Abstract: A composition comprising a mixture of particles of a bioactive glass material and a non-volatile silicone fluid.
Silicone Composition

The present invention relates to silicone based compositions, a method of manufacturing such a composition and the use of such a composition in personal and healthcare applications. In particular, although not exclusively, the composition is suitable for topical application to the skin and it may be used to treat various dermatological disorders for example psoriasis, dermatitis, acne, eczema, urticaria, and/or treat damaged skin for example, skin infections and wounds. In accordance with a preferred embodiment, the present invention provides a silicone based composition which is capable of delivering a therapeutically effective amount of a therapeutically active agent to a target site, for example the skin.

Dermatological disorders and damaged skin are not only undesirable cosmetically but also the skin may lack the functionality of normal skin, it may be more susceptible to infection and it may cause discomfort.

For example, damage to the skin produced by injury or surgery may produce wounds which typically undergo a natural healing process, whereby new tissue forms and thereafter during a final maturing phase the restored tissue stabilises while developing a less brittle and more elastic structure. A wound however, particularly during the wound healing process, is typically susceptible to infection by pathogens, such as viruses and bacteria, which may inhibit or prevent the normal healing process and/or may prevent normal skin function of the restored tissue. For example, a scar may form which may be undesirable aesthetically but also the scar may lack the functionality of normal skin as the sense of feeling may be diminished or completely lost. Weak spots may also form where the scar tissue joins uninjured tissue. Generally, an acute wound in a patient with normal blood flow having a good medical and nutritional condition typically will heal if appropriate care is provided. In chronic wounds however, healing is more difficult because the aetiology of the wound is more difficult to determine, and the measures required to reverse the medical abnormalities are often complex. Consequently, the healing process of a chronic wound differs significantly from that of acute wounds, particularly as with chronic wounds the orderly sequence of events seen in the healing of acute wounds may be come disrupted thereby resulting in non-healing, malodorous wounds typically colonised with bacteria such as Pseudomonas and Staphylococcus and containing large amounts of wound exudate. Chronic wounds suitably cause significant discomfort for the patient.
Suitably, it may be desirable to treat a wound, both a newly formed wound and during the wound healing process, with an effective amount of a therapeutic active agent, such as an antibacterial agent, to prevent or inhibit infection of the wound. Alternatively, or additionally, it may be desirable to cover the wound with a wound dressing to prevent excessive amounts of wound exudate contacting the surrounding healthy skin and loosening the healthy tissue whilst acting as a barrier to prevent a pathogen from entering the wound. Typically, the wound dressing should also allow the wound to breathe thereby promoting the wound healing process.

It is therefore desirable to provide a composition for topical application which not only acts as a barrier to pathogens contacting damaged skin but also may deliver a therapeutically effective amount of a therapeutic active agent to the target tissue, thereby promoting the healing process and the formation of new tissue which exhibits normal functional and possesses desirable aesthetics. Similarly, it is desirable to provide a composition for topical application for treating dermatological disorders which not only acts as a barrier to pathogens but also delivers a therapeutic active agent to the skin.

Although, pharmaceutical gel and cream compositions for delivering a therapeutically effective amount of a therapeutic active agent to a target tissue by topical administration are known, the universal applicability of these compositions to treat a particular target tissue site, in particular a wound, may be restricted for a number of reasons. In particular, although a gel and cream may act as a barrier to pathogens contacting the damaged tissue they may not allow the tissue to breathe during the healing process. Suitably, such compositions may inhibit or prevent the regenerated tissue from functioning normally, they may suppress the normal immune response, they may cause skin sensitivity and they may allow pathogens, such as bacteria, to evolve around the barriers they provide. Furthermore, it is desirable such compositions have the required viscosity so they remain in place at the target tissue site without the need for covering the formulations with a further protective barrier to immobilise the composition.

A further problem associated with topical gels and creams is that they may require complex formulations. For example, the compositions should be physically stable so that the component parts do not separate and the active agent does not agglomerise
within the composition. However, the compositions need to be formulated in such a manner to allow the active agent to be delivered to the target tissue. Such problems are typically magnified when the therapeutic active agent is a solid, particularly a solid that is substantially insoluble in standard pharmaceutical diluents and carriers. Furthermore, it will be appreciated that if the therapeutic active agent is released from the composition gradually over a prolonged period of time to the target tissue then this may promote the healing process and/or the formation of normal tissue. Conveniently, if the therapeutic active agent is released gradually from the composition, then the target tissue will receive a therapeutically effective amount of the therapeutic active agent over a prolonged period of time i.e. over the duration of the healing process. Suitably, such a composition will typically have to be replaced less frequently with a fresh batch during the healing process. Conveniently, the regenerating tissue will be disturbed less frequently thereby promoting healing and increasing patient compliance. Furthermore, if the composition releases a relatively large proportion of the therapeutic active agent to the target tissue over a short period of time, particularly following application to the tissue, then this may not only necessitate replacing the composition more frequently but also it may produce undesirable side effects, such as irritation to the skin and mucosa. Additionally, complex formulations may also be required to prevent degradation of the therapeutic active agent. This represents a particular problem for a therapeutic active agent which degrades and/or breaks down rapidly on contact with bodily fluids, such as the exudates from a wound.

The present invention therefore seeks to solve the aforementioned technical problems.

Thus, according to a first aspect, the present invention provides a composition comprising a mixture of particles of a bioactive glass material and a non-volatile silicone fluid. Such a composition may be referred to hereinafter as the composition of the present invention.

Suitably, the composition of the present invention seeks to solve the aforementioned technical problems associated with treating dermatological disorders and/or damaged skin. In particular, the composition of the present invention is suitable for treating a wound, namely a wound treatment composition and it may be in the form of a wound dressing.
By the term "bioactive glass material" or "bioactive glass" as used herein we mean a synthetic inorganic material comprising an oxide of silicon as its major component, wherein the bioactive glass is capable of bonding with growing tissue when contacted with physiological fluids. Bioactive glasses are well known to those skilled in the art and are disclosed, for example, in An Introduction to Bioceramics, L. Hench and J. Wilson, World Scientific, New Jersey, 1993. It will be appreciated that the bioactive glass material in the composition of the present invention may also further include an antibacterial active agent.

A number of compositional features distinguish a bioactive glass from traditional soda-lime-silica glasses and provide bioactive glass with the ability to bond with living tissue. Suitably, when a bioactive glass is exposed to physiological fluids interfacial dissolution occurs as the silica glass network is hydrolysed thereby forming surface silanol groups (Si-OH). As the number and concentration of surface silanol groups increases, they may combine to form a silicon rich surface layer. It is believed that the incorporation of organic biological constituents within the growing silicon rich layers may represent one way of triggering bonding to living tissue; a characteristic of bioactivity. Conveniently, bioactive glasses are typically biodegradable and may be employed as a resorbable solid material in a variety of medical applications, for example, bone repair, biodegradable sutures, and tissue engineering applications.

Although the use of a bioactive glass including an antibacterial agent for treating damaged skin (i.e. in wound care) or other dermatological applications has been suggested by using a mesh containing the bioactive glass, there are a number of technical problems associated with such an application. Firstly, the bioactive glass is a solid material and such a physical form does not lend itself for use in dermatological applications (i.e. wound care). Suitably, the bioactive glass needs to be formed into an article of the required shape, for example by forming fibres of the bioactive glass and then forming the fibres into a mesh. Suitably, such a process is both time consuming and laborious. Although a bioactive glass may be ground to form particles, typically such particles are much more susceptible to degradation by fluids and oxidise more quickly than larger solid forms of the bioactive glass. Consequently, fine particles of a bioactive glass need to be stored under specialised conditions (i.e. a moisture and oxygen free environment in the dark), they need to be handled carefully and they typically do not lend themselves to medical applications, particularly to those medical applications where there is a relatively large amount of bodily fluid present.
Unexpectedly, it has been found that if particles of a bioactive glass material are mixed with a non-volatile silicone fluid, then the particles in such a composition are typically more stable to exposure to fluids, such as air, moisture and bodily fluids, than particles of the bioactive glass material alone. Although only theory, it is believed that the non-volatile silicone fluid and bioactive glass material are essentially inert towards each other and the non-volatile silicone fluid may act as non-aqueous semi-occlusive barrier thereby restricting exposure of the bioactive glass to fluids (i.e. air, moisture and bodily fluids). Suitably, the rate of breakdown of the bioactive glass material is typically reduced in the composition of the present invention compared with the bioactive glass material alone. Nevertheless, the bioactive glass material in the composition of the present invention still exhibits bioactivity. Conveniently, the composition of the present invention is suitable for treating dermatological disorders and damaged skin, particularly wounds where relatively large amounts of bodily fluids are present, in particular open wounds or chronic wounds.

Conveniently, the composition of the present invention may be stored, handled and manipulated under standard conditions without the need for specialist equipment (i.e. it does not need to be stored in vacuo or an inert atmosphere). Furthermore, the composition of the present invention may be employed in a variety of medical applications where it is desirable to deliver a bioactive glass material to a target tissue over a prolonged period of time. Still further, the composition of the present invention may be employed in medical applications where it is desirable to deliver a bioactive glass material to a target tissue site containing relatively large amounts of bodily fluids, for example the application to open wounds, during the wound healing process.

The particles of the bioactive glass material are typically chemically and physically stable when mixed with the non-volatile silicone fluid. For example, the component parts of the composition of the present invention typically do not separate and the bioactive glass typically does not degrade. Additionally, the composition of the present invention may be prepared simply by mixing the particles of the bioactive glass with the non-volatile silicone fluid. Moreover, as a number of non-volatile silicone fluids are available having a range of viscosities which are suitable for use in the composition of the present invention, it is possible to formulate a composition having an appropriate viscosity for a particular medical application by using an appropriate non-volatile silicone fluid having the desired viscosity. Conveniently, the composition of the
present invention may be employed in a variety of medical applications, such as a wound treatment, without the need for further complex manufacturing steps. For example, the composition of the present invention may have an appropriate viscosity so it may be moulded to the shape of a target tissue site, applied and retained in position on the target tissue site without the need for additional adhesives or a further protective coating. The composition of the present invention may be applied by both medical and non-medical staff as it is straightforward to apply. Such methods of applications by non-medical personnel are embraced by the methods of the present invention as described hereinafter.

Suitably, the bioactive glass material may be melt-derived or sol gel-derived. Such methods of forming these type of glasses are well known to those skilled in the art as disclosed in WO 02/04606, US 6,482,444B, US 5,074,916B and WO 02/096391. Preferably, the bioactive glass material comprises a sol gel-derived bioactive glass material. More preferably, the bioactive glass material consists essentially of a sol gel-derived bioactive glass material.

As stated previously, the bioactive glass material comprises an oxide of silicon as its major component.

Suitably, the bioactive glass material comprises greater than or equal to 35% by weight, more preferably greater than or equal to 40% by weight of an oxide silicon based on the total weight of the bioactive glass material.

Suitably, the bioactive glass material comprises less than or equal to 99.9% by weight, more preferably less than or equal to 95% by weight, even more preferably less than or equal to 90% by weight of an oxide of silicon based on the total weight of the bioactive glass material.

For the avoidance of doubt, the total weight of the bioactive glass material as used herein means all components of the bioactive glass material which may also include a therapeutic active agent, if present, as described hereinafter.

A highly preferred oxide of silicon present in the bioactive glass material comprises silicon dioxide (SiO₂). Preferably, essentially all of the oxide of silicon present within the bioactive glass material is silicon dioxide.
Preferably, the bioactive glass material further includes an oxide of calcium, particularly calcium oxide (CaO).

Suitably, when the bioactive glass material includes an oxide of calcium, the oxide of calcium may be present in an amount of greater than or equal to 5% by weight, preferably greater than or equal to 10% by weight based on the total weight of the bioactive glass material.

Suitably, when the bioactive glass material includes an oxide of calcium, the oxide of calcium may be present in an amount of less than or equal to 45% by weight, preferably less than or equal to 40% by weight based on the total weight of the bioactive glass material.

Suitably, the bioactive glass material may further include an oxide of phosphorus, particularly phosphorus pentoxide (P$_2$O$_5$).

Suitably, when the bioactive glass material includes an oxide of phosphorus, the oxide of phosphorus may be present in an amount of greater than or equal to 1% by weight, preferably greater than or equal to 3% by weight based on the total weight of the bioactive glass material.

Suitably, when the bioactive glass material includes an oxide of phosphorus, the oxide of phosphorus may be present in an amount of less than or equal to 15% by weight, preferably less than or equal to 12% by weight based on the total weight of the bioactive glass material.

A preferred bioactive glass material comprises an oxide of silicon as defined herein, and an oxide of calcium as defined herein. A more preferred bioactive glass material comprises an oxide of silicon as defined herein, an oxide of calcium as defined herein and an oxide of phosphorus as defined herein.

Calcium fluoride (CaF$_2$), boron oxide (B$_2$O$_3$), aluminium oxide (Al$_2$O$_3$), magnesium oxide (MgO), potassium oxide (K$_2$O), and sodium oxide (Na$_2$O) may be included in the bioactive glass material. The preferred range for CaF$_2$ is 0 to 12.5% by weight based on the total weight of the bioactive glass material. The preferred range for boron oxide
is 0 to 10% by weight based on the total weight of the bioactive glass material. The
preferred range for aluminium oxide is 0 to 1.5% by weight based on the total weight
of the bioactive glass material. The preferred range of magnesium oxide is 0 to 5% by
weight based on the total weight of the bioactive glass material. The preferred range
for potassium oxide is 0 to 8% by weight based on the total weight of the bioactive
glass material. The preferred range for sodium oxide is 0 to 25% by weight based on
the total weight of the bioactive glass material.

Preferably, when the bioactive glass material is melt-derived the bioactive glass
material comprises between 40 to 60% by weight of silicon dioxide, 15 to 25% by
weight of sodium oxide, 15 to 25% by weight of calcium oxide, and 0 to 15% by weight
of a phosphorus pentoxide, preferably 1 to 10% by weight of phosphorus pentoxide
based on the total weight of the bioactive glass material.

Preferably, when the bioactive glass material is melt-derived and does not include a
therapeutic active agent as defined hereinafter, the bioactive glass material consists
essentially of between 40 to 60% by weight of silicon dioxide, 15 to 25% by weight of
sodium oxide, 15 to 25% by weight of calcium oxide, and 0 to 15% by weight of a
phosphorus pentoxide, preferably 1 to 10% by weight of phosphorus pentoxide based
on the total weight of the bioactive glass material.

Preferably, when the bioactive glass material is a sol gel-derived glass, the bioactive
glass material includes between 40 to 90% by weight of silicon dioxide, 6 to 50% by
weight of calcium oxide, and 0 to 12% by weight of phosphorus pentoxide, preferably
1 to 12% by weight of phosphorus pentoxide based on the total weight of the bioactive
glass material. More preferably, when the bioactive glass material is a sol gel-derived
glass, the bioactive glass material includes between 45 to 86% by weight of silicon
dioxide, 10 to 40% by weight of calcium oxide, and 3 to 12% by weight of phosphorus
pentoxide based on the total weight of the bioactive glass material.

Preferably, when the bioactive glass material is a sol gel-derived glass and does not
include a therapeutic active agent as defined hereinafter, the bioactive glass material
consists essentially of between 45 to 86% by weight of silicon dioxide, 10 to 40% by
weight of calcium oxide, and 3 to 12% by weight of phosphorus pentoxide based on
the total weight of the bioactive glass material.
The bioactive glass material used in the composition of the present invention is in particulate form (i.e. in the form of a powder). Preferably, the bioactive glass material is in the form of small, discrete particles, rather than a fused matrix of particles. It will be appreciated that under some conditions the discrete particles may tend to cling together because of electrostatic of other forces but the particles are still considered to be non-interlinked. Suitably, the particles of the bioactive glass material may have a regular or irregular shape.

Preferably, a major amount of the particles of the bioactive glass material have a maximum linear diameter of less than or equal to 1500 µm, more preferably less than or equal to 1000 µm, even more preferably less than or equal to 750 µm, even more preferably less than or equal to 500 µm, even more preferably less than or equal to 250 µm, most preferably less than or equal to 100 µm.

Preferably, a major amount of the particles of the bioactive glass material have a maximum linear diameter of greater than or equal to 1 µm, more preferably greater than or equal to 5 µm, even more preferably greater than or equal to 10 µm.

By the term "a major amount of the particles" as used herein we mean at least 75% by number of the particles, preferably greater than or equal to 80% by number, more preferably greater than or equal to 90% by number, even more preferably greater than or equal to 95% by number, even more preferably greater than or equal to 99% by number of the particles, most preferably essentially all of the particles.

By the term "maximum linear diameter" we mean the largest linear dimension which is measurable perpendicularly between a tangent line at one extreme of the particle and another tangent line at the other extreme of the particle. Suitably, when the particle is essentially spherical then the maximum linear diameter represents the diameter of the particle. Suitably, this value can be determined by scanning electron microscopy.

Suitably, the volume or mass weighted arithmetic mean diameter D (4,3) of the particles of the bioactive glass material is in the range of 1 µm to 1500 µm, preferably 1 µm to 750 µm, more preferably 1 µm to 250 µm, most preferably 1 µm to 100 µm. The weight average particle size may be determined by laser diffraction methods in accordance with ISO 13320-1 (1999-11-01) using for example a Malvern Mastersizer 2000.
Suitably, the weight average skeletal density (true density) of the particles of the bioactive glass material is between 0.5 to 5 \text{g} \text{cm}^{-3}, preferably 1 to 3 \text{g} \text{cm}^{-3}, more preferably 1 to 2 \text{g} \text{cm}^{-3}. The skeletal density may be measured by helium ultrapycnometry using a Quantachrome helium Ultrapycnometer 1000.

Suitably, the non-volatile silicone fluid forms a matrix and the bioactive glass particles are dispersed within the matrix. Conveniently, the bioactive glass particles are typically of such a size and density as defined herein that they may be suspended within the non-volatile silicone fluid. Suitably, according to a preferred embodiment of the present invention, the composition of the present invention comprises a matrix of the non-volatile silicone fluid containing particles of the bioactive glass material suspended therein. More, preferably, the bioactive glass material is uniformly dispersed within the non-volatile silicone fluid.

Preferably, the bioactive glass material in the composition of the present invention is a resorbable solid i.e. it breaks down on contact with a liquid such as bodily fluids. Suitably, the bioactive glass material is a porous solid. The bioactive glass material may be porous melt-derived bioactive glass or a porous sol-gel derived bioactive glass. Preferably, the bioactive glass is a porous sol-gel derived bioactive glass. The pore volume and porosity of the bioactive glass material may be adjusted by techniques well known to those skilled in the art for example: altering the chemical composition of the bioactive glass; the method of manufacture of the bioactive glass; subjecting the bioactive glass to a sintering and/or foaming treatment and leaching out materials contained within the bioactive glass. Such techniques are described for example in US Patent no. 6,482,444B.

Suitably, the particles of the bioactive glass material have an average pore diameter of 1 \text{µm} to 750 \text{µm}, preferably 5 \text{µm} to 600 \text{µm}, more preferably 20 \text{µm} to 500 \text{µm}. By the term "average pore diameter" we mean the average pore size of all of the pores of all of the particles of the bioactive glass material present in the composition of the present invention.

Suitably, the degree of porosity of the bioactive glass material may be between 0 and 85% by volume (i.e. up to 85% by volume of the bioactive glass material consists of pores), preferably between 30 and 80%, more preferably between about 40 and 60%
by volume. By the term "degree of porosity" we mean the percentage by volume of the bioactive glass material which is in the form of pores based on the total volume of the bioactive glass material in the composition the present invention. The porosity may be determined by nitrogen sorption and the pore size may be calculated from the desorption data by the BJH method (Barret E.P. et al J. Am. Chem. Soc, 73, 1951, P373-380).

Bioactive glass material with high porosity may be prepared, for example, by incorporating a leachable substance into the bioactive glass and subsequently leaching the substance out of the glass. The resulting voids have roughly the same size as the size of the material that has been leached out. The size of the pores and the degree of porosity also depends on the amount of leachable material included in the bioactive glass. Suitable leachable substances are well known to those skilled in the art and include, for example, sodium chloride and other water-soluble salts. When leaching the glass composition with a suitable solvent, care should be taken not to leach out significant amounts of those components which add to the bioactivity of the glass (e.g. calcium and phosphorus oxides) or the therapeutic active agent, if present.

The pore volume of the bioactive glass material may also be adjusted using a sintering and/or foaming process. Typically, subjecting the bioactive glass to a sintering and/or foaming process may increase the pore volume. Suitably, particles of bioactive glass material which are melt-derived or sol gel-derived and have been subjected to a subsequent sintering and/or foaming treatment are also suitable for use in the composition of the present invention. The porosity of the glass may also be adjusted by altering the chemical composition of the glass. For example, higher concentrations of calcium oxide typically provides larger pore volumes in the glass.

The porosity and average pore diameter of the bioactive glass may be measured by techniques well known to those skilled in the art, for example gas-sorption.

As mentioned previously, the most preferred bioactive glass is a sol-gel derived bioactive glass. Typically, sol-gel derived bioactive glasses have a higher surface area than melt derived bioactive glass. Typically, sol-gel derived bioactive glass particles have a weight average surface area of 10 to 250 m²g⁻¹, more preferably 50 to 200 m²g⁻¹, even more preferably 100 to 150 m²g⁻¹, especially 110 to 130 m²g⁻¹. In contrast, melt derived bioactive glass particles have an average surface area of 1 to 10 m²g⁻¹,
preferably 1 to 5 m²g⁻¹. The surface area may be determined by the BET method which is based upon the measurement of quantities of gas physisorbed onto a surface at equilibrium pressure. Advantageously, the higher surface area of the sol-gel derived bioactive glass promotes enhanced bioactivity and resorbability compared with the melt derived bioactive glass.

The bioactive glass material may be produced in a variety of ways.

**Sol-Gel Method**

Sol-gel derived bioactive glass may be prepared in accordance with the methods disclosed in US 6,482,444B. Typically, sol-gel derived bioactive glass is prepared by synthesising an inorganic network by mixing metal alkoxides in solution, followed by hydrolysis, gelation and firing to produce a porous matrix or a dense glass. The firing can be performed at relatively high temperatures (600 to 1100 °C) or low temperatures (200 to 250 °C). Heating at the higher temperature range typically densifies the bioactive glass material. The glass may be milled to produce particles of the bioactive glass material. Suitably, if present, the therapeutic active agent may be incorporated in the bioactive glass material during the synthesis of the glass. For example, a silver containing bioactive glass material formed by the sol-gel method may be formed from tetraethoxyxilane (TEOS), phosphorus alkoxide, calcium nitrate and silver oxide in a water ethanol solution. Sol-gel glasses produced this way typically have a higher specific surface area compared with melt-derived glass or porous melt-derived glass.

**Melt-Derived Glass**

A melt-derived glass composition may be prepared, for example, by preparing an admixture of the individual metal oxides, other components and the therapeutic active agent (i.e. silver oxide), if present, which are present in the glass, blending the admixture, melting the admixture, and cooling the mixture. The melting temperature is determined in a large part by the glass composition, and ranges, for example, from about 900-1500 °C, preferably between about 1250 and 1450 °C. The melt is preferably mixed, for example, by oxygen bubbling, to ensure a thorough homogenation of the individual components.
The mixture can be cooled, for example by casting the molten admixture into a suitable liquid such as deionized water, to produce a glass frit. The glass frit may then be ground to produce particles of the bioactive glass material. Porosity may be introduced by mixing the powder with a foaming agent, and hot pressing the mixture under vacuum and at an elevated temperature. For example, the glass may be ground to form particles having a weight average particle size of between about 2 to 70 µm, the vacuum is preferably less than 50 MPa, and the hot pressing is preferably performed at a temperature above 400 °C, preferably between about 400 and 500 °C. Suitable foaming agents include compounds which evolve carbon dioxide and/or water at elevated temperatures, for example metal hydroxides, metal carbonates, and peroxides such as hydrogen peroxide. Preferred metal carbonates are sodium bicarbonate, sodium carbonate and calcium carbonate. The foaming agents are preferably added in a range of between about 1-5, more preferably 203 percent by weight of the glass powder. The preparation of melt-derived porous glass is described, for example in US Patent No. 5,648,301 to Ducheyne and El Ghannam. It will be appreciated that particles of sol-gel derived glass may also be subjected to such a foaming process.

**Sintering Process**

The bioactive glass materials may be sintered using known methodology. In one embodiment, an aqueous slurry of the glass powder and a foaming agent with a suitable binder, such as polyvinyl alcohol, is formed. The slurry is then poured into a mold, allowed to dry, and sintered at high temperatures. These temperatures can range, depending on the glass composition and foaming agent used, between about 450 and 1000 °C, more preferably between about 550 and 800 °C.

**Leaching Process**

To aid in preparing glass compositions with high porosity, the glass composition can include a material which can be preferably leached out of the glass composition, and in doing so, provide the composition with high porosity. For example, minute particles of a material capable of being dissolved in a suitable solvent, acid or base can be mixed with or melted into the glass, and subsequently leached out. The resulting voids have roughly the same size as the particle that was leached out. The size of the pores and degree of porosity depends on the amount of added material relative to the
amount of glass. For example, if the leached material constituted about 80% of the glass, then the glass would be approximately 80% porous when the material was leached out. When leaching the glass composition, care should be taken not to leach out those components which add to the bioactivity of the glass, i.e. the calcium, silica and phosphorus oxides.

Suitably, the particles of the bioactive glass material may be present in an amount of less than or equal to 40% by weight, preferably less than or equal to 35% by weight, more preferably less than or equal to 30% by weight, even more preferably less than or equal to 25% by weight, even more preferably less than or equal to 20% by weight, even more preferably less than or equal to 10% by weight, most preferably less than or equal to 8% by weight based on the total weight of the composition of the present invention.

Suitably, the particles of the bioactive glass material may be present in an amount of greater than or equal to 0.5% by weight, preferably greater than or equal to 1% by weight, more preferably greater than or equal to 1.5% by weight, even more preferably greater than or equal to 3% by weight, most preferably greater than or equal to 5% by weight based on the total weight of the composition of the present invention.

Suitably, the non-volatile silicone fluid may represent the balance of the composition of the present invention. Alternatively, the composition of the present invention may include one or more additional components as described herein.

According to a preferred aspect of the present invention the bioactive glass material includes a therapeutic active agent. Unexpectedly, it has been found that when the bioactive glass includes a therapeutic active agent and such a bioactive glass is used in the composition of the present invention, then the therapeutic active agent is released from the composition of the present invention in a controlled and/or sustained manner. Suitably, the therapeutic active agent forms a part of the bioactive glass material, for example the therapeutic active agent is incorporated in the bioactive glass material.

Although, bioactive glasses including a therapeutic active agent are known, as disclosed in US 6,482,444B, it is typically difficult to control the rate of release of the
active agent from the bioactive glass, particularly over a prolonged period of time, as
the rate of release of the active agent typically depends on the rate of dissolution of
the bioactive glass. Suitably, if particles of a bioactive glass including a therapeutic
active agent are applied to a target tissue (i.e. a wound) which includes relatively large
amounts of bodily fluids (i.e. wound extrudate), then the active agent is typically
released over a short period of time as the bioactive glass readily dissolves. This is
not only undesirable as the therapeutic active agent is not released gradually during
the healing process or the majority of the healing process, but also such a rapid
release of all the active agent may promote unwanted side effects. A further problem
associated with a relatively rapid release of the active agent is that the active agent
will typically be exposed to high concentrations of bodily fluids for prolonged periods
of time. The active agent may be relatively unstable when subjected to prolonged
exposure to bodily fluids which may result in a decrease and/or elimination of
therapeutic activity.

Unexpectedly, it has further been found that when the bioactive glass includes a
therapeutic active agent and such a bioactive glass is used in the composition of the
present invention, then the therapeutic active agent may be released from the
composition of the present invention even if the composition of the present invention
is not contacted directly with a liquid. Suitably, the non-volatile silicone fluid appears to
promote the release of the therapeutic active agent from the bioactive glass in a
controlled and/or sustained manner, whilst functioning as a semi-occlusive barrier
protecting the bioactive glass from exposure to bodily fluids. Suitably, it will be
appreciated that the composition of the present invention is suitable for delivering a
therapeutic active agent to a target site (i.e. target tissue such as skin) where there is
relatively low amounts of fluid, but also target sites which include relatively large
amounts of fluid. The composition of the present invention is particularly suitable for
treating a wound, particularly an open wound which includes relatively large amounts
of bodily fluids.

Preferably, the bioactive glass material includes a therapeutically effective amount of
the therapeutic active agent. The term "therapeutically effective amount" as used
herein in respect of the bioactive glass material refers to an amount of a therapeutic
agent present in the bioactive glass material to produce a therapeutic response at the
target site (i.e. tissue such as skin) when the composition of the present invention is
applied to the target site. It will be appreciated by those skilled in the art that this
amount may vary depending on a variety of factors, for example, the type of treatment, the target site and the type of therapeutic active agent. It will further be appreciated by those skilled in the art that such a therapeutically effective amount of the therapeutic active agent may be determined by routine experimental techniques.

By the term "therapeutic active agent" we include any agent and derivatives thereof which may be used for the therapeutic, curative and/or prophylactic treatment of a medical or cosmetic condition of a human or animal in need thereof.

Suitable therapeutic active agents include antibiotics, antiseptics, antifungals, antibacterials, antivirals, anti-inflammatory agents, hormones, anti-cancer agents, cardiovascular agents, bronchodilators, analgesics, antiarrhythmic, antihistamines, vitamins, anti-aging agents, beta blockers and anticonvulsants. Preferred therapeutic active agents are pharmaceutical active agents, which include derivatives thereof (i.e. salts and pro-drugs), which may be used for the therapeutic, curative and/or prophylactic treatment of a medical condition of a human or animal in need thereof.

Highly preferred therapeutic active agents include those with antibacterial activity (i.e. bacteriostatic and/or bacteriocidal activity), antiviral activity, antifungal activity, antibiotics, and antiseptics. Especially preferred therapeutic active agents include antibacterial agents and antiviral agents, particularly antibacterial agents.

Preferably, the antibacterial active agent comprises an inorganic compound. More preferably, the antibacterial active agent consists essentially of one or more inorganic compounds. Any inorganic compound possessing antibacterial activity may be used which may be incorporated into the bioactive glass material.

Preferably, the antibacterial active agent comprises a metal cation which exhibits antibacterial activity. Preferably, the metal cation is selected from the group of silver, copper, zinc, mercury, tin, lead, bismuth, cadmium, chromium and thallium cations or mixtures thereof. Even more preferably, the antibacterial active agent comprises a silver, copper or zinc cation. A particularly preferred metal cation is silver. Most preferably, the antibacterial active agent consists essentially of a silver cation. Suitably, a preferred therapeutic agent comprises a metal cation, particularly a metal cation as defined herein.
Suitably, when the antibacterial active agent comprises an inorganic compound, the inorganic compound preferably includes a metal cation as defined herein. More preferably, the inorganic compound comprises a salt of the one or more metal cations (e.g. silver, zinc or copper) as defined herein. Any suitable anion which forms a salt with the one or more metal cations may be used. Suitable anions/salts comprise oxides, halides (particularly bromides and chlorides), sulfides, nitrates, acetates and silicates. Preferred inorganic compounds include silver oxide, silver bromide, silver chloride, silver acetate, silver nitrate, copper oxides, copper sulphide, zinc oxide or zinc sulphide. An especially preferred inorganic compound having antibacterial activity comprises silver oxide (Ag₂O). Most preferably, the antibacterial active agent consists essentially of silver oxide.

Suitably, the bioactive glass material comprises greater than or equal to 0.1% by weight, preferably greater than or equal to 1% by weight, more preferably greater than or equal to 2% by weight, most preferably greater than or equal to 3% by weight of the therapeutic active agent based on the total weight of the bioactive glass material.

Suitably, the bioactive glass material comprises less than or equal to 15% by weight, preferably less than or equal to 14% by weight, even more preferably less than or equal to 12% by weight, more preferably less than or equal to 10% by weight, most preferably less than or equal to 18% of the antibacterial active agent based on the total weight of the bioactive glass material.

For the avoidance of doubt, when the bioactive glass material includes a therapeutic active agent then the other components of the bioactive glass material, for example oxides of silicon, calcium, phosphorus and sodium may be present in the preferred amounts as specified hereinbefore.

Thus, when the bioactive glass material is a sol gel-derived glass the bioactive glass material includes between 40 to 90% by weight of silicon dioxide, 6 to 50% by weight of calcium oxide, 0 to 12% by weight, preferably 1 to 12% by weight, of phosphorus pentoxide and 0.1 to 15% by weight of a therapeutic active agent as defined herein based on the total weight of the bioactive glass material. More preferably, the sol gel-derived bioactive glass material includes 45 to 86% by weight of silicon dioxide, 10 to 40% by weight of calcium oxide, 3 to 12% by weight of phosphorus pentoxide and 3 to
12% by weight of a therapeutic active agent based on the total weight of the bioactive glass material.

Suitably, when the bioactive glass material is a melt-derived bioactive glass, the melt-derived bioactive glass comprises 40 to 60% by weight silicon dioxide, 15 to 25% by weight of sodium oxide, 15 to 25% by weight of calcium oxide, 0 to 15% by weight, preferably 1 to 10% by weight of phosphorus pentoxide and 0.1 to 15% by weight of a therapeutic active agent as defined herein based on the total weight of the bioactive glass material.

Preferably, the bioactive glass material in the composition of the present invention is a sol gel-derived glass, especially a sol gel-derived glass which includes a therapeutic active agent as defined herein.

Preferably, the non-volatile silicone fluid is present in an amount of greater than or equal to 20% by weight, more preferably greater than or equal to 30% by weight, even more preferably greater than or equal to 40% by weight, even more preferably greater than or equal to 45% by weight, even more preferably greater than or equal to 50% by weight based on the total weight of the composition of the present invention.

Preferably, the non-volatile silicone fluid is present in an amount of less than or equal to 80% by weight, more preferably less than or equal to 75% by weight, more preferably less than or equal to 70% by weight, even more preferably less than or equal to 60% by weight based on the total weight of the composition of the present invention.

By the term "non-volatile silicone fluid" we mean a silicone fluid that does not substantially evaporate from the composition of the present invention at normal body temperature (i.e. up to and including 38°C) and atmospheric pressure. Preferably, the non-volatile silicone fluid does not substantially evaporate from the composition at room temperature (i.e. up to and including 25°C) and at atmospheric pressure.

Suitably, the non-volatile silicone fluid per se does not exhibit an appreciable vapour pressure at ambient temperature. Preferably, the volatile content of the non-volatile silicone fluid per se at 150°C is less than or equal to 0.8% by weight, more preferably less than or equal to 0.6% by weight, even more preferably less than or equal to 0.4%
by weight, most preferably less than or equal to 0.3% by weight based on the total weight of the non-volatile silicone fluid 

per se.

Suitably, the non-volatile silicone fluid component forms the base for the composition of the present invention. Preferably, the non-volatile silicone fluid is a silicone polymer.

Preferably, the non-volatile silicone fluid is a non-volatile silicone oil. Preferably, the non-volatile silicone fluid has a viscosity at 25°C of greater than or equal to 500 centistokes, more preferably greater than or equal to 5,000 centistokes, most preferably greater than or equal to 10,000 centistokes when measured by ASTM D-445, IP71 using a glass capillary viscometer such as an Ubbelohde available from Fisher Scientific Co., Pittsburgh, PA, USA. Preferably, the silicone fluid has a viscosity at 25°C of less than or equal to 200,000 centistokes, more preferably less than or equal to 100,000 centistokes, most preferably less than or equal to 50,000 centistokes. Suitably, viscosities up to 100,000 centistokes may be measured by ASTM D-45, IP71 using a glass capillary viscometer. Viscosities above 100,000 centistokes may be measured using rotational viscometers such as a Brookfield Synchro-lectric viscometer or a Wells-Brookfield Core/Plate viscometer available from Brookfield Engineering Laboratories, Stoughton, MA, USA employing test methods ASTM D-1084 (for a cup/spindle viscometer) and ASTM D-4287 (for a cone/plate viscometer). Suitably, when measuring viscosities above 100,000 centistokes, viscometers designed for the high viscosity region (HA and HB models) are employed. Highly preferred non-volatile silicone fluids have a viscosity at 25°C of about 30,000 centistokes when measured by ASTM D-445, IP71 using a glass capillary viscometer.

Preferably, the non-volatile silicone fluid comprises a silicone polymer, particularly a linear silicone polymer, especially a linear dimethicone polymer. Highly preferred non-volatile silicone fluids comprise a polydimethylsiloxane polymer, especially a linear polydimethylsiloxane polymer.

It will be appreciated that by increasing the viscosity of the non-volatile silicone fluid in the composition of the invention may produce a composition having increased durability and resistance to removal from the target site (i.e. target tissue site such as the skin and a wound). Similarly, by lowering the viscosity of the non-volatile silicone fluid component produces a composition which may be more easily applied to and removed from the target site. By using the full range of silicone oil viscosities, the
composition of the present invention may be tailored to the unique needs of each case. Silicone fluids having viscosities at 25°C of about 30,000 centistokes are especially preferred as they provide a balance of residual durability and ease of applicability. A particularly preferred non-volatile silicone fluid is Dow Corning 200 having a viscosity at 25°C of about 30,000 centistokes produced by Dow Corning Inc. (Midland, Michigan).

Suitably, the ratio by weight of the particles of the bioactive glass material to the non-volatile silicone fluid is preferably in the range of 1:100 to 1:1.5, preferably 1:50 to 1:5, even more preferably 1:20 to 1:7.

Suitably, the composition of the present invention is in the form of a gel. Preferably, the composition of the present invention comprising the bioactive glass material, the non-volatile silicone fluid and optionally a silicone elastomer as defined hereinafter but not including an optional volatile diluent as defined hereinafter, has a kinematic viscosity of greater than or equal to 27,000 centistokes, more preferably greater than or equal to 30,000 centistokes when measured at 25°C using a glass capillary viscometer using test method ASTM D-445, IP71 at 25°C. Preferably, the composition of the present invention comprising the bioactive glass material, the non-volatile silicone fluid and optionally a silicone elastomer as defined hereinafter but not including an optional volatile diluent as defined hereinafter, has a kinematic viscosity of less than or equal to 45,000 centistokes, more preferably less than or equal to 40,000 centistokes, most preferably less than or equal to 35,000 centistokes after evaporation of the volatile diluent when measured using a glass capillary viscometer using test method ASTM D-445, IP71 at 25°C.

It will be appreciated that when the composition of the present invention includes a volatile diluent, then typically the composition of the present invention has a viscosity which is lower than the above stated ranges. However, the resulting composition after evaporation of the volatile diluent from the composition of the present invention (i.e. after application) typically has a kinematic viscosity within the ranges as stated in the preceding paragraph.

In a preferred embodiment of the present invention, the composition of the present invention consists essentially of particles of the bioactive glass material as defined
herein, which may include a therapeutic active agent, and the non-volatile silicone fluid as defined herein.

In an alternative embodiment of the present invention, the composition of the present invention further includes a volatile diluent, namely a composition comprising particles of the bioactive glass material as defined herein, the non-volatile silicone fluid and a volatile diluent. Conveniently, the inclusion of a volatile diluent in the composition of the present invention allows the viscosity of the composition to be modified further. The composition may be prepared in the form of a flowable liquid, gel, oil, spreadable cream or light grease which may be applied to the target tissue site easily, so that after the composition is in place evaporation of the diluent therefrom produces a resulting composition having increased viscosity and durability. Such compositions are typically desirable when the composition is applied to a sensitive target tissue site, for example an open wound, as the patient experiences less discomfort when the composition is applied to the wound.

By the term "volatile diluent" we mean a diluent that substantially evaporates at normal body temperature (i.e. up to and including 38°C) and atmospheric pressure. Preferably, the volatile diluent substantially evaporates at room temperature (i.e. 25°C) and atmospheric pressure.

Suitably, the volatile diluent exhibits appreciable vapour pressure at ambient temperature. Preferably, the volatile diluent exhibits a heat of vaporization at 25°C of greater than or equal to 50 kJkg⁻¹, more preferably greater than or equal to 75 kJkg⁻¹, even more preferably greater than or equal to 100 kJkg⁻¹, most preferably greater than or equal to 125 kJkg⁻¹. Preferably, the volatile diluent exhibits a heat of vaporization at 25°C of less than or equal to 275 kJkg⁻¹, more preferably less than or equal to 250 kJkg⁻¹, even more preferably less than or equal to 225 kJkg⁻¹, most preferably less than or equal to 200 kJkg⁻¹.

Suitably, the volatile diluent exhibits a low viscosity when measured at 25°C. The viscosity of the volatile diluent may be measured using a glass capillary viscometer such as a Ubbelohde available from Fisher Scientific Co., Pittsburgh, PA, USA, employing test method ASTM D-445, IP71.
Preferably, the volatile diluent has a kinematic viscosity of greater than or equal to 0.5 mmV$^1$, more preferably greater than or equal to 2 mmV$^1$, particularly greater than or equal to 3 mmV$^1$ when measured in accordance with the above method. Preferably, the volatile diluent has a kinematic viscosity of less than or equal to 10 mmV$^1$, more preferably less than or equal to 9 mm$^2$s$^{-1}$, particularly less than or equal to 8 mmV$^1$ at 25°C when measured in accordance with the above method.

Preferably, the volatile diluent is a volatile silicone fluid (such as a liquid) as these are typically compatible with the non-volatile silicone fluid. Suitably, the volatile silicone fluid comprises a silicone polymer, particularly a cyclomethicone silicone polymer. Preferred volatile silicone fluids are selected from a polydimethyl-cyclosiloxane, such as cyclohexasiloxane, cyclopenta-siloxane, dodecamethylcyclohexasiloxane, decamethylcyclo-pentasiloxane, octamethylcyclo-tetrasiloxane; a polymethyldisiloxane such as hexamethyldisiloxane; or a polymethyltrisiloxane such as octamethyltrisiloxane. Highly preferred volatile silicone fluids comprise the polydimethylcyclosiloxanes, in particular cyclopentasiloxane and cyclohexasiloxanes, especially dodecylmethylcyclohexasiloxane and decamethyl-cyclopentasiloxane.

Examples of suitable volatile silicone fluids are Dow-Corning 244 which comprises a cyclomethicone octamethylcyclo-tetrasiloxane, Dow-Corning 245 which comprises a cyclomethicone decamethylcyclopentasiloxane Dow Corning 246 which comprises a cyclomethicone dodecamethyl cyclohexasiloxane and Dow Corning 345 which comprises a cyclomethicone decamethylcyclopentasiloxane.

Preferably, the weight average molecular weight (Mw) of the volatile diluent is greater than or equal to 150 Da, more preferably greater than or equal to 250 Da, most preferably greater than or equal to 300 Da. Preferably, the weight average molecular weight of the volatile diluent is less than or equal to 1,000 Da, more preferably less than or equal to 800 Da, even more preferably less than or equal to 600 Da, most preferably less than or equal to 500 Da.

Mixtures of volatile silicone fluids may also be used to alter the rate of volatilization if desired. The volatile diluent may be added to the mixture of non-volatile silicone fluid and the bioactive glass, in any proportion required to reduce the viscosity of the composition of the present invention to produce an easy to apply oil or light grease. At very high dilution, for example if 1 part by weight of a mixture of non-volatile silicone
fluid and the bioactive glass is added to 1000 parts by weight of the volatile diluent, then the product can be applied as a mobile fluid with a suitable applicator, such as a roll-on applicator, or even as a spray from a spray bottle. At the other extreme, as little as 1 part by weight of the volatile diluent may be added to 99 parts by weight of the non-volatile silicone and bioactive glass mixture to produce a more viscous composition to assist in its application.

Suitably, the volatile diluent is present at greater than or equal to 1%, more preferably greater than or equal to 5%, even more preferably greater than or equal to 10% by weight based on the total weight of the composition of the present invention. Suitably, the volatile diluent is present at less than or equal to 99.9%, preferably less than or equal to 80%, preferably less than or equal to 70%, preferably less than or equal to 60%, even more preferably less than or equal to 50%, even more preferably less than or equal to 40% by weight, even more preferably less than or equal to 30% by weight, most preferably less than or equal to 20% by weight based on the total weight of the composition of the present invention.

Preferably, when the composition of the present invention includes a volatile diluent (i.e. bioactive glass material, non-volatile silicone fluid, volatile diluent and optionally silicone elastomer) the composition has a kinematic viscosity of greater than or equal to 1,000 centistokes, preferably greater than or equal to 5,000 centistokes, more preferably greater than or equal to 10,000 centistokes when measured using a glass capillary viscometer using test method ASTM D-445, IP71 at 25°C. Preferably, when the composition of the present invention includes a volatile diluent the composition has a kinematic viscosity of less than or equal to 25,000 centistokes, more preferably less than or equal to 22,000 centistokes, most preferably less than or equal to 20,000 centistokes at 25°C when measured using a glass capillary viscometer using test method ASTM D-445, IP71.

In a further alternative embodiment of the present invention the composition of the present invention further includes a silicone elastomer and a volatile diluent as defined herein, namely a composition comprising particles of the bioactive glass material as defined herein, the non-volatile silicone fluid, the volatile diluent and a silicone elastomer.
Suitably, the inclusion of a silicone elastomer may promote evaporation of the volatile diluent from the composition without significantly effecting the viscosity of the composition. Convenienly, if the composition is applied to a target tissue, for example a wound, it is typically not necessary to immobilise the target tissue for prolonged periods of time whilst the volatile diluent evaporates to form a resulting composition having the desired viscosity, adhesive and smear proofing properties.

By the term "silicone elastomer" we mean a silicone polymer which, at room temperature, is capable of recovering substantially in shape and size after removal of a stretching force provided the elastic limit is not exceeded. Suitably, the silicone elastomer is a thixotropic solid so that the viscosity of the silicone elastomer decreases with time when a shear force is applied thereto.

Suitably, the silicone elastomer has a weight average molecular weight (Mw) of greater than or equal to 150,000, preferably greater than or equal to 200,000, more preferably greater than or equal to 250,000, even more preferably greater than or equal to 300,000.

Preferably, the silicone elastomer comprises a silicone polymer. More preferably, the silicone elastomer is a silicone cross-polymer (i.e. a cross-linked silicone polymer). Even more preferably, the silicone elastomer comprises a dimethicone cross-polymer (i.e. a cross-linked dimethicone polymer). The silicone elastomer, particularly dimethicone cross-polymer, may be unsubstituted or substituted, for example substituted with a polyether such as polyethylene glycol (PEG). Most preferably, the silicone elastomer, particularly the dimethicone cross-polymer, is unsubstituted.

Suitably, when the silicone elastomer comprises a silicone cross-polymer, the silicone cross-polymer preferably comprises less than or equal to 10 wt% cross-linker, more preferably less than or equal to 8 wt% cross-linker, even more preferably less than or equal to 5 wt% cross-linker. Preferably, the silicone cross-polymer comprises greater than or equal to 1 wt% cross-linker, more preferably greater than or equal to 2 wt% cross-linker.

Suitably, when the composition of the present invention includes a silicone elastomer, the silicone elastomer may be present in an amount of greater than or equal to 0.1% by weight, preferably greater than or equal to 0.2% by weight, more preferably greater
than or equal to 0.25% by weight, more preferably greater than or equal to 0.3% by weight, most preferably greater than or equal to 0.5% by weight based on the total weight of the composition.

Suitably, when the composition of the present invention includes a silicone elastomer, the silicone elastomer may be present in an amount of less than or equal to 10% by weight, more preferably less than or equal to 5% by weight, even more preferably less than or equal to 2% by weight, even more preferably less than or equal to 1.5% by weight, most preferably less than or equal to 1% by weight based on the total weight of the composition.

An especially preferred composition of the present invention including a silicone elastomer comprises between 0.2 to 2% by weight, particularly 0.5 to 2.0% by weight of the silicone elastomer.

Conveniently, for ease of handling the silicone elastomer may be mixed with one or more lower viscosity silicone fluids, such as non-volatile silicone fluids and/or volatile silicone fluids as described herein, for example a linear dimethicone or a cyclomethicone. Suitably, employing a mixture of silicone elastomer and non-volatile silicone fluid allows the elastomer to be mixed more easily with the other components of the composition of the present invention. Suitably, when a mixture of a silicone elastomer and a further lower viscosity silicone fluid is employed in the composition of the present invention, the mixture is employed in such an amount so that the concentration of silicone elastomer in the final composition is within the preferred limits as defined hereinbefore. This may be determined routinely, for example, if the concentration of silicone elastomer in the lower viscosity silicone fluid is known.

Preferably, the silicone elastomer is mixed with one or more lower viscosity non-volatile silicone fluids, especially a non-volatile linear dimethicone. Alternatively, the silicone elastomer is mixed with one or more volatile silicone fluids, especially a cyclomethicone as defined herein, particularly decamethylpenta-siloxane or dodecamethylhexasiloxane.

It will be appreciated, that when a silicone elastomer and lower viscosity silicone fluid mixture is employed in the composition of the present invention, the lower viscosity silicone fluid of the silicone elastomer mixture may be identical to the volatile diluent or
non-volatile silicone fluid in the composition of the present invention. Alternatively, the lower viscosity silicone fluid of the silicone elastomer mixture may be different than the volatile diluent and the non-volatile silicone fluid in the composition of the present invention.

Particularly preferred mixtures of silicone elastomer and lower viscosity silicone fluids comprise a mixture of a dimethicone cross-polymer as defined herein and a non-volatile dimethicone or non-volatile cyclomethicone or pentasiloxane. Especially preferred silicone cross-polymer include a dimethicone cross-polymer as defined herein in cyclomethicone silicone fluid, for example Dow Corning 9040 Silicone Elastomer Blend obtainable from Dow Corning Inc., Midland, Michigan, USA, and a dimethicone cross-polymer in dimethicone silicone fluid, for example Dow Corning 9041 Silicone Elastomer Blend also obtainable from Dow Corning Inc.

The composition of the present invention may further include one or more pharmaceutical active agents in addition to the therapeutic active agent in the bioactive glass material i.e. a further pharmaceutical active agent not contained in the bioactive glass material. Suitable pharmaceutical active agents have been defined hereinbefore in relation to the bioactive glass material.

Preferably, the further pharmaceutical active agent possesses antibacterial, anti-inflammatory, antiviral and/or antifungal activity. An especially preferred further pharmaceutical active agent comprises an antibacterial agent. An alternative especially preferred further pharmaceutical active agent comprises an anti-inflammatory agent. It will be appreciated that the further pharmaceutical active agent when present in the composition of the present invention is physically distinct from the therapeutic active agent contained within the bioactive glass and, if present, it is incorporated essentially in the non-volatile silicone fluid.

Preferably, the further pharmaceutical active agent is present in an amount of less than or equal to 50%, more preferably less than or equal to 30%, more preferably less than or equal to 10%, most preferably less than or equal to 3% by weight based on the total weight of the composition of the present invention.

Preferably, the further pharmaceutical active agent is present in an amount of greater than or equal to 0.1%, more preferably greater than or equal to 0.5%, especially
greater than or equal to 1.0% by weight based on the total weight of the composition of the present invention.

Suitably, the further pharmaceutical active agent may be in the form of a liquid, gel or powder. Preferably, the further pharmaceutical active agent is in the form of a powder, especially a powder that is insoluble in a typical pharmaceutical acceptable diluent, such as water or alcohol.

Preferred further antibacterial agents include antibiotic zeolites, chlorohexidine, polymyxin B sulphate, benzachromium chloride, benzamycin, clindamycin, erythromycin, tetracycline, mupirocin, bacitracin zinc and neomycin sulphate. Especially preferred further antibacterial agents include antibiotic zeolites.

A preferred composition of the present invention comprises:

(a) 3 to 10% by weight of a bioactive glass material as defined herein, particularly a bioactive glass material including a therapeutic active agent, especially a sol gel-derived bioactive glass material including a therapeutic active agent as defined herein;

(b) 30 to 75% by weight of a non-volatile silicone fluid as defined herein;

(c) 5 to 20% by weight of a volatile diluent as defined herein, particularly a volatile silicone fluid as defined herein; and

(d) 0.5 to 2.0% by weight of a silicone elastomer as defined herein.

The composition of the present invention may further include other optional components, for example a silicone wax (i.e. an alkyl methyl silicone wax). Such components are typically present in amounts up to 10% by weight of the composition of the present invention.

According to a second aspect, the present invention provides a method of manufacturing a composition of the present invention comprising contacting particles of a bioactive glass material as defined herein with a non-volatile silicone fluid as defined herein. Preferably, the particles of the bioactive glass material are mixed with the non-volatile silicone fluid. Typically, such a mixing process may be performed at room temperature and pressure using stirrers and blenders suitable for blending.
silicone oils. Suitably, the resulting mixture comprises a suspension of the particles of
the bioactive glass material dispersed within the non-volatile silicone fluid.

Suitably, the other optional/preferred components present in the composition of the
present invention (i.e. volatile diluent, silicone elastomer and/or further pharmaceutical
active agent) may be mixed into the composition of the present invention. Suitably,
when a volatile diluent is included in the composition of the present invention, a
pressure vessel and condensing system may be employed to retain the diluent within
the composition.

The composition of the present invention is suitable for use in medicine, particularly
for the therapeutic, curative and/or prophylactic treatment of a medical condition for
which the application of a therapeutic active agent is indicated.

Thus, according to a third aspect, the present invention provides a composition
according to the first aspect of the present invention for use in medicine.

When the bioactive glass material includes an antibacterial agent the composition of
the present invention may exhibit antibacterial activity against a variety of bacteria, for
example the staphylococcal bacteria such as Staphylococcus aureus, methicillin-
resistant Staphylococcus aureus (MRSA). Silver ions are known in particular to exhibit
antibacterial activity against such bacteria.

Thus, according to a fourth aspect, the present invention provides the use of a
composition according to the first aspect of the present invention wherein the
bioactive glass material includes an antibacterial agent for reducing, eliminating,
inhibiting and/or preventing the presence of bacteria. Such bacteria include those of
the Staphylococcal family for example Staphylococcus aureus and MRSA, and
Pseudomonas. It will be appreciated by those skilled in the art that the presence of
bacteria may occur in both medical and non-medical situations.

Thus, according to a fifth aspect, the present invention provides a composition of the
present invention wherein the bioactive glass material includes an antibacterial agent
for the therapeutic, curative and/or prophylactic treatment of a medical condition for
which the application of an antibacterial active agent is indicated in a patient in need
thereof. Preferably, the composition of the present invention is applied topically to a
patient in need thereof. Such medical conditions include a wound, in particular an open wound or a chronic wound. Suitably, when such a composition is used for treating a wound then there is typically a noticeable reduction and/or prevention of scarring. Suitably, the composition of the present invention as defined herein is suitable for reducing and/or preventing scarring by administering the composition to a wound, cut and/or skin lesion. Additionally, when the composition is applied to an open wound or chronic wound the composition typically reduces the amount of bacteria (i.e. Pseudomonas and Staphylococcus aureus), the amount of exudate and the malodour associated with such wounds thereby promoting the wound healing process. Typical chronic wounds (i.e. wounds where the healing process has arrested, thereby typically resulting in malodorous wounds colonised with bacteria containing large quantities of exudate (e.g. pus)) include, for example, venous leg ulcers, trauma wounds, pressure ulcers and wounds in diabetic patients.

Conveniently, the composition may ameliorate or reduce existing scars when applied thereto. Suitably, the composition of the present invention is suitable for reducing and/or ameliorating scarring, particularly hypertrophic or keloid scars, by administering the composition to a scar.

Thus, according to a sixth aspect, the present invention provides a wound treatment composition comprising the composition of the first aspect of the present invention. The wound treatment composition may be in a form as described herein e.g. gel, stiff cream, film, etc. The wound treatment composition may also be in the form of a wound dressing. It will be appreciated that as the bioactive glass material exhibits bioactivity in the composition of the present invention, then it is not essential the bioactive glass material includes a therapeutic active agent when the composition is used in applications for repairing/healing damaged skin (i.e. wound treatment applications).

Suitably, the present invention comprises a method of treating a wound, particularly an open wound or cut, by applying a composition of the present invention to the wound.

As described herein, the composition of the present invention may be formulated in a range of viscosities. It may be in the form of a flowable liquid, gel, cream or light grease. The composition may have an appropriate viscosity so it may be used as a
cleanser having antibacterial activity, for example a hand and skin cleanser. With the prevalence of MRSA in hospitals such a cleanser may be used to prevent, eliminate and/or reduce the presence of MRSA in hospitals. Suitably, such cleansers may be dispensed from and contained in pump action containers, bottles, aerosols, etc.

Thus, according to an eighth aspect, the present invention provides a method of reducing, eliminating or preventing the presence of MRSA, by applying a composition of the present invention to a target site where it is desirable to reduce, eliminate, prevent or inhibit the presence of MRSA. Such target sites include hands, skin, and work surfaces e.g. kitchen worktop surfaces and operating tables in hospitals.

The composition of the present invention may be stored and dispensed from a variety of containers.

Thus according to a ninth aspect, the present invention provides a reservoir including a composition of the present invention contained therein, and a dispenser in fluid communication with the reservoir for dispensing the composition from the reservoir.

Suitable dispensers include a spray, pump-action dispenser, a roller ball or an applicator.

The invention will now be described by way of the following non-limiting examples.

Example 1 - Preparation of silver containing sol-gel derived bioactive glasses

A bioactive sol-gel glass of the three component CaO-P₂O₅-SiO₂ system, in which 1% by weight of Ag₂O has been introduced by substitution of CaO was prepared according to the methodology of US Patent 6,482,444B. The bioactive sol-gel glass is handled in the dark, using a safe light, stored in a black box to preserve it in its oxidised state.

Hydrolysis and Copolymerisation

The following compounds were added to deionised (DI) water obtained from an instant purifier Micromeg Eglostat in sequential order; 2N nitric acid (HNO₃), tetraethoxysilane (TEOS) 99% purity, triethoxyphosphate (TEP) 99% purity A.C.S., Ca(NO₃)₂·4H₂O 99% purity A.C.S., and AgNO₃ 99.99% purity. After two hours of
moderated stirring the mixture was poured into polymethylpentane pots, hermetically sealed, and left to gel at room temperature for two days.

**Aging**

5 The pots containing the gels were transferred to an oven at 60 °C. Aging took three days.

**Drying**

The aged gels were placed on a watch glass in a drying chamber above 250 ml of DI water. Thus, the near equilibrium drying conditions were realised, in which the pore liquor evaporating from the gel was supported by the vapour pressure of the water.

The drying schedule involves three stages, listed in Table 1. The temperature gradient between each step was 0.1 °C/minute.

**Table 1**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Time (hours)</th>
<th>Temperature (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>90</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>130</td>
<td>40</td>
</tr>
</tbody>
</table>

**Stabilisation**

The stabilisation was carried out in a box furnace at 450 °C for 19 hours.

After cooling the glass was milled to form particles of the bioactive glass material. A major amount of the particles had a maximum dimension of between 1 and 100 µm. The bioactive glass had the following composition:

% by weight

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO₂</td>
<td>61</td>
</tr>
<tr>
<td>CaO</td>
<td>34</td>
</tr>
<tr>
<td>P₂O₅</td>
<td>4</td>
</tr>
<tr>
<td>Ag₂O</td>
<td>1</td>
</tr>
</tbody>
</table>
Example 2 - Preparation of sol-gel derived bioactive glass

A bioactive sol-gel glass of the three component CaO-P$_2$O$_5$-SiO$_2$ system was prepared in accordance with the procedure of Example 1 except that silver oxide was not introduced into the glass. The bioactive glass had the following composition:

<table>
<thead>
<tr>
<th>% by weight</th>
</tr>
</thead>
</table>
| SiO$_2$     | 61  
| CaO         | 35  
| P$_2$O$_5$  | 4   

Example 3 - Preparation of a composition comprising a mixture of particles of a bioactive glass containing an antibacterial agent and a non-volatile silicone fluid

The bioactive glass of Example 1 (0.5% by weight) is mixed with a non-volatile silicone fluid Dow Corning 200 (99.5% by weight) using a J H Day Pony Mixer, under anhydrous conditions at room temperature for 2 hours. The resulting composition is in the form of a viscous gel having a viscosity of approximately 25,000 to 30,000 centistokes at 25°C when measured by a glass capillary viscometer by test method ASTM D-455, IP71.

Example 4 - Preparation of a composition comprising a mixture of particles of a bioactive glass and a non-volatile silicone fluid

The bioactive glass of Example 2 (0.5% by weight) is mixed with a non-volatile silicone fluid Dow Corning 200 (99.5% by weight) using a J H Day Pony Mixer, under anhydrous conditions at room temperature for 2 hours. The resulting composition is in the form of a viscous gel having a viscosity of approximately 25,000 to 30,000 centistokes at 25°C when measured by a glass capillary viscometer by test method ASTM D-455, IP71.

Examples 5 to 8

The compositions as outlined in Table 1 were prepared using the methodology of Example 3.
Table 2

<table>
<thead>
<tr>
<th>Example</th>
<th>Dow Corning 200</th>
<th>Bioglass from Example 1 % by wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>99</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>98.5</td>
<td>1.5</td>
</tr>
<tr>
<td>7</td>
<td>97</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>95</td>
<td>5</td>
</tr>
</tbody>
</table>

Example 9 - General procedure for assessing antibacterial activity

Standard agar culture plates are prepared under sterile conditions using an autoclave. A uniform concentration of a bacterial culture is added to each plate. Using a sterile cork borer, a cylinder of agar is removed from the centre of each plate. A test compound (0.5 g) is placed into the hole created by the borer. The plates are stored at 37°C for 72 hours and the inhibition of bacterial growth around the hole containing the test compound is measured every 12 hours by digital photography. The larger the zone of inhibition in mm indicates increased antibacterial activity.

Example 10 - Antibacterial activity against Staphylococcus aureus

A culture of Staphylococcus aureus is prepared and a uniform concentration added to eight agar plates. The antibacterial activity of the compositions of Examples 5 to 8 was determined in accordance with Example 9. The control samples employed are the non-volatile silicone fluid alone (Dow Corning 200) the particulate bioactive glass of Example 1, and the particulate bioactive glass of Example 2 not including any silver oxide. The results are presented in Table 3.

The results in Table 3 indicate that none of the control samples inhibited Staphylococcus aureus. Even the particulate bioactive glass of Example 1 containing silver oxide (i.e. Control 2) did not inhibit Staphylococcus aureus. It is believed that as the tests are essentially performed in a non-aqueous liquid environment, the bioactive glass will not resorb and the silver will not be released therefrom and inhibit bacterial growth.
Irrespective of the non-aqueous liquid environment of the test procedure, Examples 5 to 8 comprising a mixture of the bioactive glass containing an antibacterial agent and a non-volatile silicone fluid, exhibited antibacterial activity indicating release of silver ions from these compositions in sufficient amounts to inhibit bacterial growth. Moreover, the antibacterial activity occurred over the duration of the test, indicating a sustained release of the antibacterial agent from these compositions.

### Table 3

<table>
<thead>
<tr>
<th>Material</th>
<th>Zone of inhibition (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12 hrs</td>
</tr>
<tr>
<td>Control 1: Dow Corning 200</td>
<td>0</td>
</tr>
<tr>
<td>Control 2: Bioactive glass of Example 1</td>
<td>0</td>
</tr>
<tr>
<td>Control 3: Bioactive glass of Example 2 not including silver oxide</td>
<td>0</td>
</tr>
<tr>
<td>Example 5</td>
<td>0</td>
</tr>
<tr>
<td>Example 6</td>
<td>0</td>
</tr>
<tr>
<td>Example 7</td>
<td>0</td>
</tr>
<tr>
<td>Example 8</td>
<td>0</td>
</tr>
</tbody>
</table>

Example 11 - Preparation of a composition comprising a mixture of particles of bioactive glass material containing an antibacterial agent, a non-volatile silicone fluid, a volatile diluent and a silicone elastomer

A blend comprising 45% by weight of Dow Corning 245 (a volatile diluent comprising decamethyldimethylsiloxane), 50% by weight of a non-volatile silicone fluid Dow Corning 200, 3% by weight of the bioactive glass of Example 1 and 2% by weight of Dow Corning 9040 silicone elastomer blend (comprising a dimethicone cross-polymer in cyclomethicone and having a viscosity of 250,000 to 580,000 centistokes at 25 °C) was stirred at ambient temperature using a J H Day Pony Mixer, under anhydrous conditions, for 2 hours. The resulting product was in the form of a gel having a
viscosity of 19,000 to 21,000 centistokes at 25 °C when measured by a glass capillary viscometer by test method ASTM D-455 IP71.

Example 12 - Preparation of a composition comprising a mixture of particles of a bioactive glass material containing an antibacterial agent, a non-volatile silicone fluid and a volatile diluent

A blend comprising 47% by weight of Dow Corning 245 (a volatile diluent comprising decamethylpentasiloxane), 50% by weight of a non-volatile silicone fluid Dow Corning 200 and 3% by weight of the bioactive glass of Example 1 was stirred at ambient temperature using a J H Day Pony Mixer, under anhydrous conditions, for 2 hours. The resulting product was in the form of a gel having a viscosity of 19,000 to 21,000 centistokes at 25 °C when measured by a glass capillary viscometer by test method ASTM D-455 IP71.

Example 13 - Preparation of a composition comprising a mixture of particles of bioactive glass material containing an antibacterial agent, a non-volatile silicone fluid, a volatile diluent and silicone elastomer

A blend comprising 20% by weight of Dow Corning 245 (a volatile diluent comprising decamethylpentasiloxane), 70% by weight of a non-volatile silicone fluid Dow Corning 200, 8% by weight of the bioactive glass of Example 1 and 2% by weight of Dow Corning 9040 silicone elastomer blend (comprising a dimethicone cross-polymer in cyclomethicone and having a viscosity of 250,000 to 580,000 centistokes at 25 °C) was stirred at ambient temperature using a J H Day Pony Mixer, under anhydrous conditions, for 2 hours. The resulting product was in the form of a gel having a viscosity of 19,000 to 21,000 centistokes at 25 °C when measured by a glass capillary viscometer by test method ASTM D-455 IP71.

Example 14 - Preparation of a sol-gel derived bioactive glass

A bioactive sol-gel glass of the two component CaO-SiO₂ system was prepared by adding Ca(NO₃)₂·4H₂O 99% purity A.C.S. (1237g) to deionised water (3082 ml) and nitric acid (70% w/w, 80 ml) and the resulting solution stirred at room temperature for 5 minutes. Tetraethoxysilane (TEOS, 99% purity, 2547g) was added to the resulting mixture at a rate of 1 litre per minute and stirring continued until the mixture was at a
temperature of below 35 °C. The mixture was then transferred into coated stainless steel trays, the trays sealed and heated in an oven at 60 °C for 24 hours, then at 90 °C for 24 hours and then at 130 °C for 48 hours. The glass was finally subjected to stabilisation by heating in a furnace at 600 °C for 7 hours. This produced approximately 1 kg of bioactive glass having the following composition.

<table>
<thead>
<tr>
<th></th>
<th>% by weight</th>
<th>mole %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO₂</td>
<td>69.5</td>
<td>71.2</td>
</tr>
<tr>
<td>CaO</td>
<td>26.3</td>
<td>28.8</td>
</tr>
</tbody>
</table>

Example 15 - Preparation of a silver containing sol-gel derived bioactive glass

A bioactive sol-gel glass of the two component CaO-SiO₂ system including Ag₂O was prepared by adding Ca(NO₃)₂·4H₂O (1155.3 g) and silver nitrate (58.7 g) to water (3082 ml) and nitric acid (70% w/w 80 ml) and the resulting mixture stirred at room temperature for 5 minutes. Tetraethoxysilane (TEOS, 99% purity, 2547g) was added to the resulting mixture at a rate of 1 litre per minute and stirring continued until the mixture was at a temperature of below 35 °C. The mixture was then transferred into coated stainless steel trays, the trays sealed and heated in an oven at 60 °C for 24 hours, then at 90 °C for 24 hours and then at 130 °C for 48 hours. The glass was finally subjected to stabilisation by heating in a furnace at 600 °C for 7 hours. This produced approximately 1 kg of bioactive glass having the following composition.

<table>
<thead>
<tr>
<th></th>
<th>% by weight</th>
<th>mole %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SiO₂</td>
<td>69.7</td>
<td>72.8</td>
</tr>
<tr>
<td>CaO</td>
<td>22.7</td>
<td>25.4</td>
</tr>
<tr>
<td>Ag₂O</td>
<td>3.33</td>
<td>1.8 (Ag⁺)</td>
</tr>
</tbody>
</table>
Claims

1. A composition comprising a mixture of particles of a bioactive glass material and a non-volatile silicone fluid.

2. A composition as claimed in claim 1 wherein the bioactive glass material includes a therapeutic active agent.

3. A composition as claimed in claim 2 wherein the therapeutic active agent is selected from the group consisting of antibacterial agents, antiviral agents, antifungal agents, antibiotics, antiseptics and mixtures thereof.

4. A composition as claimed in claim 3 wherein the therapeutic active agent comprises an antibacterial agent.

5. A composition as claimed in claim 4 wherein the antibacterial agent comprises a metal cation.

6. A composition as claimed in claim 5 wherein the metal cation is selected from the group consisting of silver, copper and zinc ions or a mixture of two or more of these ions.

7. A composition as claimed in claim 5 or 6 wherein the antibacterial agent comprises an inorganic compound comprising a salt of said metal cation.

8. A composition as claimed in any one of claims 5 to 7 wherein said antibacterial agent comprises a silver salt, preferably silver oxide.

9. A composition as claimed in any one of the preceding claims wherein the bioactive glass material is an inorganic glass material having an oxide of silicon as its major component.

10. A composition as claimed in any one of the preceding claims wherein the bioactive glass material is a sol gel derived bioactive glass material.
11. A composition as claimed in any one of the preceding claims wherein the bioactive glass material further includes an oxide of calcium.

12. A composition as claimed in any one of the preceding claims wherein the bioactive glass material further includes an oxide of phosphorus.

13. A composition as claimed in any one of the preceding claims wherein the therapeutically active agent is present in an amount of 0.1 to 15 wt% of the bioactive glass material based on the total weight of the bioactive glass material.

14. A composition as claimed in any one of claims 2 to 13 wherein the bioactive glass material comprises 45 to 86% by weight of silicon dioxide, 10 to 40% by weight of calcium oxide, 3 to 12% by weight of phosphorus pentoxide and 3 to 12% by weight of a therapeutic active agent based on the total weight of the bioactive glass material.

15. A composition as claimed in any one of the preceding claims wherein the bioactive glass is present in an amount of greater than or equal to 0.5 wt% based on the total weight of the composition.

16. A composition as claimed in any one of the preceding claims wherein the bioactive glass material is present in an amount of less than or equal to 20% by weight on the total weight of the composition.

17. A composition as claimed in any one of the preceding claims wherein the non-volatile silicone fluid comprises a silicone polymer, preferably a linear dimethicone.

18. A composition as claimed in any one of the preceding claims wherein the non-volatile silicone fluid is present in an amount of greater than or equal to 30 wt% based on the total weight of the composition.

19. A composition as claimed in any one of the preceding claims wherein the non-volatile silicone fluid is present in an amount of less than or equal to 70 wt% based on the total weight of the composition.
20. A composition as claimed in any one of the preceding claims wherein the particles of the bioactive glass material have a weight average particle size of 1 µm to 250 µm.

21. A composition as claimed in any one of the preceding claims wherein the particles of the bioactive glass are dispersed within the non-volatile silicone fluid.

22. A composition as claimed in any one of the preceding claims further including a volatile diluent.

23. A composition as claimed in claim 22 wherein the volatile diluent comprises a volatile silicone fluid, particularly a cyclomethicone.

24. A composition as claimed in claims 22 or 23 wherein the composition further includes a silicone elastomer.

25. A composition as claimed in any one of the preceding claims wherein the composition includes a further pharmaceutical active agent.

26. A method of manufacturing a composition as defined in any one of claims 1 to 25 comprising contacting particles of a bioactive glass material as defined in any one of claims 1 to 25 with a non-volatile silicone fluid.

27. A composition as claimed in any one of claims 1 to 25 for use in medicine.

28. Use of a composition as defined in any one of claims 4 to 25 for reducing, eliminating, inhibiting or preventing the presence of bacteria.

29. Use as claimed in claim 28 wherein the bacteria comprises a Staphylococcal bacteria, particularly methicillin-resistant Staphylococcus aureus (MRSA).

30. A composition as claimed in any one of claims 4 to 25 for the therapeutic, curative and/or prophylactic treatment of a medical condition for which the application of an antibacterial active agent is indicated.
31. A wound treatment composition comprising the composition as defined in any one of claims 1 to 25.

32. A cleanser comprising the composition as defined in any one of claims 1 to 25.

33. A container comprising a reservoir including a composition as defined in any one of claims 1 to 25 contained therein, and a dispenser in fluid communication with the reservoir for dispensing the composition from the reservoir.

34. A composition as claimed in any one of claims 2 to 25 for the topical administration of a therapeutic active agent to a patient in need thereof.

35. A composition as claimed in any one of claims 4 to 25 for reducing, eliminating, inhibiting or preventing the presence of bacteria.

36. A composition as claimed in claim 35 wherein the bacteria comprises Staphylococcal bacteria, particularly methicillin-resistant Staphylococcus aureus (MRSA).

37. Use of a composition as defined in any one of claims 4 to 25 in the manufacture of a medicament for reducing, eliminating, inhibiting or preventing bacteria by topically administering the medicament to a patient in need thereof.

38. A method of reducing, eliminating or preventing the presence of bacteria by applying a composition as defined in any one of claims 4 to 25 to a target site where it is desirable to reduce, eliminate or prevent the presence of bacteria.

39. A method as claimed in claim 38 wherein the bacteria is MRSA.

40. A method as claimed in claim 39 wherein the target site is the human hand.

41. Use of a composition as defined in any one of claims 1 to 25 in the manufacture of a medicament for treating an open wound.