

## **ANTI-MICROBIAL COMPOSITION**

This invention relates to anti-microbial compositions and to formulations including the  
5 anti-microbial compositions. In particular, the invention relates to anti-microbial  
compositions that can be used on skin.

Micro-organisms such as bacteria and viruses, for example norovirus, polio virus and  
adenovirus, are well known to present health hazards due to infection or contamination.  
10 Along with fungi, yeasts and other micro-organisms they can also cause spoilage of items  
such as food, clothing and produce unpleasant odours. When micro-organisms are present  
on the surface of a substrate, such as skin, they can replicate rapidly to form colonies.

Many anti-microbial agents can destroy micro-organisms that are present in a wide range  
15 of environments. For example, anti-microbial agents that may be used in medical,  
industrial, commercial, domestic and marine environments are known. Many of the known  
anti-microbial agents have previously been included in compositions for use in these  
environments for various applications.

20 Known anti-microbial agents and the compositions that contain these anti-microbial agents  
act via a number of different mechanisms.

For example, many anti-microbial agents are poisonous to microorganisms and, therefore,  
destroy microorganisms with which they are contacted. Examples of this type of anti-  
25 microbial agent include hypochlorites (bleaches), phenol and compounds thereof, and salts  
of copper, tin and arsenic.

However, whilst many of these anti-microbial agents are effective against micro-organisms  
and appropriate for certain environments, their mechanisms can make them unsuitable or  
30 disadvantageous for topical application to human skin due to their detrimental effects to  
human health or on skin condition. For example, hypochlorite bleach is very effective at  
killing micro-organisms on solid surfaces, but inappropriate for application to skin due to  
its corrosive properties. Also, these materials tend to be effective in a wet environment for  
sterilization and cleansing but stop working shortly after drying.

Many skin sanitizers are alcohol-based. These are typically an alcohol-containing preparation designed for application to the hands for reducing the number of viable microorganisms on the hands. Such preparations typically contain 60%-95% ethanol or isopropanol. However, while isopropyl alcohol has established anti-bacterial properties, it has the disadvantage that, when used regularly, it can cause dryness and skin irritation. As a result, some people may be reluctant to use such creams, soaps and other compositions comprising significant levels of isopropanol.

Some anti-microbial agents are highly toxic to humans and animals and are dangerous to handle. Specialist handling, treatment and equipment are therefore required in order to handle them safely. The manufacture and disposal of compositions comprising this type of anti-microbial agent can, therefore, be problematic. There can also be problems associated with the use of compositions containing this type of anti-microbial agent, particularly in consumer materials where it is difficult to ensure that they are used for designated purposes.

Herein, unless the context indicates otherwise, “toxicity” is intended to refer to toxicity to complex organisms such as mammals. References to “toxic” are to be construed accordingly.

Increasing scrutiny of the environmental credentials of chemicals is further restricting the usage of anti-microbial agents not just for topical application on skin but for general use. For example, some anti-microbial agents once they enter the environment can harm other organisms. They can also be very stable and persist in the environment for long periods causing concerns around build-up and residual levels.

Because of these factors the list of effective and available anti-microbial agents, particularly for use on skin, is becoming more restricted and the burden of registering new anti-microbials more prohibitive. At the same time the public are becoming increasingly concerned with sanitization, both of person and property following outbreaks such as MRSA in hospitals.

There is a need to provide compositions for a variety of applications and uses, such as compositions for use on skin, for example hand sanitising agents, that have anti-microbial

properties and that address one or more of the problems set out above. However, it is not a straight forward matter to do this. There are regulations such as the Biocidal Products Regulations (Directive 98/8/EC) which regulates the use of anti-microbial agents both in terms of the nature and the amount of a given anti-microbial agent that may be used.

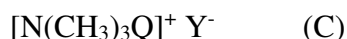
5 Additionally, the potential reactivity of an anti-microbial agent once in a composition is important as some anti-microbial agents are rendered inactive by chemical reaction. Even where an anti-microbial agent is not deactivated by chemical reaction it may have its activity suppressed by other components of the composition.

10 The present inventors have surprisingly found that the foregoing deficiencies can be overcome by certain combinations of components. It has also been found that compositions containing these combinations of components can have some surprising and unexpected properties.

15 The listing or discussion of an apparently prior-published document in this specification should not necessarily be taken as an acknowledgment that the document is part of the state of the art or is common general knowledge.

The present invention provides an anti-microbial composition comprising:

20 (i) a compound of formula (C):



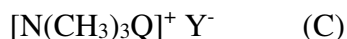
wherein Q is a C<sub>10-20</sub> (for example C<sub>12-20</sub>) hydrocarbon chain which may be saturated or unsaturated, optionally the hydrocarbon chain may be interrupted by one or more amido groups (-NHC(O)-), Y<sup>-</sup> is a halide anion (such as chloride, bromide, fluoride, iodide), an  
25 alkylsulphate (such as a C<sub>1-6</sub> alkylsulphate, for example methosulphate (or methylsulphate, CH<sub>3</sub>OSO<sub>3</sub><sup>-</sup>), sulphonate (GSO<sub>3</sub><sup>-</sup>, wherein G is an organic residue, such as a C<sub>1-6</sub> alkyl group)), saccharinate, or bicarbonate, or a mixture of compounds of formula (C);

(ii) an anti-microbial component comprising at least one anti-microbial quaternary ammonium compound and chlorhexidine or a chlorhexidine salt; and

30 (iii) a polar solvent.

### ***Component (i)***

Component (i) comprises one or more compounds of formula (C):



wherein Q is a C<sub>10-20</sub> hydrocarbon chain which may be saturated or unsaturated, such as a C<sub>12-20</sub> or C<sub>14-20</sub> hydrocarbon chain, for example a C<sub>12, 13, 14, 15, 16, 17 or 18</sub> hydrocarbon chain; optionally the hydrocarbon chain (whether saturated or unsaturated) may be interrupted by one or more amido groups (-NHC(O)-), for example one, two, three or four amido groups, such as one amido group.

By way of example, the hydrocarbon chain may be saturated or contain one or more C=C double bonds, for example one, two, three or four C=C double bonds.

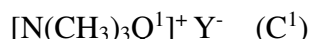
In one aspect, the hydrocarbon chain contains one or more C=C double bonds, for example one, two, three or four C=C double bonds and is interrupted by one or more amido groups (-NHC(O)-), for example one, two, three or four amido groups, such as one amido group.

Q may, for example, be a saturated and uninterrupted C<sub>12-20</sub> or C<sub>14-20</sub> hydrocarbon chain.

Q may, alternatively, be a C<sub>10-20</sub> or C<sub>12-20</sub> hydrocarbon chain that is unsaturated and/or interrupted by one or more amido groups.

Y<sup>-</sup> is a halide anion such as chloride, bromide, fluoride, iodide, or an alkylsulphate (such as a C<sub>1-6</sub> alkylsulphate, for example methosulphate (or methylsulphate, CH<sub>3</sub>OSO<sub>3</sub><sup>-</sup>), sulphonate (GSO<sub>3</sub><sup>-</sup>, wherein G is an organic residue, such as a C<sub>1-6</sub> alkyl group)), saccharinate, or bicarbonate. In one aspect, Y<sup>-</sup> is a halide anion, for example chloride or methosulphate anion.

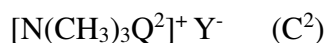
Preferred compounds of formula (C) include those of formula:



wherein Q<sup>1</sup> is an unsubstituted, uninterrupted C<sub>14-20</sub> alkyl chain, such as a C<sub>16-20</sub> alkyl chain, for example a C<sub>14, 15, 16, 17 or 18</sub> alkyl chain, wherein Y<sup>-</sup> is as defined above, for example Y<sup>-</sup> is a halide anion such as chloride.

An example of a compound of formula C<sup>1</sup> that may be used in the present invention is [N(CH<sub>3</sub>)<sub>3</sub> C<sub>16</sub> H<sub>33</sub>]<sup>+</sup> Cl<sup>-</sup>, cetyl trimethyl ammonium chloride (CTAC).

Preferred compounds of formula (C) also include those of formula:



wherein  $\text{Q}^2$  has structure  $-(\text{CH}_2)_a\text{NHC}(\text{O})(\text{CH}_2)_b\text{CHCH}_2$ , wherein  $a + b$  is an integer of from 8 to 18 (such as 10 to 18), provided that  $a$  and  $b$  are each independently an integer of from 1 to 9, for example  $a$  is from 1 to 5 and  $b$  is from 5 to 9, wherein  $\text{Y}^-$  is as defined above, for example  $\text{Y}^-$  is an alkylsulphate anion, such as methosulphate anion.

An example of the group  $\text{Q}^2$  is  $-(\text{CH}_2)_3\text{NHC}(\text{O})(\text{CH}_2)_8\text{CHCH}_2$

10 An example of a compound of formula  $\text{C}^2$  that may be used in the present invention is  $[\text{N}(\text{CH}_3)_3(\text{CH}_2)_3\text{NHC}(\text{O})(\text{CH}_2)_8\text{CHCH}_2]^+ \text{CH}_3\text{SO}_4^-$ , undecylenamidopropyltrimonium methosulfate (available commercially as Rewocid UTM 185).

### ***Component (ii)***

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The compositions of the invention comprise chlorhexidine or a chlorhexidine salt. Examples of suitable chlorhexidine salts include the acetates, formates, gluconates, hydrochlorides, isoethionates, lactates, and succinamates of chlorhexidine. For example, suitable salts include, but are not limited to chlorhexidine diphosphanilate, chlorhexidine digluconate, chlorhexidine diacetate, chlorhexidine dihydrochloride, chlorhexidine dichloride, chlorhexidine dihydroiodide, chlorhexidine diperchlorate, chlorhexidine dinitrate, chlorhexidine sulfate, chlorhexidine sulfite, chlorhexidine thiosulfate, chlorhexidine di-acid phosphate, chlorhexidine difluorophosphate, chlorhexidine diformate, chlorhexidine dipropionate, chlorhexidine di-iodobutyrate, chlorhexidine di-n-valerate, chlorhexidine dicaproate, chlorhexidine malonate, chlorhexidine succinate, chlorhexidine succinamate, chlorhexidine malate, chlorhexidine tartrate, chlorhexidine dimonoglycolate, chlorhexidine mono-diglycolate, chlorhexidine dilactate, chlorhexidine di-alpha-hydroxyisobutyrate, chlorhexidine diglucoheptonate, chlorhexidine di-isothionate, chlorhexidine dibenzoate, chlorhexidine dicinnamate, chlorhexidine dimandelate, chlorhexidine di-isophthalate, chlorhexidine isoethionate chlorhexidine di-2-hydroxy-napthoate, and chlorhexidine embonate.

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A specific example of a chlorhexidine salt that may be used in the compositions of the invention is chlorhexidine di-gluconate.

Component (ii) of the compositions of the invention also comprises at least one quaternary ammonium anti-microbial agent.

- 5 The quaternary ammonium anti-microbial agent(s) used in the present invention are typically water soluble at room temperature and pressure.

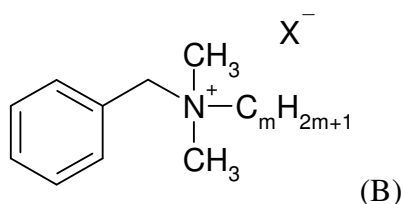
Suitable anti-microbial quaternary ammonium compounds include compounds of formula (A) shown below.



wherein  $\text{R}^1$  and  $\text{R}^2$  are each independently a straight chain, unsubstituted and uninterrupted  $\text{C}_{8-12}$  alkyl group. In one aspect, the groups  $\text{R}^1$  and  $\text{R}^2$  contain the same number of carbon atoms but this is not essential and compounds in which  $\text{R}^1$  and  $\text{R}^2$  contain different number  
15 of carbon atoms can be used.  $\text{X}^-$  is a halide anion (such as chloride, bromide, fluoride, iodide), sulphonate ( $\text{GSO}_3^-$ , wherein G is an organic residue, such as a  $\text{C}_{1-6}$  alkyl group), saccharinate, or bicarbonate.

In the compounds of formula (A) each group  $\text{R}^1$  and  $\text{R}^2$  is independently a straight chain,  
20 unsubstituted, uninterrupted  $\text{C}_{8-12}$  alkyl group, for example an alkyl group containing 8, 9, 10, 11 or 12 carbon atoms.  $\text{R}^1$  and  $\text{R}^2$  may be the same, for example  $\text{R}^1$  and  $\text{R}^2$  may both be alkyl groups containing 8, 9, 10, 11 or 12 carbon atoms, as an example both  $\text{R}^1$  and  $\text{R}^2$  may be 10.

- 25 Suitable anti-microbial quaternary ammonium compounds also include benzalkonium compounds having the formula (B) shown below.

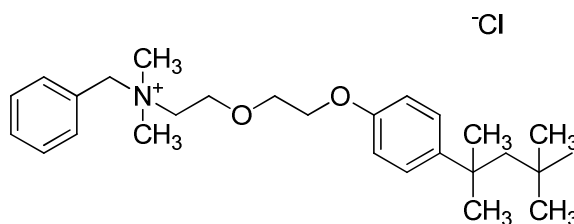


wherein  $m$  is from 8 to 18, and  $X^-$  is a halide anion such as chloride, bromide, fluoride, iodide, sulphonate ( $GSO_3^-$ , wherein  $G$  is an organic residue, such as a  $C_{1-6}$  alkyl group), saccharinate or bicarbonate.

- 5 The compounds of formula (B) are generally called benzalkonium compounds. The benzalkonium chloride is provided and/or used as a mixture of  $C_{8-18}$  alkyl groups, particularly a mixture of straight chain, unsubstituted and uninterrupted alkyl groups  $n-C_8H_{17}$  to  $n-C_{18}H_{37}$ , mainly  $n-C_{12}H_{25}$  (dodecyl),  $n-C_{14}H_{29}$  (tetradecyl), and  $n-C_{16}H_{33}$  (hexadecyl). Preferably  $m$  is 8, 10, 12, 14 and/or 16. Most preferably  $m$  is from 8 to 12 for  
 10 example 8, 10 and/or 12 or from 12 to 16, for example 12, 14 and/or 16.

By benzalkonium compounds we also include derivatives of benzalkonium compounds whereby the alkyl group  $C_mH_{2m+1}$  shown below can be substituted by another organic group. Such organic groups include but are not limited to alkenyl, phenyl, amide, ester,  
 15 alcohol, and ether groups or combinations thereof.

An example of such a derivative of a benzalkonium compound is diisobutylphenoxyethoxyethyl-dimethylbenzyl ammonium chloride, whose INCI name is benzethonium chloride (typically abbreviated to BENZ). The structure of benzethonium  
 20 chloride is shown below.



In an aspect of the invention, where the composition comprises two or more anti-microbial quaternary ammonium compounds, a compound of formula (A) and a compound of formula  
 25 (B) may be present, or the composition may comprise more than one compound of formula (A) or more than one compound of formula (B).

Examples of quaternary ammonium compounds of formula (A) include di- $n$ -decyldimethyl ammonium chloride, octyl decyl dimethyl ammonium chloride and dioctyl dimethyl  
 30 ammonium chloride.

Examples of commercially available compounds of formula (A) include Acticide DDQ 40 from Thor, Bardac 2240 from Lonza, Bardac 2280 from Lonza and Maquat 4480E, from Mason Chemical Company, USA.

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Examples of quaternary ammonium compounds of formula (B) include N,N-benzyl dimethyloctylammonium chloride, N,N-benzyl dimethyldecylammonium chloride, N-dodecyl-N-benzyl-N,N-dimethylammonium chloride, N-tetradecyl-N-benzyl-N,N-dimethylammonium chloride, N-hexadecyl-N,N-dimethyl-N-benzylammonium chloride,  
10 N,N-dimethyl N-benzyl N-octadecyl ammonium chloride and mixtures thereof.

It will be appreciated that a single CAS number often refers to more than one blend or mixture. A CAS classification for a commercial preparation typically covers blends comprising specified compounds in amounts within defined ranges. The compositions  
15 having the CAS numbers quoted above are only examples of compositions having a given CAS number that may be used in the present invention.

Examples of commercially available compounds of formula (B) include Acticide BAC 50M from Thor, Barquat MB50/80 from Lonza, Lonzagard Benzethonium Chloride USP  
20 from Lonza.

Typically, the anti-microbial quaternary ammonium compound or compounds used in the composition of the invention is selected from the group consisting of di-n-decyldimethyl ammonium chloride (DDAC (CAS number 7173-51-5)), benzalkonium chloride (BAC)  
25 such as benzalkonium chloride of formula (B) above wherein m is 8 and mixtures thereof. This benzalkonium chloride has CAS number 68424-85-1, and benzethonium chloride (BENZ).

The amount of component (i) and anti-microbial component (ii) present in the compositions  
30 of the present invention will vary depending on a number of factors, such as the intended use of composition and the particular compound(s) used.

For example, as will be appreciated by the person skilled in the art, higher concentrations of (i) and/or (ii) may be required in order to provide sterilisation compared to providing sanitisation or disinfection.

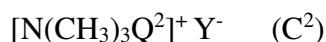
- 5 Anti-microbial component (ii) may consist essentially of at least one anti-microbial quaternary ammonium compound and chlorhexidine or a chlorhexidine salt.

Anti-microbial component (ii) may consist of at least one anti-microbial quaternary ammonium compound and chlorhexidine or a chlorhexidine salt.

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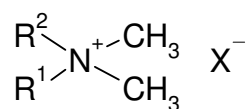
The ratio of the at least one anti-microbial quaternary ammonium compound to chlorhexidine or a chlorhexidine salt is preferably from 1:1 to 3:1 in the compositions of the invention.

- 15 A composition of the invention may, for example, comprise as component (i) a compound of formula:



- wherein  $\text{Q}^2$  has structure  $-(\text{CH}_2)_a\text{NHC}(\text{O})(\text{CH}_2)_b\text{CHCH}_2$ , wherein  $a + b$  is an integer of from 8 to 18 (such as 10 to 18), provided that  $a$  and  $b$  are each independently an integer of from 1 to 9, for example  $a$  is from 1 to 5 and  $b$  is from 5 to 9, wherein  $\text{Y}^-$  is as previously defined and;
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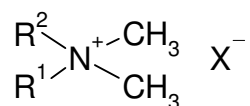
as component (ii) an anti-microbial quaternary ammonium compound of formula (A)



- wherein  $\text{R}_1$  and  $\text{R}_2$  are each independently a straight chain, un-substituted and uninterrupted  $\text{C}_{8-12}$  alkyl group and  $\text{X}^-$  is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, or bicarbonate and chlorhexidine or a chlorhexidine salt. Optionally, these compositions may contain a compound of formula (B) as defined above.
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- The composition of the invention may, for example, comprise as component (i)
- 30  $[\text{N}(\text{CH}_3)_3(\text{CH}_2)_3\text{NHC}(\text{O})(\text{CH}_2)_8\text{CHCH}_2]^+ \text{CH}_3\text{SO}_4^-$ , (undecylenamidopropyltrimonium methosulfate) and;

as component (ii) an anti-microbial quaternary ammonium compound of formula (A)



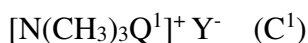
wherein R<sub>1</sub> and R<sub>2</sub> are each independently a straight chain, un-substituted and uninterrupted C<sub>8-12</sub> alkyl group and X<sup>-</sup> is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, or bicarbonate and chlorhexidine or a chlorhexidine salt.

5 Optionally, these compositions may contain a compound of formula (B) as defined above.

Examples of the compound of formula (A) suitable for use in such compositions include di-n-decyldimethyl ammonium chloride, octyl decyl dimethyl ammonium chloride, dioctyl dimethyl ammonium chloride and mixtures thereof.

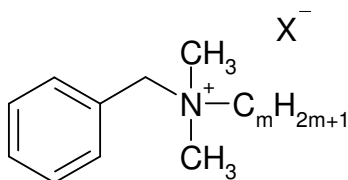
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A composition of the invention may, for example, comprise as component (i) a compound of formula:



wherein Q<sup>1</sup> is an unsubstituted, uninterrupted C<sub>14-20</sub> alkyl chain, and wherein Y<sup>-</sup> is as previously defined and as component (ii) at least one benzalkonium compound of formula (B)

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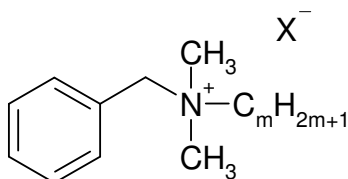


wherein m is from 8 to 18 and X<sup>-</sup> is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, or bicarbonate; and/or benzethonium chloride and chlorhexidine or a chlorhexidine salt. Optionally, these compositions may contain a compound of formula (A) as defined above.

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The composition of the invention may, for example, comprise as component (i) [N(CH<sub>3</sub>)<sub>3</sub>C<sub>16</sub>H<sub>33</sub>]<sup>+</sup> Cl<sup>-</sup>, cetyl trimethyl ammonium chloride (CTAC) and as component (ii) at least one benzalkonium compound of formula (B)

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wherein m is from 8 to 18 and X- is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, or bicarbonate; and/or benzethonium chloride and chlorhexidine or a chlorhexidine salt. Optionally, these compositions may contain a compound of formula (A) as defined above.

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Examples of the compound of formula (B) suitable for use in such compositions include benzalkonium chloride (BAC) and/or benzethonium chloride (BENZ).

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The compositions of the invention may additionally comprise other suitable anti-microbial agent(s) (b), such as those described in the EPA (United States Environmental Protection Agency) Listing and Annex I and Annex 3 of the EC Biocides Directive.

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Typically, the compounds used as anti-microbial agents are those that are suitable for application to the skin. For example, compounds that meet the required regulatory approval for human hygiene, such as those compounds approved by the European Commission, when used in products of Product-type 1 as listed in Annex II of the European Commission's delegated regulation (EU) No. 1062/2014 of 4 August 2014 and/or those approved by the FDA (Food and Drugs Administration).

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Suitable additional anti-microbial agents (b) that may be included in the anti-microbial component (ii) include anti-microbial agents that are not quaternary ammonium compounds. Preferably, these additional anti-microbial agent(s) are water soluble at room temperature and pressure.

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Examples of suitable additional anti-microbial agents include but are not limited to polymeric biguanidines (e.g. polyhexamethylene biguanidine (PHMB)), hydrogen peroxide, lactic acid, silver, salts of silver (for example silver chloride, silver carbonate, silver citrate, silver dihydrogen citrate), octenidine HCl, amphoteric compounds, iodophores, phenolic compounds, amine anti-microbial agents and nitrogen based heterocyclic compounds, ortho phenyl phenol (OPP), and nitro bromopropanes (e.g. bronopol (INN), 2-bromo-2-nitropropane-1,3-diol), naturally derived biocidal compounds (e.g. honey and extracts of honey such as those comprising methyl glyoxal), flavenoid based anti-microbials, and essential oils.

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In one aspect, the compositions of the invention are free of inorganic anti-microbial agents such as those comprising silver. In this aspect, any additional anti-microbial agent is an organic anti-microbial agent.

- 5 In one aspect, the compositions of the invention do not comprise PHMB or they may be free of polymeric biguanides. For example, they do not contain a biguanide in addition to chlorhexidine.

10 In one aspect of the invention the anti-microbial composition does not comprise any isothiazalones and/or any nitrobromopropanes such as bronopol and/or any hypochlorites.

In one aspect of the invention the anti-microbial composition does not contain anti-microbial compounds that are poorly soluble in water such as phenolic compounds.

- 15 Typically, when formulated as a ready to use composition, the amount of component (i) may be from about 0.01 to 5% by weight of the composition, for example from about 0.05 to about 2% by weight of the composition, such as from about 0.08 to about 0.5% by weight of the composition.

- 20 Typically, when formulated as a ready to use composition, the total amount of anti-microbial component (ii) and component (b) if present (ie the combined amount of anti-microbial quaternary ammonium compound and chlorhexidine or a salt thereof and any additional anti-microbial component (b)), may be from about 0.01 to about 5% by weight of the composition, for example from about 0.02 to about 2% by weight of the composition,  
25 such as from about 0.05 to about 0.6% by weight of the composition.

When the composition of the invention formulated for use as a hand sanitizer, the amount of anti-microbial component (ii) may be from about 0.05 to about 0.6% by weight.

- 30 The anti-microbial component (ii) may comprise equal amounts of quaternary ammonium compound and chlorhexidine, or salt thereof. For example, if the total amount of anti-microbial component is about 0.2% by weight of the composition, the amount of quaternary ammonium compound would be about 0.1% and the amount of chlorhexidine or salt thereof would be about 0.1%. Alternatively, the anti-microbial component may comprise different

amounts of quaternary ammonium compound and chlorhexidine. For example, the ratio of the quaternary ammonium compound to the chlorhexidine or salt thereof may from about 4:1 to 1:2, preferably from 1:1 to 3:1.

- 5 Typically, in the compositions of the invention, the ratio of component (i) to anti-microbial component (ii) ranges from 15:1 to 1:10 or from 5:1 to 1:5.

Examples of compositions of the invention include wherein the ratio of the at least one anti-microbial quaternary ammonium compound to chlorhexidine or a chlorhexidine salt is from  
10 1:1 to 3:1 and the ratio of component (i) to component (ii) is from 15:1 to 1:10 or from 5:1 to 1:5. In such compositions, the amount of component (i) may be from about 0.01 to about 5% by weight of the composition and the amount of component (ii) and component (b) if present is from may be from about 0.05 to about 0.6% by weight of the composition.

- 15 The compositions of the invention comprise a polar solvent (iii). Suitable polar solvents include, but are not limited to, water, alcohols, glycol ethers and mixtures thereof.

Suitable alcohols include, but are not limited to, straight or branched chain C<sub>1</sub> to C<sub>5</sub> alcohols, (such as methanol, ethanol, n-propanol, iso-propanol, mixtures of propanol  
20 isomers, n-butanol, sec-butanol, tert-butanol, iso-butanol), mixtures of butanol isomers, 2-methyl-1-butanol, n-pentanol, mixtures of pentanol isomers and amyl alcohol (mixture of isomers), and mixtures thereof.

Preferred polar solvents for use in the compositions of the invention include, but are not  
25 limited to, water, ethanol, isopentydiol, mono propylene glycol, hexylene glycol, 3-methoxy-3-methyl-1-butanol (MMB), n-propanol, isopropanol, ethylene glycol ethers, propylene glycol ethers, butyl diglycol (BDG) and mixtures thereof. In one aspect, the composition comprises water, or a mixture of water and one or more alcohols selected from the alcohols described above. In such mixtures, water is preferably the major component.  
30 The polar solvent may consist essentially of water or consist of water.

If the compositions of the invention comprise an alcohol, the alcohol is typically present in an amount lower than the amount necessary for the alcohol to provide an anti-microbial effect, but at a level that it is believed improves drying of the composition on skin. For

example, the compositions of the invention may comprise up to about 30% by weight alcohol, such as between 20 and 30% by weight alcohol or less than about 20% by weight alcohol, such as from about 15 to about 20% by weight alcohol.

- 5 It will be appreciated that the percentage of alcohol may depend on the use of the composition. For example, when used on a wipe, the composition of the invention may comprise up to 20% alcohol.

In one aspect, the compositions of the invention are substantially free of alcohol. For  
10 example, the compositions may contain 1% or less by weight alcohol. For example, the compositions may contain less than 1% or less than 0.5% by weight or 0.1% by weight or less of an alcohol such as isopropanol. As an example, compositions of the invention may comprise no isopropanol or may comprise no alcohol.

- 15 In another aspect, the compositions of the invention may comprise an alcohol up to a level of 70% by weight, e.g. up to about 50% by weight.

The composition may comprise water or a mixture of water and one or more alcohols selected from the alcohols described above. In such mixtures, water is preferably the major  
20 component.

For example, the polar solvent may consist of or consist essentially of water. As another example, the polar solvent may be water and from about 0 to about 20% by weight, such as from about 15 to about 20% by weight of an alcohol, for example ethanol or isopropanol.

- 25 The compositions of the invention can be provided in concentrated form for dilution before use or in ready to use form. It is preferred that the compositions of the invention are provided in ready to use form and, unless otherwise stated, information about amounts (such as weight% or ppm) provided in this document relate to ready to use compositions.

The pH of the compositions and formulations used can vary within wide limits, for example  
30 from about pH 2 to about pH 12, more preferably from about pH 3 to about pH 10 or about pH 4.5 to 8. The pH of a formulation used in the invention may be similar to that of known formulations which are intended to be used for the same purpose or a similar purpose. For example, a formulation that is intended to come into contact with the skin such as a personal care or first aid formulations will typically have a pH which will not irritate the skin, for

example from about pH 3 to about pH 8, such as from about pH 3.5 to about pH 7.5 or from about pH 4 to about pH 7.

When used as a hand sanitizer, the pH of the compositions of the invention is typically from  
5 about 4 to about 7.

It will be appreciated that the compositions of the invention can comprise other ingredients commonly used in the art. The nature of any other ingredients used will depend on the nature and intended purpose of the composition. The person of ordinary skill in the art will  
10 know which additional ingredients are suitable for use in compositions for different applications.

The compositions of the present invention may comprise additional materials such as surfactants, complexing agents, buffering agents, thickening agents, skin conditioning  
15 compounds, polar solvents and fragrances.

The selection of surfactants will depend on the nature of and the intended purpose of the composition. Suitable surfactants for use in formulations intended for different purposes will be within the knowledge of the person of ordinary skill in the art. Likewise, the  
20 selection of suitable amounts of surfactant will be within the knowledge of the person of ordinary skill in the art. Suitable surfactants may be selected from non-ionic, cationic or amphoteric and mixtures thereof.

Some compositions of the invention may comprise a non-ionic surfactant. Suitable non-  
25 ionic surfactants include, but are not limited to, amine oxides, alkyl polyglucosides, linear and branched 1° and 2° alcohol ethoxylates, and ethoxylated/propoxylated (EPO) block polymers.

In one aspect, the composition is substantially free of or free of anionic surfactant. In  
30 another aspect, the compositions of the invention do not comprise an amphoteric surfactant.

Some compositions of the invention may comprise an amphoteric surfactant. Suitable amphoteric surfactants include but are not limited to C<sub>6</sub>-C<sub>20</sub> alkylamphoacetates or amphodiacetates (such as cocoamphoacetates), C<sub>10</sub>-C<sub>18</sub> alkyl dimethyl betaines, C<sub>10</sub>-C<sub>18</sub>

alkyl amidopropyldimethyl betaines. Examples include but are not limited to coconut amphoteric surfactant cocoamidopropyl betaine (CAPB) (Surfac B4, CAS 61789-40-9), coco imidazoline betaine, oleo amido propyl betaine, and tall oil imidazoline.

- 5 Some compositions of the invention may comprise a cationic surfactant. Suitable cationic surfactants include but are not limited to undecylenamidopropyltrimonium methosulphate and cetrimonium chloride.

Typically, the amount of surfactant present in the compositions of the invention is from  
10 about 0.01 to 20% by weight. The amount of surfactant depends on a number of factors such as the pH of the composition and the intended use of the composition.

The compositions of the invention may comprise complexing agents. The terms sequestering agents or chelates are sometimes used interchangeably with the term  
15 complexing agents. For the purpose of describing this invention, the term complexing agents include both sequestering agents and chelates. Complexing agents can be used to help provide a clear composition even when the compositions of the invention are used with hard water. Examples of suitable complexing agents include but are not limited to EDTA (Ethylenediaminetetraacetic acid), Gluconate, GLDA (Glutamic acid diacetic acid)  
20 - Trade name Dissolvine GL, EDDS (Ethylenediamine-N,N'-disuccinic acid), citrates and gluconates or salts of glutaric, adipic and succinic acids and mixtures thereof. If the complexing agent contains a counter ion that counter ion is preferably metallic. Suitable metallic counter ions include but are not limited to Na, Ca, Fe, K, Zn, Mg and Mn.

- 25 Preferred complexing agents are GLDA (Dissolvine) and EDTA.

The complexing agents are typically present in an amount of from about 100 to 10,000 ppm, preferably from about 400 to 3,000 ppm, for example from about 500 to 2000ppm.

- 30 Buffering agents may be included to adjust the pH of the composition to the required value and maintain it at or close to that pH value during storage and use.

Suitable pH modifiers include but are not limited to acids such as citric, sulfamic, hydrochloric, phosphoric, nitric, lactic, formic, acetic glycolic or gluconic acids or other

mineral or organic acids or bases such as sodium or potassium hydroxide, triethanolamines and carbonates and mixtures thereof.

Thickening agents can be included to adjust the viscosity of the composition to the required value for such purposes as to make the composition more stable; facilitate application of the composition; or for aesthetic benefits. Examples of thickening agents include but are not limited to hydroxypropylmethylcellulose stearoxy ether supplied commercially by Daido chemical corporation under the tradename Sangelose 90, and a polyquaternium 37 supplied by Rheo Lab under the tradename Kleasol 200ST.

10

The compositions of the invention may contain skin conditioning compounds. Suitable skin conditioning compounds include, but are not limited to, panthenol, tocopheryl acetate, glycerine, polyquaternium compounds, PEG-7-glyceryl cocoate, and silicones and mixtures thereof. Typically, the compositions of the invention do not comprise mucopolysaccharides.

15

The compositions of the invention may alternatively or additionally contain salts such as the halides of alkali metals or alkaline earth metals such NaCl or KCl. In some situations, the use of salts can facilitate the formation of a stable composition.

20

The compositions of the invention may also contain other ingredients that are standard in the art such as colorants, fragrances, emollients, antioxidants and mixtures thereof.

The compositions of the invention may be free of anionic materials. Within the meaning of anionic materials, we do not include counterions that may for present in any of the ingredients used in the invention, such as counterions associated with a quaternary ammonium compound. The compositions of the invention may, for example, be free of anionic polyelectrolytes, such as high molecular weight, anionic mucomimetic polymers, polystyrene sulfonic acid polymers and cationic exchange resins.

25

30

It has been found that in use compositions of the invention have advantageous anti-microbial effects, and particularly when applied to the surface of skin. For example, such compositions have an anti-microbial effect when initially applied to a surface (so called "wet kill") and they can also have a residual anti-microbial effect in that they control,

reduce or prevent the formation of new microbial colonies at the surface (so called “dry kill”) that may otherwise result in the formation of more persistent biofilms.

The compositions of the invention are also resistant to washing with water and to wiping.

5 This means that the compositions of the invention provide a residual anti-microbial effect even when the surface which has been treated is subsequently wiped and/or washed or rinsed with water.

The compositions of the invention are particularly suitable for use as skin or hand sanitizers  
10 or on other surfaces. Some compositions are suitable for use on other surfaces. The compositions of the invention typically provide a residual anti-microbial effect.

Such compositions may be used in a wide variety of formats and applications for the purpose of skin sanitization. For example, the compositions of the invention are particularly  
15 suitable for formulation into mousses, gels, creams, lotions, liquids, sprays and wipes to be used in body or skin sanitisation, such as hand sanitizers.

When used in a wipe format, the substrates used to prepare the wipes may be made of any suitable woven or non-woven material. Suitable wipe materials include, but are not limited  
20 to, non-woven fibrous sheet materials and those made of fibres from natural sources such as wood pulp, and viscose or other cellulose based materials, silk fibres and keratin fibres. The materials comprise from 1 to 100% by weight of a cellulosic material. For example, 100% cellulosic materials such as viscose or wood pulp may be used. Other preferred materials include blends of cellulosic and non-cellulosic materials, such as blend of viscose  
25 with synthetic substrates such as polyester or polypropylene. Blended materials may comprise from 1 to 99.9 % by weight of a cellulosic material such as viscose, for example from 20 to 80% by weight or from 30 to 70 % by weight of a cellulosic material such as viscose.

30 The compositions of the invention can be used on humans and animals for both therapeutic and non-therapeutic purposes. Examples of products for non-therapeutic uses include personal care and personal hygiene products. Examples of products for therapeutic purposes include first aid and skin care products.

Compositions of the invention may also be in the form of a liquid and packed into suitable dispensers to provide a foam, mousse or spray in use. Compositions of the invention may be used for foot hygiene products, including those for direct use on the foot and those for the treatment/deodorisation of footwear, particularly sports footwear. Compositions of the invention can also be used in other personal care products which are used for direct application on skin or hair for example soap, bath and shower products, hair care products including shampoo, and anti-dandruff shampoos, hair conditioners hair styling products such as hair mousses, gels and sprays, skincare products such as shaving products, cosmetics and products for hair removal, deodorant and antiperspirant products, baby products including baby cleaning and cleansing products such as baby bath, soaps, wipes, moisturisers, nappy rash cream, products for cleaning surfaces that have regular and high incidence of infant and baby contact.

Compositions of the invention may be used as hygienic cleansers in pet products for direct application to the skin surface of the animal or its coat or fur for the purpose of eradicating or inhibiting micro-organisms which may otherwise have a detrimental effect on the animal's health, well-being or cleanliness. Such compositions can also be applied to materials such as surfaces which come into contact with animals and to which micro-organisms may be transferred from the animal. The benefit of such applications is again to eradicate or inhibit such micro-organisms which otherwise may be transferred to another animal or human and also to control or eliminate the by-products that such organisms may produce such as malodour. Such pet applications may include but not be limited to stain and odour removal sprays, disinfectant sprays and wipes, outdoor hutch cleaners, cage cleaners, anti-bacterial cat litter tray sprays and wipes, dog shampoos and spritzers and dog ear cleaning wipes.

Compositions of the invention may be used for First Aid topical applications to skin to sanitize abrasions or wounds on the surface of the skin to prevent or deter infection, or to prevent minor infections such as athletes' foot, verruca, warts, spot/acne prevention/treatment products. Thus, the invention provides products for these uses, such as wound care or first aid products that comprise a composition of the invention.

Compositions of the invention may also be used for medical applications such as sterilization of catheters, dialysis and other medical equipment; inhibiting or eradicating

viruses such norovirus, polio virus or adenovirus; and prevention or eradication of persistent biofilms.

Compositions of the invention may also be used on surfaces other than skin. Examples of applications of the invention to surfaces other than skin include but are not limited to: surface cleaners such as those intended for use in bathrooms, kitchens, living areas; hard floor cleaners; carpet cleaners; furniture cleaners; glass/mirror cleaners; toilet care products including solid toilet cleaners such as rim devices and those designed to be placed in the cistern; liquid toilet cleaners excluding those comprising hypochlorite bleaches; dishwashing products such as washing up liquids and preparations from dishwashing machines such as dishwashing solids (in powder or tablet format) & liquids; Laundry products such as solid detergents (in powder or tablet format); liquid detergents; fabric conditioners and “2 in 1” products comprising detergent and fabric conditioner; cleaning products intended for use outdoors such as those for cleaning for wood, stone, concrete or plastics, for example patio cleaner, garden furniture cleaners/treatments, BBQ cleaners, wall and fence cleaners/treatments; plant sprays such as those intended to remove insects such as aphides from plants; food sprays, such as those suitable for use in food preservation.

For the avoidance of doubt, in this specification when we use the term “comprising” or “comprises” we mean that the composition or formulation or component being described must contain the listed ingredient(s) but may optionally contain additional ingredients. When we use the term “consisting essentially of” or “consists essentially of” we mean that the composition or formulation or component being described must contain the listed ingredient(s) and may also contain small (for example up to 5% by weight, or up to 1% or 0.1% by weight) of other ingredients provided that any additional ingredients do not affect the essential properties of the composition, formulation or component. When we use the term “consisting of” we mean that the composition or formulation or component being described must contain the listed ingredient(s) only. These terms can be applied in an analogous manner to processes, methods and uses.

By “substantially free” we mean that the composition or formulation or component being described contains less than 3% by weight, preferably less than 1%, more preferably 0.1% or less by weight of the stated ingredient. For example, the compositions of the invention

that are substantially free of alcohol contain less than 3% by weight of alcohol, preferably less than 1% by weight of alcohol, more preferably 0.1% or less alcohol.

By the term “anti-microbial” we mean a compound or composition that kills and/or inhibits the growth of microbes (microorganisms). The term “microbiocidal” is used to refer to compounds or compositions that kill microbes. The compositions of the invention are anti-microbial and/or microbiocidal.

By the term “sanitising” or “sanitizer” we mean the reducing in the total number of microbes on a surface.

By the term “sterilising” we mean the elimination of microbiological organisms to achieve asepsis (a sterile microbial environment).

A microorganism or microbe is an organism that is microscopic (too small to be seen by the human eye). Examples of microorganisms include bacteria, fungi, yeasts, moulds, mycobacteria, algae spores, archaea and protists. Microorganisms are generally single-celled or unicellular organisms. However, as used herein, the term “microorganisms” also includes viruses.

The compositions of the invention may be anti-bacterial, anti-fungal, anti-algal, anti-sporal, anti-viral, anti-yeast and/or anti-mould.

The compositions of the invention are particularly suitable for use against bacteria, such as E.coli.

As used herein, the terms anti-bacterial, anti-fungal, anti-algal, anti-viral, anti-yeast and anti-mould agents are intended to refer to agents that inhibit the growth of the respective microorganisms but do not necessarily kill the microorganisms and agents that kill the respective microorganisms. Thus, for example, within the term anti-bacterial we include agents that inhibit the growth of bacteria but may not necessarily kill bacteria and bactericidal agents that do kill bacteria.

Examples of anti-bacterial agents include myobactericides and tuberculocides. Preferably, the compositions of the invention comprise at least one agent selected from anti-bacterial, anti-fungal, anti-algal, anti-sporal, anti-viral, anti-yeast and anti-mould agents and mixtures thereof. More preferably, the compositions of the invention comprise at least one anti-bacterial, anti-viral, anti-fungal and/or anti-mould agent.

The compositions of the invention can be effective against a wide range of organisms, including Gram negative and Gram positive bacteria, fungi, yeasts, viruses and some spore forming bacteria

An advantage of the invention is that it is possible to prevent a broad range of microorganisms from adhering and attaching to the surface, and, therefore, from forming a biofilm. Large numerous colonies are also substantially prevented from forming. Thus, the ability of the colony to grow is substantially reduced or even prevented. The invention is therefore general in its control of microorganisms.

In an aspect of the invention, the compositions may be used to reduce or control the formation of a biofilm.

As described previously, the compositions of the invention advantageously provide a residual anti-microbial effect whereby the anti-microbial action continues for a significant period after the initial application of the composition.

Typically, the compositions of the invention do not need to contain materials that are highly toxic to mammals. The anti-microbial agents used in the anti-microbial compositions are typically well known and widely understood and tested anti-microbial agents. The efficacy of the known anti-microbial agents is amplified in the formulations of the invention. Therefore, anti-microbial agents that have a low toxicity can be used in the anti-microbial compositions. In contrast, many “new” anti-microbial agents for known techniques of sanitization use “stronger”, more toxic and/or little tested materials.

The anti-microbial compositions of the invention do not contain materials that produce highly persistent residues or rinsates or products that contain heavy metals and their salts. Thus, there is a greatly reduced risk of long term hazards.

The anti-microbial compositions of the invention do not interfere with the biochemical reproductive pathways of the micro-organisms they control. The risk of resistance build up and the development of resistant strains is, therefore, low.

- 5 The anti-microbial compositions of the invention can have a dual effect in that not only do they provide an anti-microbial effect in use but they can also have a preservative effect on the composition. This means that it is typically not necessary to include additional preservatives in the formulations of the invention.
- 10 The compositions of the invention do not typically give surfaces to which they are applied a greasy feel.

According to a further aspect of the invention, there is provided the use of composition of the invention to control, reduce or prevent the formation of colonies of micro-organisms on  
15 a surface at which it is provided.

The present invention provides a method for providing a residual anti-microbial benefit to a surface such as a hard surface or skin, which method comprises applying a composition as defined herein to that surface or skin. The composition may, for example, be applied to  
20 the surface or skin by spraying the composition on the surface or wiping the composition onto the surface or skin. In one method of the invention, it is not necessary for the method to include any steps in addition to simply applying the composition to the surface. Thus, a method that consists essentially of or consists of applying the composition to the surface or skin is provided.

25 In an aspect of the invention, the surface to which the composition of the invention is applied is a surface of the body, such as skin.

The anti-microbial compositions of the invention can typically degrade when submersed in  
30 water, to provide a rinsate/leachate of low toxicity and which has a short residence time in the environment.

According to a further aspect of the invention, there is provided the use of an anti-microbial composition of the invention to reduce or prevent the formation of colonies of microorganisms on a surface at which it is provided, such as skin.

- 5 The anti-microbial compositions of the invention are typically made by a process as described below.

A process for preparing an anti-microbial composition as herein described comprising:

- (i) combining component (iii) and component (ii) with stirring; and  
 10 (ii) adding component (i) to components (iii) and (ii).

In some aspects, the pH of the solution obtained after step (ii) may require adjusting. Therefore, the present invention also describes a process in which (iii) the pH of the solution is adjusted after step (ii).

15

Preferences and options for a given aspect, feature or parameter of the invention should, unless the context indicates otherwise, be regarded as having been disclosed in combination with any and all preferences and options for all other aspects, features and parameters of the invention.

20

The present invention is illustrated by the following non-limiting Examples:

#### Preparation of Test Examples and Comparative Examples

- 25 The compositions as described in Table 1 were prepared using the method of described below. The commercially available compounds used in the compositions are listed below.

Rewocid UTM 185 supplied by Evonik (REW): a 48% solution of  
 $[N(CH_3)_3(CH_2)_3NHC(O)(CH_2)_8CHCH_2]^+ CH_3SO_4^-$ , undecylen-amidopropyltrimonium  
 30 methosulfate

*Acticide DDQ 40* supplied by Thor (DDAC): contains 40% *di-n-decyldimethyl ammonium chloride* (DDAC). This is an example of component (ii) of the invention, being of Formula Type A.

*Acticide BAC 50M* supplied by Thor (BAC): contains 50% *Benzalkonium chloride* (BAC) is also an example of component (ii) of the invention, being of Formula Type B.

- 5    *Chlorhexidine di-gluconate (CHDG)*, supplied by Evonik: a 20% solution is a further example of component (ii) of the invention.

*Benzethonium Chloride USP* supplied by Lonza (Benz): a Benzalkonium derivative and contains 100% Diisobutylphenoxyethoxyethyl-dimethylbenzyl ammonium chloride  
10    (BENZ) otherwise known as Benzethonium Chloride. It is a further example of component (ii) of the invention.

The polar solvent (component (iii)) was placed in a suitably sized vessel (typically of 1 litre capacity). A small amount of the polar solvent was retained to allow for final weight  
15    adjustment. The required amount of the biocide(s) (component (ii)), was then added to the vessel, with the vessel being stirred for 5 minutes after addition of each biocide before the next biocide is added. The required amount of the REW (component (i)) was then added and the vessel stirred for a further 5 minutes. The pH was checked and was adjusted using lactic acid or sodium hydroxide solution if required. The solution was then made up to  
20    100% by weight by adding the retained polar solvent and stirred for a final 10 minutes.

The Comparative Examples were prepared following the same method but by leaving out one or more of the components (i) or (ii) of the invention.

- 25    In Table 1 the ppm of REW refers to the amount of the primary chemical component present in Rewocid UTM 185, namely undecylenamidopropyltrimonium methosulfate and the ppm of the components (ii) of the invention refers to the amount of the active chemical component, namely DDAC-*di-n-decyldimethyl ammonium chloride*; CHDG-*Chlorhexidine digluconate*; BENZ-*Benzethonium Chloride*; or BAC-*Benzalkonium*  
30    *Chloride*.

Table 1

|                                  | <b>BEN<br/>Z<br/>ppm</b> | <b>DDA<br/>C<br/>ppm</b> | <b>BAC<br/>ppm</b> | <b>CHD<br/>G<br/>ppm</b> | <b>REW<br/>ppm</b> | <b>(QUAT +<br/>CHDG) ppm</b> | <b>REW/(QUA<br/>T<br/>+ CHDG)</b> |
|----------------------------------|--------------------------|--------------------------|--------------------|--------------------------|--------------------|------------------------------|-----------------------------------|
| <b>Example 1</b>                 | 0                        | 1800                     | 0                  | 600                      | 600                | 2400                         | 0.25                              |
| <b>Example 2</b>                 | 0                        | 1800                     | 0                  | 600                      | 1200               | 2400                         | 0.5                               |
| <b>Example 3</b>                 | 0                        | 1800                     | 0                  | 600                      | 2400               | 2400                         | 1                                 |
| <b>Example 4</b>                 | 0                        | 1800                     | 0                  | 600                      | 4800               | 2400                         | 2                                 |
| <b>Example 5</b>                 | 0                        | 0                        | 1000               | 1000                     | 4800               | 2000                         | 2.4                               |
| <b>Example 6</b>                 | 1000                     | 0                        | 0                  | 1000                     | 4800               | 2000                         | 2.4                               |
| <b>Example 7</b>                 | 0                        | 1000                     | 0                  | 1000                     | 4800               | 2000                         | 2.4                               |
| <b>Example 8</b>                 | 0                        | 1800                     | 0                  | 600                      | 7200               | 2400                         | 3                                 |
| <b>Example 9</b>                 | 0                        | 1800                     | 0                  | 600                      | 9600               | 2400                         | 4                                 |
| <b>Example 10</b>                | 1800                     | 0                        | 0                  | 600                      | 19200              | 2400                         | 8                                 |
| <b>Example 11</b>                | 1800                     | 0                        | 0                  | 600                      | 24000              | 2400                         | 10                                |
| <b>Example 12</b>                | 1800                     | 0                        | 0                  | 600                      | 36000              | 2400                         | 15                                |
| <b>Comparative<br/>Example 1</b> | 0                        | 0                        | 0                  | 0                        | 4800               | 0                            | $\infty$                          |
| <b>Comparative<br/>Example 2</b> | 0                        | 2100                     | 0                  | 0                        | 0                  | 2100                         | 0                                 |
| <b>Comparative<br/>Example 3</b> | 0                        | 1800                     | 0                  | 600                      | 0                  | 2400                         | 0                                 |
| <b>Comparative<br/>Example 4</b> | 0                        | 0                        | 1300               | 1300                     | 0                  | 2600                         | 0                                 |
| <b>Comparative<br/>Example 5</b> | 0                        | 0                        | 1300               | 1000                     | 0                  | 2300                         | 0                                 |
| <b>Comparative<br/>Example 6</b> | 0                        | 0                        | 0                  | 2000                     | 4800               | 2000                         | 2.4                               |
| <b>Comparative<br/>Example 7</b> | 1000                     | 1000                     | 0                  | 0                        | 1200               | 2000                         | 0.6                               |
| <b>Comparative<br/>Example 8</b> | 0                        | 1250                     | 0                  | 350                      | 0                  | 1600                         | 0                                 |
| <b>Comparative<br/>Example 9</b> | 0                        | 1500                     | 0                  | 300                      | 0                  | 1800                         | 0                                 |

|                               |   |      |   |     |   |      |   |
|-------------------------------|---|------|---|-----|---|------|---|
| <b>Comparative Example 10</b> | 0 | 1750 | 0 | 250 | 0 | 2000 | 0 |
| <b>Comparative Example 11</b> | 0 | 1750 | 0 | 300 | 0 | 2050 | 0 |
| <b>Comparative Example 12</b> | 0 | 1750 | 0 | 350 | 0 | 2100 | 0 |

### Evaluation of Residual Anti-Microbial Efficacy of Examples and Comparative Examples

- 5 25 micro litres (0.025ml) of test sample was applied to a 2cm x 2cm section of Vitro-Skin (as supplied by IMS, Inc.) in duplicate in a Petri dish. The test sample was spread on the vitro-skin® surface with a sterile inoculation loop ensuring that approximately a 0.5 cm perimeter was left untreated to the edge. The test sample was allowed to dry on the vitro-skin®\*<sub>2</sub> at 20°C in an oven with the Petri dish lid left off for one hour. The Petri dish was
- 10 then removed from the oven and a strip of polypropylene wipe saturated with a sterile tryptone/saline solution placed inside. The lid was closed and then placed back in the oven for 4 hours at 20°C. After this time the Petri dish was removed from the oven and 10ul of a  $1-1.5 \times 10^8$  cfu/ml. suspension of *E. coli* K12\*<sub>1</sub> prepared in tryptone/saline solution was added to the surface of the vitro-skin® containing the test sample and spread with a sterile
- 15 inoculation loop ensuring the suspension stayed within the treated area of the vitroskin. The bacterial suspension was left in contact with the vitroskin for 5 minutes. After this time the vitro-skin® was removed from the petri dish and placed in a test tube containing 10ml of neutralisation solution. It was shaken gently and left for a further 5 minutes after which the tube was vortex mixed for 1 minute to recover the bacteria from the surface of the vitroskin.
- 20 A 1 ml sample of this suspension was then plated with tryptone soya agar and incubated for 48 hours at 37°C. After this time the log reduction in *E. coli* K12 was calculated by comparison with the water-treated control.

\*<sub>1</sub> NB. *E. coli* K12 suspension prepared from a '2a' culture grown on tryptone soya agar  
25 for 24 hours at 37 °C, as described in BS EN microbiology standards e.g. EN1276:2009)

\*<sub>2</sub> vitro-skin® is a testing substrate that mimics the surface properties of human skin. It is a synthetic non-biological product that has been formulated to have topography, pH, critical surface tension and ionic strength that are similar to human skin. It is a well-known and

used substrate for those trained in the art to evaluate the benefits of topological applications of skin-care products to skin, which includes the evaluation of biocidal efficacy of actives applied to skin. Examples of published, peer-reviewed work with vitro-skin include US2009/0202463 which describes a method for evaluating antimicrobial compositions that provide enhanced immediate and residual anti-viral and antibacterial efficacy on the surface of skin; evaluation of the efficacy of organic acids in Hand Cleansers for the prevention of rhinovirus infections as described in the Journal of Antimicrobial Agents and Chemotherapy; 48(7); 2004 July; 2595-2598; US2012/0141396 describes disinfectant compositions that provide a prolonged antimicrobial property to a variety of surfaces, including skin, evaluated using vitro-skin.

The Examples and Comparative Examples were made to the compositions described in Table 1 following the method described above. The Examples and Comparative Examples Samples were then tested for anti-microbial efficacy using the method described above. The results of these tests are shown in Table 2 below.

Table 2

|                              | <b>Log R e-Coli vitro skin</b> |
|------------------------------|--------------------------------|
| <b>Example 1</b>             | > 4.24**                       |
| <b>Example 2</b>             | > 5.14**                       |
| <b>Example 3</b>             | > 4.24**                       |
| <b>Example 4</b>             | > 4.19**                       |
| <b>Example 5</b>             | > 5.23**                       |
| <b>Example 6</b>             | > 5.23**                       |
| <b>Example 7</b>             | > 5.23**                       |
| <b>Example 8</b>             | > 4.24**                       |
| <b>Example 9</b>             | > 4.24**                       |
| <b>Example 10</b>            | > 4.24**                       |
| <b>Example 11</b>            | > 4.19**                       |
| <b>Example 12</b>            | > 4.19**                       |
| <b>Comparative Example 1</b> | 1.92                           |
| <b>Comparative Example 2</b> | 2.48                           |

|                               |       |
|-------------------------------|-------|
| <b>Comparative Example 3</b>  | 2.84  |
| <b>Comparative Example 4</b>  | TNTC* |
| <b>Comparative Example 5</b>  | TNTC* |
| <b>Comparative Example 6</b>  | 2.86  |
| <b>Comparative Example 7</b>  | 2.74  |
| <b>Comparative Example 8</b>  | TNTC* |
| <b>Comparative Example 9</b>  | TNTC* |
| <b>Comparative Example 10</b> | 3.39  |
| <b>Comparative Example 11</b> | 3.3   |
| <b>Comparative Example 12</b> | 3.59  |

\*TNTC = too numerous to count - Where the number of recoverable organisms post-testing on the recovery media exceeds the countable limits. This indicates that the organisms have largely remained unaffected in the test, and so the test sample has not performed well.

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\*\* Where a value is preceded by > it indicates Total Kill, this means that no bacterial colonies were present post-testing on the recovery media, meaning that the test sample has performed very well.

- 10 The results in Table 2 show that the compositions of the invention have superior residual anti-microbial performance compared to the Comparative Examples that are missing at least one feature of the compositions of the invention.

Comparative Example 1 shows that REW has almost no anti-microbial activity.

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## Claims

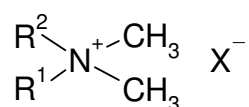
1. An anti-microbial composition comprising:

(i) a compound of formula:



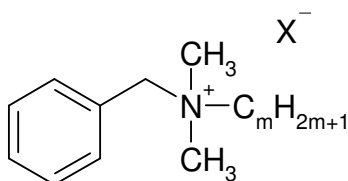
wherein  $\text{Q}^2$  has structure  $-(\text{CH}_2)_a\text{NHC}(\text{O})(\text{CH}_2)_b\text{CHCH}_2$ , wherein  $a + b$  is an integer of from 8 to 18, provided that  $a$  and  $b$  are each independently an integer of from 1 to 9, wherein  $\text{Y}^-$  is a halide anion, alkylsulphate, sulphonate, saccharinate, or bicarbonate, or a mixture of compounds of formula  $(\text{C}^2)$ ;

10 (ii) at least one anti-microbial quaternary ammonium compound of formula (A)



wherein  $\text{R}_1$  and  $\text{R}_2$  are each independently a straight chain, un-substituted and uninterrupted  $\text{C}_{8-12}$  alkyl group and  $\text{X}^-$  is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, or bicarbonate and/or at least one

15 benzalkonium compound of formula (B)



wherein  $m$  is from 8 to 18, optionally  $m$  is 8, 10 or 12, and  $\text{X}^-$  is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, or bicarbonate; and/or benzethonium chloride,

20 diisobutylphenoxyethoxyethyl-dimethylbenzyl ammonium chloride (otherwise known as Benzethonium Chloride) or benzyl-cocoalkyl-dimethyl-ammonium chloride; and

chlorhexidine or a chlorhexidine salt; and

(iii) a polar solvent.

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2. A composition according to claim 1, wherein in the compound of formula  $(\text{C}^2)$   $a$  is from 1 to 5 and  $b$  is from 5 to 9.

3. A composition according to claim 1 or 2, wherein component (i) comprises  

$$[\text{N}(\text{CH}_3)_3(\text{CH}_2)_3\text{NHC}(\text{O})(\text{CH}_2)_8\text{CHCH}_2]^+ \text{CH}_3\text{SO}_4^-$$
undecenylamidopropyltrimonium methosulfate.
- 5 4. A composition according to claim 1, wherein the benzalkonium compound of  
formula (B) is benzyldimethyl-n-tetradecyl-ammonium chloride, benzyldimethyl-  
n-dodecyl-ammonium chloride, benzyl-C<sub>12</sub>-C<sub>16</sub>-alkyl-dimethyl-ammonium  
chloride, and/or the compound of formula (A) is di-n-decyldimethyl ammonium  
10 chloride, octyl decyl dimethyl ammonium chloride or dioctyl dimethyl ammonium  
chloride,  
optionally wherein the anti-microbial quaternary ammonium compound is selected  
from the group consisting of di-n-decyldimethyl ammonium chloride (DDAC),  
benzalkonium chloride (BAC), and benzethonium chloride (BENZ) and mixtures  
15 thereof.
5. A composition according to any one of the preceding claims comprising a  
quaternary ammonium compound of CAS number 7173-51-5 and/or 68424-85-1.
- 20 6. A composition according to claim 1, wherein the compound of formula (A) is di-  
n-decyldimethyl ammonium chloride, octyl decyl dimethyl ammonium chloride or  
dioctyl dimethyl ammonium chloride or a mixture thereof, optionally wherein the  
compound of formula (A) is di-n-decyldimethyl ammonium chloride, and wherein  
the composition optionally additionally comprises a compound of formula (B) as  
25 defined in claim 4 and/or diisobutylphenoxyethoxyethyl-dimethylbenzyl  
ammonium chloride (otherwise known as Benzethonium Chloride) or benzyl-  
cocoalkyl-dimethyl-ammonium chloride.
7. A composition according to any one of the preceding claims, wherein the  
30 chlorhexidine is chlorhexidine di-gluconate.
8. A composition according to any one of the preceding claims, wherein

- (a) the amount of component (i) is from 0.01 to 5% by weight of the composition or from 0.05 to 2% by weight of the composition, optionally wherein the amount of component (i) is from 0.08 to 0.5% by weight of the composition; and/or
- (b) the amount of component (ii), and if present an additional antimicrobial component (b) is from 0.01 to 5% by weight of the composition or from 0.02 to 2% by weight of the composition, optionally wherein the amount of component (ii) and component (b) if present is from 0.05 to 0.6% by weight of the composition; and/or
- (c) the ratio of component (i) to component (ii) is from 15:1 to 1:10 or from 5:1 to 1:5; and/or
- (d) the ratio of the at least one anti-microbial quaternary ammonium compound to chlorhexidine or a chlorhexidine salt is from 1:1 to 3:1.
9. A composition according to any one of the preceding claims, wherein
- (a) the pH of the composition is from 4 to 7; and/or
- (b) the polar solvent is selected from water, ethanol, n-propanol, isopropanol, ethylene glycol ethers, propylene glycol ethers, butyl diglycol (BDG) and dipropylene glycol methyl ether (Trade name Dowanol DPM) and mixtures thereof; and/or
- (c) the composition is substantially free of alcohol.
10. A composition according to any one of the preceding claims, wherein the ratio of the at least one anti-microbial quaternary ammonium compound to chlorhexidine or a chlorhexidine salt is from 1:1 to 3:1 and the ratio of component (i) to component (ii) is from 15:1 to 1:10 or from 5:1 to 1:5; optionally wherein the amount of component (i) is from 0.01 to 5% by weight of the composition and the amount of component (ii) and component (b) if present is from 0.05 to 0.6% by weight of the composition.
11. The use of a composition according to any one of the preceding claims to substantially reduce or control the formation of microbial colonies on or at a surface, wherein the surface is selected from hard surfaces optionally selected from bathroom surfaces, kitchen surfaces, living area surfaces, hard floors, carpets, furniture, glass/mirrors, toilet surfaces, outdoor surfaces such as wood,

stone, concrete or plastics, BBQ surfaces, walls, fences; plant surfaces and food surfaces, optionally wherein the use comprises reducing or controlling the formation of biofilms.

- 5     12.     A method of substantially reducing or controlling the formation of microbial colonies on or at a surface, wherein the surface is selected from hard surfaces optionally selected from bathroom surfaces, kitchen surfaces, living area surfaces, hard floors, carpets, furniture, glass/mirrors, toilet surfaces, outdoor surfaces such as wood, stone, concrete or plastics, BBQ surfaces, walls, fences; plant surfaces and food surfaces, which method comprises applying a composition according to any one of claims 1 to 10 to that surface, optionally wherein the method is to reduce or control the formation of biofilms.
- 10
13.     A method of disrupting, preventing or reducing the adhesion and/or attachment of micro-organisms to a surface, wherein the surface is selected from hard surfaces optionally selected from bathroom surfaces, kitchen surfaces, living area surfaces, hard floors, carpets, furniture, glass/mirrors, toilet surfaces, outdoor surfaces such as wood, stone, concrete or plastics, BBQ surfaces, walls, fences; plant surfaces and food surfaces; which method comprises applying a composition according to any one of claims 1 to 10 to that surface.
- 15
14.     A hand sanitizer, wound care product or anti-microbial wipe comprising an anti-microbial composition as defined in any one of claims 1 to 10.
- 20
15.     A composition according to any one of claims 1 to 10 for use to reduce or control the formation of microbial colonies on the skin or a wound; optionally wherein the use comprises the reducing or controlling the formation of biofilms.
- 25
16.     A composition according to any one of claims 1 to 10 for use in a method of preventing or reducing the adhesion and/or attachment of micro-organisms to the skin.
- 30