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(71) Applicants and
(72) Inventors: **TAGG, John, Robert** [AU/NZ]; 39 Braeview Crescent, Dunedin (NZ). **CHILCOTT, Christopher, Norman** [NZ/NZ]; 55 Silverton Street, Andersons Bay, Dunedin (NZ). **ALQUMBER, Mohammed, Abdullah, Ali** [SA/NZ]; Cumberland Hall, 250 Castle Street, Dunedin (NZ).

(74) Agents: **ADAMS, Matthew, D.** et al.; A J Park, 6th Floor Huddart Parker Building, Post Office Square, P O Box 949, Wellington, 6015 (NZ).

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(54) Title: SKIN TREATMENT COMPOSITIONS

(57) Abstract: The present invention relates to compositions containing *Micrococcus luteus*. The compositions are useful for controlling skin disorders in which bacteria are a causative component. The invention also provides a new strain of *Micrococcus luteus* useful in these compositions.

SKIN TREATMENT COMPOSITIONS

FIELD OF THE INVENTION

This invention relates to *Micrococcus luteus* containing compositions useful for controlling skin disorders, more particularly, the invention relates to compositions intended for topical application to prevent or treat skin disorders in which bacteria are a causative component, for example, body odour, skin infections and acne. A new strain of Micrococcus luteus useful in these compositions is also provided.

BACKGROUND OF THE INVENTION

Skin disorders including malodour are often attributable to the action of microorganisms on the skin. A range of products including proteins, lipids, salts and acids are secreted by glands in the skin. While the fresh secretions are often odourless, microbial decomposition of the secreted products can result in offensive odours being produced.

Control of body odour is most commonly addressed through the use of antiperspirants or deodorants. Deodorants are generally designed to mask offensive odours or to prevent production of same. Antiperspirants are intended to prevent or control perspiration on the skin, and may also function as a deodorant.

Most deodorant or antiperspirant products make use of aluminium salts or zinc salts. These compounds can cause irritation, itching and burning on individuals with sensitive skin. There exists a health concern amongst various groups of consumers about the health effects of using aluminium or other metal salts particularly in deodorants. Studies such as *Graves et al.*, 1990 Journal of Clinical Epidemiology vol. 43. 35-44 and P.D Dabre., 2003 Journal of Applied Toxicology vol 23, Issue 2, 89-95 imply a link between aluminium and Alzheimer's, and aluminium and breast cancer.. Accordingly, development of an aluminium or zinc free deodorant or antiperspirant product is desirable.

Skin infections may be caused by a range of bacteria including *Staphylococcus* species, (particularly *S. aureus)*, *Propionibacterium acnes*, *Corynebacterium sps*, and *Streptococcus* species as well as aerobic diphtheroids. Examples of such infections are toe infections, impetigo, folliculitis, cellulitis, boils, carbuncles, mastitis, and acne. Treatment often involves topical or oral administration of antibiotics, antifungals and in some cases steroids. Antibiotics and antifungals can also kill off non-pathogenic beneficial microorganisms leading to reinfection. Moreover, microorganisms are becoming increasingly antibiotic resistant see for example Antibiotic Resistance; Stephen Gillespie ed; Humana Press, 1 September 2000. Accordingly, there is a constant need for alternative forms of treatment.

The present invention is broadly directed to compositions and methods for controlling skin disorders using *Micrococcus luteus* strains, or at least provides the public with a useful choice.

SUMMARY OF THE INVENTION

In a first aspect, the invention provides a biologically pure culture of *M. luteus* strain Q24 on deposit at Deutsche Sammlung von Mikroorganisms Und Zellkulturen GmbH, Braunschweig, Germany, under accession number DSM 17172, or a culture having the identifying characteristics thereof.

The invention also provides a composition comprising *M. luteus* strain Q24 or a culture having the identifying characteristics thereof together with a diluent, carrier and/or excipient.

In a further aspect, the invention provides a composition comprising a strain of *M. luteus* effective to at least inhibit one or more bacteria selected from the group consisting of *Staphylococcus* species, *Propionibacterium* species, *Corynebacterium* species, and *Streptococcus* species, and aerobic diphtheroids.

In a further aspect, the invention provides a composition comprising a strain of *M. luteus* effective to at least inhibit growth of one or more bacteria selected from the group consisting of *Propionibacterium acnes*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*, *Staphylococcus simulans*, *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Corynebacterium minutissium*, *Corynebacterium tenuis, Streptococcus pyogenes Streptococcus agalactiae,* and *Streptococcus dysgalactiae* together with a diluent, carrier and/or excipient.

In one embodiment, the *M. luteus* strain inhibits at least four of the group of bacteria above, preferably eight and more preferably all eleven.. These bacteria are generally recognised as skin bacteria.

In one embodiment the *Staphylococcus aureus* is methicillin resistant.

Preferably the *M. luteus* is strain Q24.

Preferably the composition is formulated for topical administration.

Topically administrable forms include powders, emulsions, unguents, pastes, oils, gels, lotions, creams, suspensions, nasal sprays, roll ons, sticks or aerosol sprays, semi-solid and solid formulations.

In a further aspect, the invention provides a method for at least inhibiting the growth of bacteria sensitive to *M. luteus*, the method comprising contacting the sensitive bacteria with an inhibitory effective amount of an *M. luteus* strain or a composition of the invention.

The invention also provides a prophylactic or therapeutic method of treatment for skin disorders in an individual in need thereof. The method comprising administering to said individual an *M. luteus* strain, or a composition of the invention in an amount effective to at least inhibit growth of one or more bacteria causing the skin disorder, or in an amount to allow effective colonisation of the skin of the individual by the *M. luteus*.

In a further aspect, the invention provides a method of controlling the incidence and/or severity of a skin disorder, the method comprising introducing to the skin of the individual an amount of *M. luteus*, or composition of the invention, effective to control the incidence or severity of said skin disorder.

Skin disorders amenable to treatment according to the present invention include skin infections, such as impetigo, erysiphelas, folliculitis, acne, boils, carbuncles, cellulitis, pitted keratolysis, intertrigo, trichomycosis, mastitis, toe infections such as tinea, and body odour.

Bacteria responsible for skin disorders that may be controlled according to the present invention include *Propionibacterium* species, including *Propionibacterium acnes*, *Streptococci* species including *Streptococcus pyogenes*, *Streptococcus agalactiae*, and *Streptococcus dysgalactiae*, *Staphylococcus* species including *Staphylococcus simulans*, *Staphylococcus saprophyticus* and *Staphylococcus aureus*, *Corynebacterium* species including *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Corynebacterium tenuis* and *Corynebacterium minutissimum*. Included in this group are aerobic diphtheroids. This is a group of Corynebacterium commonly regarded as responsible at least in part for body odour.

Optionally, the existing population of skin microflora is reduced prior to, or simultaneously with treatment using a method of the invention.

The invention also relates to the use of *M. luteus*, or compositions of the invention in the methods discussed above. Particularly, to the use of *M. luteus* in the preparation of medicament for use in treating skin disorders as above including body odour, skin infections (particularly acne), and toe infections.

Although the invention is broadly as described above, it will be appreciated by those persons skilled in the art that it is not limited thereto but also includes embodiments of which the following description gives examples.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is directed in a first aspect to *M. luteus* strain Q24. This *M. luteus* strain was deposited by the assignee under the terms of the Budapest Treaty with Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH, Braunschweig, Germany on 10 March 2005, and assigned Accession No. 17172.

M. luteus is a gram positive spherical saprophytic bacterium. The organism is a natural inhabitant of the human skin, and can occasionally be found in the mucous membranes. It is considered non-pathogenic and can be spread through direct contact. It is common in the environment but survives for only a limited time in soil or water. The species is a non-spore forming, obligate aerobe that produces creamy white to yellow insoluble pigments. A full morphological description is provided in the accompanying examples. Also contemplated herein are *M. luteus* strains having the identifying characteristics of Q24 as set forth in the examples. These strains may be mutants which are natural products or artificially produced by manipulations such as chemical or UV mutagenesis, or genetic modification.

M. luteus Q24 and other *M. luteus* strains having the identifying characteristics thereof are useful for at least inhibiting the growth of bacteria such as *Propionibacterium* species including *Propionibacterium acnes; Staphylococcus* species including *Staphylococcus aureus* (all of 24 tested strains were sensitive including 20 that were methicillin resistant), *Staphylococcus saprophyticus;* and *Staphylococcus simulans; Corynebacterium* species including, *Corynebacterium diphtheriae, Corynebacterium ulcerans, Corynebacterium tenuis, Corynebacterium minutissimum, Streptococcus pyogenes, Streptococcus agalactiae* and *Streptococcus dysgalactiae.* Included in this group are aerobic diphtheroids. This is a group of Corynebacterium commonly regarded as being at least in part responsible for body odour.

Without wishing to be bound by theory, it is currently believed that *M. luteus* serves as an effector strain to replace bacteria involved in causing skin disorders. An effector strain is one which can compete successfully with the disorder-causing organism either via

competitive action (eg for attachment sites; or inhibition by other metabolism-associated by-products; or a combination thereof).

The *M. luteus* of the invention exhibit broad spectrum antibacterial activity. The *M. luteus* are therefore useful as an antibacterial agent *per se* as well as therapeutically. The *M. luteus* are also useful as an antifungal agent *per se*. In this context, "therapeutic" includes prophylactic treatment. Therapeutic uses include the treatment or prevention of bacterial infections, particularly *Staphylococcus*, *Streptococcus*, *Propionibacterium*, and *Corynebacterium* infections. The *Micrococcus luteus* of the invention are particularly suitable for use against the bacteria *S. aureus*, *P. acnes*, *Corynebacterium minutissimum* and *S. pyogenes* Conditions amenable to treatment with the strains or compositions of the invention include skin infections (including acne), toe infections, and body odour.

Common skin disorders and the organisms which are at least in part causative of the disorder are as follows:

Table A

Disorder	**Bacteria**
Impetigo	*Streptococcus pyogenes* and/or *Staphylococcus aureus*
Erysiphelas	*Streptococcus pyogenes*
Folliculitis	*Staphylococcus aureus*
Boils	*Staphylococcus aureus*
Carbuncles	*Staphylococcus aureus*
Acne	*Propionibacterium acnes*
Pitted Keratolysis	Coryneform bacteria/Aerobic diphtheroids
Intertrigo[1]	Overgrowth of resident and transient bacteria
Erythasma	*Corynebacterium minutissimum*
Trichomycosis	*Corynebacterium tenuis*
Toe web infection[2]	Coryneform bacteria/aerobic diphtheroids
Body odour	Aerobic diphtheroids

Tinea[3]	*Staphylococcus* species and *Streptococcus* species
Mastitis[4]	*Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalatiae*

[1]Intertrigo is polymicrobial disorder like many skin diseases the infection often results from infection by normal commonsal organisms of the skin. Resident and transient bacteria most usually include *Staphylococcus* species, *Streptococcus* species *Propionibacteria* species, aerobic diphtheroids and some *Candida* species.

[2] Toe web infection

A polymicrobial infection involving coryneform bacteria aerobic diphtheroids, Brevibacterium and Gram-negative rods

[3] Tinea is a polymicrobial infection usually involving dermatophyte fungi such as *Trichophyton*, *Epidermophyton* and *Microsporum*. Secondary bacterial infections are also commonly implicated in Tinea's. Causative organisms include *Staphylococcus* species, *Streptococcus* species, *Pseudomonas*, and *Corynebacterium minutissimum*. (See *Gupta AK et.*, Dermatology Clinics vol 21; p431-62, 2003 Treatments of Tinea pedis).

[4] Mastitis is also a polymicrobial infection. Key causative organisms include *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Escherischia coli*, and *Klebsiella pneumoniae*.

The term "skin disorders" as used herein is therefore to be broadly understood as encompassing bacterial diseases of the skin, and mucosa. caused at least in part by one or more bacteria of the genera *Staphylococcus*, *Streptococcus*, *Corynebacterium*, and *Propionibacterium* or by bacteria of the group aerobic diphtheroids.

Specific skin disorders herein are those caused at least in part by *S. saprophyticus, S. simulans, S. aureus, S. pyogenes, S. agalactiae, S. dysgalactiae, C. diphtheriae, C. ulcerans, C. minutissium, C. tenuis and P. acnies.*

For treatment of skin disorders, topical therapeutic formulations are particularly useful. The term "topical" refers to compositions suitable for application to skin or mucosal surfaces of the body. Mucosal surfaces include the nasal cavity.

A "therapeutic formulation" is a formulation appropriate for administration of an *M. luteus* strain to an individual in need of same, particularly an individual susceptible to skin disorders. In general, therapeutic formulations of the invention are composed of an *M. luteus* strain of the invention and an acceptable carrier, diluent and/or excipient.

An "acceptable carrier, diluent and/or excipient" means a vehicle for delivery of a *M. luteus* strain of the invention, to the individual, in which the vehicle is compatible with bacterial cell viability. Acceptable carriers suitable for use in the administration of viable *M. luteus* strains of the invention are well known to those skilled in the art. Suitable carriers are generally inert and can be either solid or liquid.

In one embodiment, the carrier is a pharmaceutically acceptable carrier. Pharmaceutically acceptable carriers suitable for use with the *M. luteus* strains herein include, but are not limited to buffered saline solutions (e.g., phosphate-buffered saline), pharmaceutically acceptable culture media (e.g. TSB), or other solutions which maintain the viability of the bacterium. Additionally, such pharmaceutically acceptable carriers may be non-aqueous solutions, suspensions, and emulsions. A variety of pharmaceutically acceptable carriers suitable for administration of viable or lyophilized bacteria are well known in the art (see, for example, *Remington's Pharmaceutical Sciences*, 18th ed., Gennaro, ed., 1990, Mack Publishing Co., Easton, Pa., incorporated herein by reference. Suitable solid carriers known in the art include, for example, magnesium carbonate; magnesium stearate; celluloses; talc; sugars such as fructose, sucrose, dextrose, trehalose, mannitol, lactose; starches; and flours; but are not limited thereto.

Oleaginous carriers suitable for use in the compositions of the invention include glycerol, mineral oils, essential oils, fats, fatty acids and esters thereof, glycerides, propylene glycol, lanolin, and derivatives, lecithin and derivatives, white petrolatum petroleum jelly, emulsions formed from oil(s) and water, and may be mixed to form liquids, gels, creams,

emulsions, pastes, suspensions, semi-solids, solids or aerosols amongst others. Detergents and surfactants such as Tween 80 may also be added.

Currently preferred for use are oils and fats such as cocco butter, shea butter, grapeseed oil and chamomile oil.

Phase formulations including aqueous and oil phases with the *M. luteus* or composition of the invention in an oil phase are also feasible. In one embodiment the phase formulation is a two phase formulation with one oil and one aqueous phase.

The compositions may also include excipients such as known art preservatives; thickening agents; opacifiers; binders; antioxidants; emulsifiers; buffers; colourings; anti-caking agents; fillers; mineral salts; essential oils; botanical extracts; and fragrances as appropriate. Nutrients (for example carbohydrates such as xylitol, lactose and maltose or the like, and/or proteins such as casein) to maintain viability of *M. luteus* may also be included. Emollients to improve cosmetic properties and facilitate application of the composition can also be included. Examples of emollients are silicones such as DC246 and DC556 (Dow Corning, USA), fatty acid esters such as Esto/RTM1517 (Unichem) but are not limited thereto. The carriers and excipients selected must not significantly affect the antibacterial, activity of the *M. luteus*.

A currently preferred composition includes a salt such as rock salt or sodium chloride but not limited thereto. Because many bacteria and fungi involved in skin disorders are salt sensitive, the inclusion of salt in the composition also helps to reduce the bacterial populations on the skin. nails or mucosa. This allows for more effective colonisation by the *M. luteus* strain.

Salt is most usually included at a concentration of 1 to 10%, preferably 3 to 7%, and more preferably 5% by weight of the composition

The *M. luteus* strains of the invention can be formulated in any of a variety of compositions suitable for topical administration, including mucosal administration. For

example, the *M. luteus* strains can be formulated for administration as a lyophil or cell paste prepared from a *M. luteus* culture, or can be directly administered to the site of the skin disorder. The strain can also be administered in the form of a cream, gel, emulsion, oil, paste, lotion, wash, suspension, spray (including nasal spray), powder, stick, roll-on or aerosol, solid or semi-solid but the forms are not limited thereto.

For treatment of body odour, roll-on powder, aerosol or stick deodorant formulations are feasible. Currently preferred for use are stick formulations. All formulations can be readily produced according to known art techniques. For example a deodorant stick may be produced by melting cocco and shea butter, and mixing in freeze-dried *M. luteus* powder. The mixture is then poured into a deodorant stick container and cooled until solid.

For acne treatment the *M. luteus* can be a component of a face wash, soap, lotion, cream unguent gel, emulsion or the like. The *M. luteus* may conveniently form part of an existing skin treatment regime product. For example, a face wash, cleanser or moisturiser.

For skin infections including tinea the *M. luteus* can be formulated as a powder, oil, wash, cream, soap, ungent lotion, or spray (including nasal sprays).

Formulations such as bath oils, and soaps are useful for treating skin infections identified herein.

For general antimicrobial use, formulations may also be produced for other methods of administration including transdermal administrable formulations, but not limited thereto.

The *M. luteus*, compositions and formulations of the invention may also be topically administered indirectly, such as in material for contacting the skin or mucosa. For example, in nappies, wet wipes, sanitary pads, clothing articles and the like. The *M. luteus* can be applied to the material by known art techniques such as spraying and drying.

The formulations and compositions of the invention may further comprise one or more secondary antibacterial agents. These secondary agents may, for example, be antibiotics,

or other antibacterial agents or antibacterial producing microorganisms. Useful antibacterials include bacteriocin-like inhibiting substances (BLIS) such as nisin, epidermin and salivaricins A, A_1, A_2 and B for example. Other antibacterial compounds such as potassium alum may also be included. Any antibacterial must also be compatible with *M. luteus* viability. The secondary antibacterial may be included at a concentration of 1 to 20%, commonly 3 to 15%, preferably 4 to 10%, more preferably 1 to 9%, by weight of the composition and even more preferably 7.5%.

The *M. luteus* comprise about 0.01% to about 99% by weight of the final composition, commonly 0.05 to 50%, preferably 0.075 to 20%, more preferably 0.1 to 10% by weight of the composition or formulation suitable for topical administration.

In the treatment of skin disorders, *M. luteus* strains of the invention can be administered to any susceptible individual.

The term "individual" as used herein includes humans, horses, dogs, cats, pigs, sheep, cattle, goats but is not limited thereto. Preferably, the individual is a human. The *M. luteus* strains can be administered to the individual at any age, e.g. childhood, adolescence, or adulthood.

The *M. luteus* of the invention can be administered in a variety of ways. For example, in the form of compositions or formulations discussed above, or as suspensions, sustained release formulae or lyophil powders. The *M. luteus* strains can also be administered by direct application of a lyophil, culture, or cell paste to the affected skin, nail or mucosal surface of the individual. Any mode of administration is suitable as long as the therapeutic formulation is applied to the skin, or mucosa.

In general, the amount of *M. luteus* administered to the individual will be an amount effective for replacement of skin disorder causing bacteria or fungi on the skin of the individual. "An amount effective for replacement of skin disorder causing bacteria on the skin of the individual means an amount effective for skin colonisation by the *M. luteus* strain, and significant reduction of the resident skin disorder-causing bacteria (e.g. by

competition between the bacteria for attachment sites, nutrients and/or by antibacterial action).

The term "unit dose" when used in reference to a therapeutic formulation of the present invention refers to physically discrete units suitable as unitary dosage for the individual, each unit containing a predetermined quantity of active material (viable *M. luteus*) calculated to produce the desired therapeutic effect in association with the required diluent, carrier, or excipient.

Specific dosages can vary widely according to various individual variables including size, weight, age, disease severity (e.g. the tenacity and/or number of skin disorder causing resident bacteria, or fungi) and responsiveness to therapy (e.g. the susceptibility of the individual's skin to colonisation). Methods for determining the appropriate route of administration and dosage may be determined by the consumer as they deem appropriate, or on a case-by-case basis by an attending doctor, pharmacist, or other clinician. Such determinations are routine to one of ordinary skill in the art (see for example, *Remington's Pharmaceutical Sciences*, 8th ed., Gennaro, ed., Mack Publishing Company, Easton, Pa., 1990).

In general, the number of *M. luteus* administered to the individual will range from about 10^2 to 10^{15} bacteria, preferably from about 10^3 to 10^{10} bacteria, more preferably from about 10^4 to 10^8 bacteria, normally about 10^6 to 10^7 colony forming units (CFU) per dose.

Multiple doses of the *M. luteus* strain can be administered to achieve colonisation and replacement of the resident, skin disorder causing bacteria or fungi. The *M. luteus* strains may need to be administered to the patient once only or repeatedly. Repeat treatments may be once a month, once a week, once a day, two or three times a day, or as may otherwise be required. Conveniently, the administration may be effected as part of the patient's routine grooming.

For treatment of body odour the *M. luteus* or composition of the invention should be applied to affected body parts such as axilla, groin, feet and skin folds. Most conveniently application is made after showering.

Acne treatment is most commonly required on the face. Applications of *M. luteus* may be in the form of a face wash, cleanser, moisturiser or similar used in routine grooming, or may be applied in the form of a cream or the like.

Skin infections can affect a variety of surfaces and body parts including skin folds. Tinea commonly occurs on the feet *(Tinea pedis)*, groin *(Tinea cruris)*, body *(Tinea corporis)*, toenails *(Tinea unguium)*, or scalp *(Tinea capitis)* As discussed above Tinea is a polymicrobial skin infection. Athlete's foot is usefully treated by direct application of the organism or composition of the invention to the affected area. Oils and powders are particularly useful for this purpose.

Many infections also arise at sites of trauma, for example scratches, grazes and cuts. These trauma sites allow colonisation by normal commensal organisms of the skin. Common skin infectious agents treatable using *M. luteus* or compositions of the invention are listed above and include *S. pyogenes, S.aureus, P. acnes,* and aerobic coryneforms.

Staphylococcus aureus (including methicillin resistant strains) are commonly carried on the skin and in the nasal passages and lungs. Nasal sprays of the invention can be used to treat or eliminate the carriage of *S. aureus* and similar pathogens. Therapeutic treatment of health and food workers to eliminate resistant *S. aureus* from skin, and nasal passages is desirable to prevent spread of infection.

Mastitis involves mammary gland infection by skin bacteria. Prevention or treatment of mastitis is usefully achieved by teat or nipple washes.

To facilitate colonisation, in one embodiment the treatment method of the invention includes a preliminary step of pre-treating the individual to at least reduce the normal microflora present on the skin surface. This pre-treatment may be as simple as carrying

out normal grooming procedures such as washing with soap and water, or using a salt scrub, showering, skin cleansing, and usual treatments for acne. *M. luteus* of the invention is then administered to the depopulated environment to repopulate same.

Successful colonisation of the individual's skin by the *M. luteus* strain can be established by culturing the bacteria of the individual's skin, and identifying the *M. luteus* using methods well known in the art for bacterial strain identification such as 16 sRNA identification.

The methods and uses of the invention may further comprise the use of one or more secondary antibacterial agents, as discussed above.

The *M. luteus* and compositions of the invention may also be used in conjunction with existing treatment products such as acne treatment products, deodorants and antiperspirants, cleansers, toners and moisturisers but not limited thereto.

Where the term comprise, comprises, comprised or comprising are used in this specification, they are to be interpreted as specifying the presence of the stated features, integers, steps or components referred to, but not to preclude the presence or addition of one or more other features, integers, steps, components or groups thereof.

Various aspects of the invention will now be illustrated in a non-limiting way by reference to the following experimental section.

EXAMPLES

Example 1

Isolation and Characterisation of *Micrococcus luteus* Q24

M. luteus strain Q24 was isolated from the skin of a healthy adult male subject and cultured into blood agar plates. The plates were incubated at 35-37°C, 5% CO_2 in air.

Comparison of the amplified 16S rRNA variable gene region with data bases established the organism to be *Micrococcus luteus*. Its appearance on blood agar is consistent with *Micrococcus luteus*. Individual colonies are convex, circular, entire, smooth and become creamy-yellow-pigmented on prolonged incubation. Gram-stained appearance was of Gram-positive cocci (1 micrometre diameter) in irregular clumps.

Physiological and Biochemical Characteristics of *M. luteus* Q24

The biochemical characteristics were determined using the ID32 Staph and API 50 CH kits (bioMérieux).

Pigmentation	yellow
Urease	positive
Nitrate reduction	negative
Acetoin production	negative
Novobiocin sensitivity	sensitive
Esculin hydrolysis	negative
Casein hydrolysis	positive
Fermentation:	
Glycerol	negative
Erythritol	negative
D-Arabinose	negative
L-Arabinose	negative
D-Xylose	negative
Adonitol	negative
α-Methyl-xyloside	negative
Galactose	negative
D-Glucose	negative
D-Fructose	negative
L-Sorbose	negative
Maltose	negative
Lactose	negative
Trehalose	negative
D-Mannose	negative
Raffinose	negative
Mannose	negative
Mannitol	negative
Ribose	negative
Dulcitol	negative
Inositol	negative
Sorbitol	negative
Saccharose	negative
N-acetylglucosamine	negative
D-Turanose	negative
Arabinose	negative
Cellobiose	negative
α-Methyl-D- mannoside	negative

α-Methyl-D-glucoside	negative
Amygdaline	negative
Salicin	negative
Melibiose	negative
Inulin	negative
Melezitose	negative
Amidon	negative
Glycogen	negative
Xylitol	negative
β-Gentiobiose	negative
D-Tagatose	negative
D-Fucose	negative
L-Fucose	negative
D-Arabitol	negative
L-Arabitol	negative
Gluconate	negative
2 ceto-gluconate	negative
5 ceto-gluconate	negative
β-Galactosidase	negative
Arginine phosphatase	positive
Pyrrolidonyl acrylamidase	negative
β-Glucouronidase	negative
Arginine dihydrolyase	negative
Ornithine decarboxylase	negative

Inhibitory activity of *Micrococcus luteus*

A. The ability of *M. luteus* strain Q24 to inhibit bacteria associated with skin disorders was assessed in a deferred antagonism test against nine standard indicator strains.

The P-typing test involves first growing the test strain on blood agar as a diametric streak culture. After removing this growth, the agar surface is sterilized with chloroform vapour, aired and the 9 standard indicator bacteria (set out in table 1) are cross-streaked across the line of the original test strain inoculum. Following incubation, interference with growth of the indicators in the vicinity of the original producer streak is taken as indicative of inhibitory activity. Relative zone size is indicated qualitatively on a scale of +-(reduction in growth on indicator in a zone approximately the width of the original producer streak) to +++ (Clear inhibition zone three times the width of the original producer streak).

The results are given below in Table 1.

Table 1

Indicator designation	Strain specification	Activity
I1	*Micrococcus luteus* strain T-18	+++
I2	*S. pyogenes* (Group-A)[2] strain FF22, M-type 52, T-pattern 3/13	++
I3	*S. anginosus* (Group-F) strain T-29	+
I4	*S. uberis* (Group-E) strain T-6, (ATCC 27958)	+
I5	*S. pyogenes* (Group-A) strain 71-679, M-type 4, T-pattern 4	++
I6	*Lactococcus lactis* (subspecies lactis) (Group-N) strain T-21	+++
I7	*S. pyogenes* (Group-A) strain 71-698, M-type 28, T-pattern 28	++
I8	*S. pyogenes* (Group-A) strain W-1,, M-type M87, T-pattern 6	+
I9	*S. equisimilis* (Group-C) strain T-148	++

[1] Tagg and Bannister "Fingerprinting" beta-haemolytic streptococci by their production of and sensitivity to bacteriocine-like inhibitors. *J Med Microbiol* **12,** 397-411.
[2] Lancefield group designation

The table 1 shows a P-type 777 pattern signifying inhibitory activity against all nine indicators. Activity was particularly strong against a *Micrococcus* strain, *S. pyogenes*, *L. lactis* and *S. equisimilis*.

By using this deferred antagonism test, the inhibitory spectrum of *M. luteus* Q24 was further assessed and the results are shown in Table 2.

Table 2. Activity against additional potential indicator strains

Species	**Number Tested**	**Sensitive to *M. luteus* Q24**
Staphyococcus aureus *	24	24
Staphylococcus simulans	1	1
Staphylococcus xylosus	1	1
Staphylococcus saprophyticus	1	1
Staphylococcus carnosus	1	1
Staphylococcus cohnii	1	0

Streptococcus mutans	9	0
Streptococcus dysgalactiae	3	3
Streptococcus salivarius	10	0
Streptococcus agalactiae	3	3
Corynebacterium minutissimus	1	1
Corynebacterium diphtheriae	1	1
Corynebacterium ulcerans	1	1
Lactobacillus casei	1	1
Lactobacillus acidophilus	1	1
Micrococcus lysodiekticus	1	1
Kocuria varians (variacin producer)	1	0
Enterococcus faecalis	3	1
Candida albicans	4	0
Prevotella intermedia	2	2
Porphyromonas gingivalis	2	2
Propionibacterium acnes	1	1
Propionibacterium propionicus	1	1
Pseudomonas aeruginosa	1	0
Micrococcus luteus Q24 (Producer strain)	1	0

* strains tested included 20 methicillin resistant strains.

Example 2

A. Topical Application to Prevent Body Odour

A saline suspension of *M. luteus* Q24 with a concentration of approximately 1 x 10^6 CFU per dose was inoculated by swabbing one axilla of each of several test subjects after showering.

The inoculated strain has been shown to persist for at least 24 hours. Subjective comparison of the body odour of the two axilla by the subjects and by "blinded"

assessors found the Q24 inoculated axilla to be relatively odour free when compared with the control axilla.

B. Effect of *M. luetus* Q24 on axilla odour

Deodorant Stick formulation

Cocco butter	16 g
Shea butter	12 g
Potasium alum	2.3 g
Q24 freeze-dried powder	0.04 g

The deodorant stick was prepared by melting cocco and shea butter at 40°C. *M. luteus* Q24 freeze-dried powder was mixed with the molten butter and poured into a deodorant stick container. The mixture was cooled at 4°C until solid.

The Q24 cell count for the deodorant stick was 5×10^6 cfu/g

The subject had a shower as per usual and then applied the Q24 deodorant stick to the left axilla. The right axilla was used as a control. A cotton swab was soaked in sterile saline/1% Tween 80 and used to swab the axilla region. The swab sample was resuspended in 1 ml saline/1% Tween 80. Ten fold dilutions of the sample were spiral plated onto Blood agar plates or Corynebacterium isolation medium (Columbia blood agar base 22 g, Calcium carbonate 0.5 g, Lecithin 0.5 g, Tween 80 2.5 ml, Human blood agar 20 ml, sodium tellurite 10 ml, distilled water 500 ml). The plates were incubated at 37°C, 5% CO_2 in air. Staphlococci counts were determined from the Blood agar plates after 24 hour incubation and the corynebacterial counts on the selective media after 2 days.
Body odour was self assessed by smelling their own axilla (0 – no odour, 1 slight odour, 3- strong odour, 5- very strong odour).

Table 3. Effect of *M. luteus* Q24 on staphylococcus and corynebacterial axilla populations.

Time (hours)	Staphylococcus counts		Corynebacterium counts	
	Left axilla	Right axilla	Left axilla	Right axilla
0	1.6×10^5	3.4×10^5	3.8×10^3	4.5×10^3
7	8.2×10^4	6.4×10^5	9.0×10^2	3.5×10^4
24	1.0×10^5	4.2×10^6	3.3×10^3	8.2×10^4

Table 4. Effect of M. luteus on axilla odour

Time (hours)	Odour score	
	Left	Right
0	0	0
7	0	3
24	1	5

The *M. luteus* Q24 had a slight effect on the staphylococcus cell counts while there was a 0.6 log reduction in the corynebacterial cell counts at 7 hours (Table 3). The odour score on the control axilla increased over 24 hours while the treated axilla only slightly increased (Table 4).

These results confirm the earlier assessment that Q24 is effective in reducing body odour. This is believed to be by action against the aerobic diphtheroids commonly implicated in body odour.

Example 3

Effect of *M luteus* Q24 on Athlete's Foot

Formulation:

Grapeseed oil	2.0 g
Chamomile oil	0.06 g
Q24 freeze-dried powder	0.1 g

The oil formulation was prepared by mixing *M. luteus* freeze-dried powder with the oils to produce a suspension formulation.

The Q24 cell count for the deodorant stick was 1.2×10^7 cfu/g.

The formulation was applied to the infected area of five subjects with athlete's foot daily for three days. Within 10 minutes the itchy symptoms had disappeared. After three days no further application was required due to cessation of the signs of infection.

All references including patents and publications cited in this specification are incorporated herein by reference.

WHAT WE CLAIM IS:

1. A biologically pure culture of *M. luteus* strain Q24 on deposit at Deutsche Sammlung von Mikroorganisms Und Zellkulturen GmbH, Braunschweig, Germany, under accession number DSM 17172, or a culture having the identifying characteristics thereof.

2. A composition comprising an *M. luteus* strain according to claim 1 together with a diluent, carrier and/or excipient.

3. A composition comprising a strain of *M. luteus* effective to at least inhibit one or more bacteria selected from the group consisting of *Staphylococcus* species, *Propionibacterium* species, *Corynebacterium* species, *Streptococcus* species, and aerobic diphtheroids.

4. A composition comprising a strain of *M. luteus* effective to at least inhibit growth of one or more bacteria selected from the group consisting of *Propionibacterium acnes*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*, *Staphylococcus simulans*, *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Corynebacterium minutissium*, *Corynebacterium tenuis*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, and *Streptococcus dysgalactiae* together with a diluent, carrier and/or excipient.

5. A composition of claim 4 effective to inhibit at least four of the group of bacteria above, preferably eight, and preferably all eleven.

6. A composition of claim 4 wherein the Staphylococcus aureus is methicillin resistant.

7. A composition of any one of claims 3 to 6 wherein the *M. luteus* is strain Q24.

8. A composition of any one of claims 2 to 7 which is formulated for topical administration.

9. A composition of claim 8 which is a wash, cream, lotion, gel, oil, emulsion, unguent, suspension, powder, aerosol spray, nasal spray, roll-on, stick, semi-solid or solid formulation.

10. A composition of any one of claims 2 to 8 which further comprises one or more secondary antibacterial agents.

11. A composition of claim 10 wherein the secondary antibacterial agent is a bacteriocin-like inhibitory substance (BLIS).

12. A composition of claim 11 wherein the BLIS is selected from nisin, epidermin and salivaricin A, salivaricin A_1, salivaricin A_2, and salivaricin B.

13. A composition of claim 10 wherein the secondary antibacterial agent is potassium alum.

14. A composition of any one of claims 2 to 13 which is in unit dosage form.

15. A composition of claim 14 which contains from about 10^4 to 10^8, preferably 10^6 to 10^7 CFU of *M. luteus* per dose.

16. A composition of any one of claim 2 wherein the *M. luteus* comprises 0.01 to 99%, preferably 0.05 to 50%, preferably 0.075 to 20%, preferably 1 to 10% by weight of the composition.

17. A composition of any one of claims 2 to 16 which is a therapeutic formulation.

18. A composition of claim 9 which is a deodorant in the form of a powder, roll on, stick or aerosol spray.

19. A composition of claim 18 which is in the form of a stick deodorant.

20.. A composition of claim 9 which is a skin infection treatment composition in the form of a wash, cream, lotion, gel, oil, emulsion, unguent or suspension.

21. A composition of claim 20 which is an acne treatment composition.

22. A composition of claim 9 which is a tinea treatment composition in the form of a powder, or oil.

23. A composition of claim 9 which is formulated as a nasal spray.

24.. A method for at least inhibiting the growth of bacteria sensitive to *M. luteus*, the method comprising contacting the sensitive bacteria with an inhibitory effective amount of an *M. luteus* strain or a composition of any one of claims 2 to 23.

25. A prophylactic or therapeutic method of treatment for skin disorders in an individual in need thereof, the method comprising administering to said individual an *M. luteus* strain, or a composition of any one of claims 2 to 23 in an amount effective to at least inhibit growth of one or more bacteria causing at least in part the skin disorder, or in an amount to allow effective colonisation of the skin of the individual by the *M. luteus*.

26. A method of controlling the incidence and/or severity of a skin disorder, the method comprising introducing to the skin of the individual an amount of *M. luteus*, or composition of any one of claims 2 to 23, effective to control the incidence or severity of said skin disorder.

27. A method of claim 25 or claim 26 wherein the skin disorder is selected from skin infections, toe infections, and body odour.

28. A method of claim 27 wherein the skin disorder is impetigo, erysipelas, folliculitis, boils, carbuncles, cellulites, acne, pitted leeratolysis, intertrigo, erythraemia, or trichomycosis.,

29. A method of claim 27 wherein the toe and infection is toe web infection or tinea.

30. A method of claim 27 wherein the skin disorder is body odour.

31. A method of any one of claims 25 to 27 wherein the skin disorder is caused at least in part by one or more of *Propionibacterium* species, *Staphylococcus* species, *Streptococcus* species, *Corynebacterium* species, and aerobic diphtheroids.

32. A method of any one of claims 25 to 27 wherein the skin disorder is caused by one or more of *Propionibacterium acnes*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Staphylococcus aureus*, *Staphylococcus saprophytucus*, *Staphylococcus simulans*, *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Corynebacterium minutissimum*, and *Corynebacterium tenuis*.

33. A method of any one of claims 25 to 32 which includes the preliminary step of reducing the existing population of skin microflora.

34. A method of treating body odour in an individual the method comprising applying to affected areas a composition of any one of claims 2 to 9 and 18.

35. A method of treating a skin infection in an individual the method comprising applying to an affected area a composition of any one of claims 2 to 9 and 20.

36. A method of claim 35 wherein the skin infection is acne or mastitis.

37. A method of treating tinea in an individual the method comprising applying to a tinea affected area a composition of any one of claims 2 to 9 and 22.

38. A method of claim 37 wherein the tinea is tinea pedis (athlete's foot).

39. Use of a biologically pure culture of claim 1 in the manufacture of a composition for treatment of skin disorders in an individual in need thereof.

40.. Use of a biologically pure culture of claim 1 in the manufacture of a composition for controlling the incidence and/or severity of a skin disorder in an individual in need thereof.

41. Use of claim 39 or claim 40 wherein the skin disorder is selected from skin infections, toe infections, and body odour.

42. Use of claim 41 wherein the skin disorder is impetigo, erysipelas, folliculitis, boils, carbuncles, cellulites, acne, pitted leeratolysis, intertrigo, erythraemia, or trichomycosis.,

43. Use of claim 41 wherein the toe and infection is toe web infection or tinea.

44. Use of claim 41 wherein the skin disorder is body odour.

45. Use of any one of claims 39 to 41 wherein the skin disorder is caused at least in part by one or more *Propionibacterium* species, *Staphylococcus* species, *Streptococcus* species *Corynebacterium* species, and aerobic diphtheroids.

46. Use of any one of claims 39 to 41 or 45 wherein the skin disorder is caused by one or more of *Propionibacterium acnes*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*, *Staphylococcus simulans*, *Corynebacterium diphtheriae*, *Corynebacterium ulcerans*, *Corynebacterium minutissimum* and *Corynebacterium tenuis*.

47. Use of a biologically pure culture of claim 1 in the manufacture of a composition for treating body odour in an individual in need thereof.

48. Use of a biologically pure culture of claim 1 in the manufacture of a composition for treating a skin infection in an individual in need thereof.

49. Use of claim 48 wherein the skin infection is acne or mastitis.

50. Use of a biologically pure culture of claim 1 in the manufacture of a composition for treating tinea in an individual in need thereof.

51. Use of claim 50 wherein the tinea is *Tinea pedis* (athlete's foot).

52.. Use of a biologically pure culture of claim 1 in the manufacture of a composition for treating a methicillin resistant *S.aureus* infection.

Applicant's or agent's file reference 538871 TVG	International application No. PCT/NZ(PCT/NZ2006/000060)

INDICATIONS RELATING TO DEPOSITED MICROORGANISM OR OTHER BIOLOGICAL MATERIAL

(PCT Rule 13*bis*)

A. The indications made below relate to the deposited microorganism or other biological material referred to in the description on page 2, line 19.

B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet ☐

Name of depositary institution
DSMZ DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH

Address of depositary institution *(including postal code and country)*
Mascheroder Weg 1b, D-38124
Braunschweig
Germany

Date of deposit	Accession Number
10 March 2005	DSM 17172

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* This information is continued on an additional sheet ☐

SEE ATTACHED SHEET 'A'

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

AE; AG; AL; AM; AP; AT; AU; AZ; BA; BB; BE; BF; BG; BJ; BR; BY;; BZ; CA; CF; CG; CH; CI; CM; CN; CO; CR; CU; CY; CZ; DE; DK; DM; DZ; EA; EC; EE; EP; ES; FI; FR; GA; GB; GD; GE; GH; GM; GN; GQ; GR; GW; HR; HU; ID; IL; IN; IT; IS; JP; KE; KG; KP; KR; KZ; LC; KI; LK; LR; LS; LT; LU; LV; MA; MC; MD; MG; MK; ML; MN; MR;M MW; MX; MZ; NE; ML; NO; NZ; OA; PH; PL; PT; RO; RU; SC; SD; SE SG; SI; SK SL; SN; SZ; TD; TG; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VC; VN; YU; ZA; ZM; NW

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application	☐ This sheet was received by the International Bureau on:
Authorized officer Bev Stephens	Authorized officer

C. Additional Indications (continued)

AUSTRALIA
The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations.

CANADA
The applicant hereby requests that, until either a Canadian patent has been issued on the basis of the application or the application has been refused or abandoned and no longer subject to reinstatement, or is withdrawn, the furnishing of a sample of deposited biological material referred to in the application only be effected to an independent expert nominated by the Commissioner of Patents.

CROATIA
The applicant hereby requests that the samples, upon request, be made available between the publication of the application and the granting of the patent to anyone requesting them, or, if the applicant so requests, only to an independent expert, or to, after the patent has been granted, and notwithstanding cancellation or revocation of the patent, anyone requesting them.

DENMARK
The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent and Trademark Office), or has been finally decided upon by the Danish Patent and Trademark Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

EUROPEAN PATENT
In respect of those designations in which a European Patent is sought a sample of the deposited microrganism will be made available until the publication of the mention of the grant of the European patent or until the date on which the application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28(4) EPC).

FINLAND
The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Registration), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

FRANCE
The applicant hereby requests that, until the publication of the grant of the patent, the withdrawal or refusal of the application, the deposited culture shall only be accessible to an expert designated by the applicant.

ICELAND
The applicant hereby requests that, until a patent has been granted or a final decision taken by the Icelandic Patent Office concerning the application which has not resulted in a patent, the furnishing of a sample shall only be effected to an expert in the art.

IRELAND
The applicant hereby requests that, until the preparations for publication of the patent application have been completed by the Comptroller, a sample of the microorganism should be made available only to an expert.

NETHERLANDS
The applicant hereby requests that until the date of grant of a patent or date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in Rule 31F(1) of the Patent Rules only by issue of a sample to an expert.

NORWAY
The applicant hereby requests that, until the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

SINGAPORE
The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert.

SPAIN

The applicant hereby requests that until the date of grant of a patent or date on which the application is refused or withdrawn or lapsed, the biological material shall be made available as provided in Article 45 SPL only by issue of a sample to an expert.

SWEDEN
The applicant hereby requests that, until the application has been laid open for public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM
The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert.

OTHER NOMINATED DESIGNATIONS

Where such provisions exists, the applicant hereby requests that, until the publication or grant of a patent, the withdrawal or refusal of the application, the deposited culture shall only be effected to an expert in the art.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ2006/000060

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl.

C12N 1/00 (2006.01) ***A61P 31/04*** (2006.01) ***A61K 35/74*** (2006.01) ***A61P 31/04*** (2006.01)
A61K 8/99 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPIDS, CAPLUS, MEDLINE, BIOSIS, BIOTECHABS (Skin, Disorder, Diseas?, Bacteri?, Infect?, Prohibit?, Inhibit?, Treat?, Prevent?, Anti(W)Microbial, Luteus, DSM17172, Micrococcus(W)Luteus, Acne, Tinea, Mastitis, Body()Odour)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Bibel D J et. al., "Inhibition of diptheroid esterase by *Micrococcus luteus*". Canadian Journal of Microbiology, October 1977, **23**(10), pg 1319-1326 See whole document	3-5, 8-38
A	DE 10027928 (SIEMENS P M et al) 3 January 2002 See whole document especially Abstract and Page 2	1-52
A	WO 1997 048408 (NOVARTIS AG) 24 December 1997 See whole document especially Abstract and Pages 3 and 7	1-52

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 June 2006	30 JUN 2006
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer **David Olde** Telephone No : (02) 6283 2569

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ2006/000060

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO1995 030751 (CIBA-GEIGY AG) 16 November 1995 See whole document especially Abstract and Pages 3 and 4	1-52
A	Cleveland R F et. al., "Inhibition of Bacterial Wall Lysins by Lipoteichoic Acids and Related Compounds". Biochemical and Biophysical Research Communications, 1975, **67**(3), pg 1128-1135 See whole document	1-52

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/NZ2006/000060

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
WO	1995 030751	AU	24086/95	CA	2186621	EP	0759077
WO	1997 048408	AU	33410/97	BR	9709812	CA	2251779
		CN	1222081	EP	0934075	US	6187800
DE	10027928	NONE					

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX