 lux. Results show that there was no significant difference in bactericidal efficacy. Further testing at lower light levels are underway.

12. Would differences in lighting type affect the efficacy of AMG Antimicrobial gloves (for example – LED, fluorescent, incandescent light bulb)?

No. The AMG is activated by any white light source. It is specifically activated by light in the 600 - 700 nm region but all white light sources contain this, otherwise they would be coloured.

13. Will the dye be depleted if the AMG Antimicrobial Gloves are continually exposed to light?

No. As long as there is light and oxygen, the gloves are active. Heat aged AMG gloves (accelerated aging equivalent to 3 years shelf life) did not show significant difference in bactericidal efficacy compared to fresh AMG gloves.

AMG gloves were also exposed to "light" (equivalent to 30 days in an open box environment). Again, there was no significant difference in bactericidal efficacy compared to fresh AMG gloves.

14. What are the different classifications of bacteria?

Bacteria are classified into Gram-positive or Gram-negative. This classification came from a staining property observed by Hans Gram in 1884. It was observed that some bacteria could be stained with a dye, and others could not. It was later found that bacteria have different cell wall structure. Gram-positive bacteria allow substances to cross the cell wall more easily. The cell wall of Gram-negative bacteria is multi-layered and so it is harder for substances to cross the cell wall.

15. What are some examples of Gram-negative bacteria?

Gram-negative bacteria include *Esherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Acinetobacter baumannii* among others.

16. What are some examples of Gram-positive bacteria?

Gram-positive bacteria include MRSA, *Staphylococcus aureus, Enterococcus faecium, Streptococcus pyogenes, Enterococcus faecalis* (VRE) among many others.

17. What type of bacteria survive longer on surfaces, which allow the possibility of infection transfer?

Based on a study conducted by Hirai,[12] which measures the survival of different types of bacteria on cotton lint, the results showed that Gram-positive bacteria have longer lifetimes on surfaces, which may have implications that these bacteria are available for transfer to cause HAIs. Gram-negative bacteria are known to die more quickly on surfaces, especially if the surface is dry.

18. How about in a clinical environment? Is there a survival difference between Gram-positive and Gram-negative bacteria?

The pattern of lower survival of Gram-negative bacteria is also seen in the clinical environment. In Wilson et al study,[13] Gram-positive bacteria such as *Staph* a. were found in numerous locations in the hospital environment, but Gram-negative bacteria such as *E. Coli* were not found on any surfaces sampled, despite having a number of patients in the ward with E. *Coli* infections.

19. Do biocides kill Gram-positive or Gram-negative bacteria easily?

All bacteria respond to biocides differently, requiring different contact times and concentrations for inactivation. In general, Gram-negative bacteria are harder to kill with biocides.[14]

20. How is the bactericidal efficacy of AMG Antimicrobial gloves measured?

AMG Antimicrobial Glove will start generating singlet oxygen and start killing bacteria immediately upon exposure to light and oxygen. Based on the requirements of ASTM D7907-14, the contact time in which the bacteria have been exposed the external surface of the glove containing antimicrobial agent needs to be measured at intervals of 5 mins, 10 mins, 20 mins and 30 mins.

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At the end of each contact time, the glove is transferred into a validated neutraliser to stop the bactericidal activity. This will stop the singlet oxygen killing activity on the microbes, which will in turn allow the calculation of bacteria kill.

Additional testing has been conducted at shorter contact times of 1 min and 2 mins on *Staphylococcus aureus* with bacteria kill rates of 99.898% and 99.998% respectively.

21. Does AMG glove has any efficacy on virus?

We believe AMG can kill viruses apart from bacteria. This is why we choose to name it Antimicrobial instead of the more limited Antibacterial. However, all our tests are based on ASTM D7907 Standard Test Methods for Determination of Bactericidal Efficacy on the Surface of Medical Examination Gloves. This test method specified the glove to be tested against 4 specific bacteria. As AMG is a new invention, there is no other standard that we can use to test for viral efficacy. Nevertheless, we are working on adapting D7907 to test for viruses. This work will take a longer time to complete. One of the challenge is that viruses only replicate inside the living cells; once expose to the environment they will be destroyed quickly, therefore making it difficult for us to test.

Meanwhile, we have decided to launch AMG with D7907 test data as we believe most HAIs attributable to hand-surface contamination are bacteria. Viruses like Hepatitis and HIV are spread through fecal-oral route or transmission through contaminated syringes, needles or sharps, infected blood transfusions. The more common flu virus is mainly spread to others by droplets made when people with flu, cough, sneeze or talk. These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs. Less often, a person might get flu by touching a surface or object that has flu virus on it and then touching their own mouth, nose, or possibly their eyes.[15]

22. What is the medical device classification for AMG Antimicrobial Gloves in MDD93/42/EEC?

European Union MDD 93/42/EEC Annex IX:
Class I (Rule 5) includes "*All invasive devices with respect to body orifices, other than surgically invasive devices and which are not intended for connection to an active medical device...".*

As such, the Antimicrobial Nitrile Powder Free Examination gloves are an invasive device intended for short transient use (I. Definitions, 1.1) for examinations on intact skin and also involve body orifices (I. Definitions, 1.2). All other parts of rule 5 do not apply.

Based on rule 5 (III. Classification, section 2, 2.1), the Antimicrobial Nitrile Powder Free Examination Gloves are classified as a medical device class I.

23. What is the intended use and indication for AMG Antimicrobial Gloves in the technical file?

The Antimicrobial Nitrile Powder Free Examination Gloves are intended to be used in the framework of medical examinations and diagnostic and therapeutic procedures conducted under non-sterile conditions. Furthermore, the use of the device is intended to help prevent cross contamination.

Its indication is stated as "Any medical condition requiring an examination, a diagnostic or therapeutic procedure on the intact skin or mucosa under non-sterile conditions".

24. Does AMG Antimicrobial Gloves require registration by EU Biocidal Regulation?

The Biocides Regulation (EU) No. 528/2012 is not applicable for medical devices unless they are intended to be used for other purposes not covered by the medical device directive, in which case the Biocides Regulation shall also apply to that product insofar as those purposes are not addressed by those instruments. In our understanding, this would mean that the biocides regulation is only applicable if the gloves are intended for other non-medical purposes or if the antibacterial feature would not be within the original purpose of the medical device. As the gloves' medical purpose is to prevent infection of the patient and the antimicrobial feature supports this purpose, we believe that the biocides regulation is not applicable.[16]

ANTIMICROBIAL GLOVES **Appendix:**

Appendix: Commonly Found Bacteria in Healthcare Facilities that Cause HAI

No.	Microbe	Type	Impact
1	*Enterococcus faecalis*/ Vancomycin-resistant enterococci (VRE)	Gram-positive Bacteria	According to the Centers for Disease Control and Prevention (CDC), *Enterococcus faecalis* is responsible for approximately 80% of human infections.[17] It is one of the bacteria that is becoming resistant to vancomycin, an antibiotic, and sometimes other standard therapies. Vancomycin-resistant enterococci (VRE) are leading causes of nosocomial bacteraemia, surgical wound and urinary tract infections.
2	*Enterococcus faecium*	Gram-positive Bacteria	*Enterococcus faecium* has been a leading cause of multi-drug resistant enterococcal infections over *Enterococcus faecalis* in the U.S. Approximately 40% of medical intensive care units reportedly found that the majority of device-associated infections were due to vancomycin- and ampicillin-resistant *E. faecium*.[18] The rapid increase of VRE has made it difficult for physicians to fight infections caused by *E. faecium* since not many antimicrobial solutions are available.[19]
3	Methicillin-resistant *Staphylococcus aureus* (MRSA)	Gram-positive Bacteria	Commonly transmitted through direct contact, open wounds and contaminated hands, MRSA is a type of staph bacteria resistant to many antibiotics. Due to this, it is sometimes also called a "superbug". MRSA can cause severe problems such as bloodstream infections, pneumonia and surgical site infection in healthcare settings such as hospitals and nursing homes. Every year, MRSA infects about 72,444 people with 9,194 related deaths in the U.S.[20]
4	*Staphylococcus aureus*	Gram-positive Bacteria	According to CDC, about 30% of people carry this microbe in their noses.[21] Usually staph does not cause any harm; however in healthcare settings, it can sometimes cause infections that are serious or fatal. These infections include bacteraemia or sepsis, pneumonia, endocarditis (infection of the heart valves) and osteomyelitis (bone infection).
5	*Streptococcus pyogenes*	Gram-positive Bacteria	It is estimated that 5 - 15% of healthy individuals carry it on the skin or in the respiratory tract without showing symptoms of illness.[22] It can rapidly colonise and multiply within a host, causing mild infections like "strep throat" or impetigo. When it becomes invasive, it can destroy fat, skin and muscle tissues, leading to necrotising fasciitis (flesh-eating disease).
6	*Enterobacter cloacae*	Gram-negative Bacteria	*E. cloacae* has been reported as a multidrug-resistant opportunistic pathogen infecting people in hospital wards for the last three decades. These Gram-negative bacteria have been responsible for several outbreaks of HAIs in Europe, particularly in France.[23]
7	*Escherichia coli*	Gram-negative Bacteria	*E. coli* can cause diarrhoea, urinary tract infections, respiratory illness, bloodstream infections, and other illnesses. The types of *E. coli* that can cause illness can be transmitted through contaminated water or food, or through contact with animals or people.
8	*Klebsiella pneumoniae*	Gram-negative Bacteria	These bacteria have become resistant to the class of antibiotics called carbapenems. Unfortunately, carbapenem antibiotics often are the last line of defence against Gram-negative infections that are resistant to other antibiotics.[24] The bacteria are not spread through the air, but through physical contact. It can cause pneumonia, bloodstream infections, wound or surgical site infections, and meningitis.