

COMMONWEALTH of AUSTRALIA

PATENTS ACT 1952

APPLICATION FOR A STANDARD PATENT

617812

We, **INTERFACE RESEARCH CORPORATION**, of 100 Galleria Parkway, Suite 1875, Atlanta, Georgia 30339, **UNITED STATES OF AMERICA**

hereby apply for the grant of a Standard Patent for an invention entitled:

"BIOCIDAL DELIVERY SYSTEM AND METHOD OF PREPARATION THEREOF"

which is described in the accompanying complete specification.

Details of basic application(s):-

<u>Number</u>	<u>Convention Country</u>	<u>Date</u>
190,370	United States of America	5 May 1988

We request that the patent may be granted as a patent of addition to Patent No. 589,142 (49658/85) in the name of **INTERFACE RESEARCH CORPORATION**. We request that the term of the patent of addition be the same as that for the main invention or so much of the term of the patent for the main invention as is unexpired.

The address for service is care of **DAVIES & COLLISON**, Patent Attorneys, of 1 Little Collins Street, Melbourne, in the State of Victoria, Commonwealth of Australia.

Dated this 19th day of March, 1991.



(a member of the firm of **DAVIES & COLLISON**
for and on behalf of the Applicant).

To: **THE COMMISSIONER OF PATENTS**

Davies & Collison, Melbourne and Canberra

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

DECLARATION IN SUPPORT OF CONVENTION OR NON-CONVENTION APPLICATION FOR A PATENT OF ADDITION

Insert title of invention.

In support of the Application made for a patent ^{of addition} for an invention
entitled: "Biocidal delivery system and method of
preparation thereof"

Insert full name(s) and address(es)
of declarant(s) being the appli-
cant(s) or person(s) authorized to
sign on behalf of an applicant
company.

I
~~WE~~ David W. Porter
of Interface Research Corporation
of 100 Galleria Parkway, Suite 1875
Atlanta, Georgia 30339
United States of America

Cross out whichever of paragraphs
or 1(b) does not apply
1(a) relates to application made
by individual(s)
1(b) relates to application made
by company; insert name of
applicant company.

do solemnly and sincerely declare as follows:-

1. (a) ~~I am the applicant~~ ~~XXXXXX~~
~~We are~~
or (b) I am authorized by

Interface Research Corporation

Cross out whichever of paragraphs
2(a) or 2(b) does not apply
2(a) relates to application made
by inventor(s)
2(b) relates to application made
by company(s) or person(s) who
are not inventor(s); insert full
name(s) and address(es) of inven-
tors.

the applicant..... for the patent ^{of addition} to make this declaration on ^{its} behalf.

2. (a) ~~I am the actual inventor~~ ~~XXXXXX~~
~~We are~~
or (b) 1. Robert H. MCINTOSH Jr. of
1820 Kello Drive, Greensboro, NC, 27405
2. Albin F. TURBAK of 7140 Brandon Mill
Road, N.W., Sandy Springs, GA, 30328
3. Robert H. MCINTOSH Sr. of
1710 Hobbs Road, Greensboro, NC, 27403

All of United States of America

~~are~~ the actual inventor(s)..... of the invention and the facts upon which the applicant.....
is
~~are~~ entitled to make the application are as follows:-

State manner in which applicant(s)
derive title from inventor(s)

The actual inventors assigned the invention
to the said applicant.

Cross out paragraphs 3 and 4
for non-convention applications.
For convention applications,
insert basic country(s) followed
by date(s) and basic applicant(s).

3. The basic application..... as defined by Section 141 of the Act ^{was} made
in United States of America ^{on the} 5 May 1988
by Robert H. MCINTOSH Jr, Albin F. TURBAK and
in Robert H. MCINTOSH Sr.
by
in
by on the

4 The basic application..... referred to in paragraph 3 of this Declaration ^{was}
the first application..... made in a Convention country in respect of the invention the subject
of the application.

Insert place and date of signature

Declared at *Atlanta, Ga. USA* this *6th* day of *January, 1990*

Signature of declarant(s) (no
attestation required)

David W. Porter
David W. Porter
Vice President and General Counsel

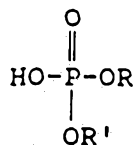
Note Initial all alterations

DAVIES & COLLISON, MELBOURNE and CANBERRA.

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- (57) Claim

1. A biocidal composition comprising
- (a) an inert carrier selected from the group consisting of diatomaceous earth, attapulgite clay, colloidal silica, zeolite, protein, polysaccharide, collagen, chitin, chitosan and gelatin; and
- (b) a biocidally effective amount of a phosphate ester having the general formula:



wherein R and R' are selected from the group consisting of alkyl, aryl, aralkyl and alkaryl groups, one or R or R' can be H, and
the phosphate ester is bound to the carrier.

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(21) International Application Number: PCT/US89/01955 (22) International Filing Date: 4 May 1989 (04.05.89) (30) Priority data: 190,370 5 May 1988 (05.05.88) US (71) Applicant: INTERFACE RESEARCH CORPORATION [US/US]; 100 Galleria Parkway, Suite 1875, Atlanta, GA 30339 (US). (72) Inventors: MCINTOSH, Robert, H., Jr. ; 1820 Kello Drive, Greensboro, NC 27405 (US). TURBAK, Albin, F. ; 7140 Brandon Mill Road, N.W., Sandy Springs, GA 30328 (US). MCINTOSH, Robert, H., Sr. ; 1710 Hobbs Road, Greensboro, NC 27403 (US).		(74) Agents: PABST, Patrea, L. et al.; Kilpatrick & Cody, 100 Peachtree Street, Suite 3100, Atlanta, GA 30303 (US). (81) Designated States: AT (European patent), AU, BE (European patent), BR, CH (European patent), DE (European patent), DK, FI, FR (European patent), GB (European patent), IT (European patent), JP, KR, LU (European patent), NL (European patent), NO, SE (European patent). Published <i>With international search report.</i>
(54) Title: BIOCIDAL DELIVERY SYSTEM AND METHOD OF PREPARATION THEREOF (57) Abstract A biocidal phosphate ester in combination with an inert inorganic or organic particulate or polymeric carrier. The biocidal-carrier composition is useful in extending the effective lifetime of the biocidal phosphate ester when incorporated into a variety of materials including plastics, fibrous materials, and solutions. Applications of the disclosed carrier compounds include preparation of mildew resistant paints and plastics having extended antimicrobial properties despite extensive washing and wear of the surface.		

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**BIOCIDAL DELIVERY SYSTEM
AND METHOD OF PREPARATION THEREOF**

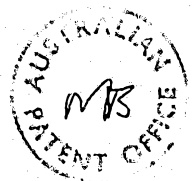
Technical Field

The present invention relates to biocidal
5 compositions and methods for their delivery.

Background

~~This application is a continuation-in-part to
U.S. Serial No. 047,561, filed April 27, 1987,
entitled "Microbiocidal Composition and Method of
10 Preparation Thereof" by Robert H. McIntosh, which is a
continuation-in-part of U.S.S.N. 781,710 filed October
2, 1985; U.S.S.N. 635,728 filed October 9, 1984, now
abandoned; U.S.S.N. 713,445 filed March 19, 1985, now
abandoned; U.S.S.N. 736,652 filed May 21, 1985, now
15 U.S. Patent No. 4,647,601; U.S.S.N. 744,730 filed June
13, 1985, now abandoned; all of which are
continuations-in-part of U.S.S.N. 570,952 filed March
8, 1984, a continuation of U.S.S.N. 523,734 filed
August 16, 1983, now abandoned, which is a
20 continuation of U.S.S.N. 226,006 filed January 19,
1981, now abandoned, which is a continuation of
U.S.S.N. 930,879 filed August 4, 1978, now abandoned.~~

Bacteria, fungi, viruses, algae and other
microorganisms are always present in our environment.
25 Such microorganisms are frequently an essential part
of ecological systems, industrial processes, and
healthy human and animal bodily functions, such as
digestion. In other instances, however,
microorganisms are highly undesirable as a cause of
30 illness, odors and damage or destruction of a wide
variety of materials.



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The species and numbers of microorganisms present vary depending on the general environment, on the nutrients and the moisture available for the growth of the microorganisms, and on humidity and temperature of the local environment. Nutrients for microorganisms abound in the normal environment. Furthermore, many materials, including plastic coatings and objects, wood, paper and other natural fibers can serve as nutrients for microorganisms which will degrade those materials. In addition, certain bacteria are capable of remaining viable in a dormant state on floors or on objects for long periods of time until they are deposited in the proper media for growth. Consequently, potentially harmful microorganisms can be transported merely by walking on floors, brushing against walls or furniture or by handling objects.

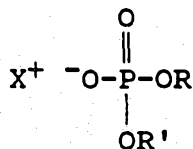
It is well recognized that a major difficulty in health care facilities is the spread of infectious diseases caused by a wide variety of microorganisms. The problem is exacerbated in these facilities because many of the patients are in a weakened condition or immunosuppressed. One of the most common means by which these organisms are spread is health care personnel. Another important source of infection are the floors, furniture and other plastic objects routinely used in these settings. Conventionally, the plastic products in these facilities are periodically cleaned with strong disinfecting cleansers to remove or kill accumulated microorganisms. Between cleanings, however, it is possible for the plastic products to constitute a major vector for cross-infection or spread of infectious diseases.

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Pathogenic microorganisms can also be deposited on fabrics such as towels, clothes, laboratory coats and other fabrics where they remain viable for long periods of time. When the microorganisms grow on or in a plastic product, fiber, or fabric, they form unsightly colonies and can eventually break down the plastic, fiber, fabric, or other material. Washing with conventional detergents does not always kill or remove the microorganisms.

The control of microbial growth is a major problem in both industry and the home. It has proved difficult, however, to develop a microbiocidal composition that is effective in controlling the growth of a wide variety of unwanted microorganisms and is, at the same time, safe for use around human beings and animals. Another difficulty is the extreme variability of response of various microorganisms to conventional microbiocidal agents. Even within bacteria, Gram-negative and Gram-positive bacteria respond differently to antibiotics. Further, the antibiotics that are effective against procaryotic organisms are usually ineffective against eucaryotic microorganisms such as fungi and yeasts.

U.S. Serial No. 047,561 entitled "Microbiocidal Composition and Method of Preparation" filed April 27, 1987 by Robert H. McIntosh disclosed a broad spectrum, safe, biocidal composition having the following general formula:



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wherein R and R' are an alkyl, aryl, aralkyl or alkaryl group, one of R or R' can be H, X is a Group I metal ion, Group II metal ion, transition metal ion, or an organic ion such as an ammonium ion, and there is at least one free hydroxyl group. Examples of the alkyl, aryl, aralkyl and alkaryl include straight chains, branched chains or cyclic alkyl groups having from 2 to 24 carbon atoms, polyoxyethylene or polyoxypropylene having from 2 to 12 ethylene oxide or propylene oxide units respectively, alkyl phenoxy polyoxyethylene containing from 2 to 12 ethylene oxide units, alkyl phenoxy polyoxyethylene containing ethylene oxide units and from 2 to 24 carbon atoms in the phenolic alkyl chain, or a polyhydroxy compound such as ethylene glycol, glycerol, or sorbitol. The positively charged ion does not appear to be essential for biocidal activity against all types of organisms, although the charge of the phosphate ester does affect the degree of biocidal activity. The relative ratios of mono- and di-esters also appears to affect the antimicrobial activity. As used herein, the general compound is referred to as a "phosphate ester". When the salt is specifically required or utilized, the compound is referred to as a "phosphate ester salt".

This compound has previously been demonstrated to be effective when incorporated into epoxy resins, combined with a surfactant for use as an antimicrobial detergent, used as a coating for fabric, wood or plastics, or a preservative when applied to an absorbent material. Despite the successful use of these compounds in a variety of ways, there remains a need for a means of incorporating the compounds into polymeric materials which results in effective antimicrobial control over an extended period of time,

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wherein the unbound phosphate ester or salt is not extensively removed by washing and surface wear. Further requirements for such a system are that it cannot decrease the stability and biocidal activity of the phosphate compounds.

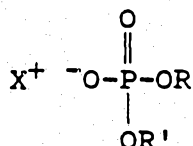
Accordingly, it is an object of the present invention to provide the biocidally effective phosphate esters in combination with carrier materials to yield products having biocidal properties which are resistant to washing and wear over an extended period of time.

Another object of the present invention is to provide methods for incorporating the biocidally effective phosphate esters into carrier materials which are relatively easy and inexpensive.

A further object of the present invention is to provide methods and means for the application of the biocidally effective phosphate esters to the surface of both synthetic and natural fibers, fabrics and fibrous surfaces to thereby impart biocidal properties to the materials which are resistant to washing.

Summary of the Invention

The present invention includes methods to incorporate a biocidal compound having the general formula



wherein R and R' are an alkyl, aryl, aralkyl or alkaryl group, one of R or R' can be H, X is a Group I

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metal ion, Group II metal ion, transition metal ion, or an organic ion such as an ammonium ion, and there is at least one free hydroxyl group. This compound, while more accurately termed a phosphoric acid, is described herein as a "phosphate ester" or salt thereof.

In the preferred embodiment, the biocidal compound is incorporated onto the surface, or absorbed within the structure, of a carrier material. Examples of carrier materials include diatomaceous earth or other high-surface area particulate inert materials, polymers which can bind the phosphate ester such as cationic synthetic resins and natural polymers, for instance, chitin, gelatin and collagen having quarternary amine sites or free amine functions, and polymeric microcapsules.

In one embodiment, the biocidal compound is adsorbed onto diatomaceous earth to provide a dusting powder with slow release of the biocidal compound. In another embodiment, the biocidal compound is adsorbed onto a powder such as celite for use as an additive to house paint to retard decomposition of the paint due to mold or bacterial growth. In yet another embodiment, the biocidal compound is mixed with or bound to a cationic resin or monomers which can be subsequently polymerized for use, for example, as a preservative of canvas used for outdoor activities. The biocidal compound can also be bound to polymers for use in wound coverings or filtration of either air or liquid. In still another embodiment, the biocidal compound is microencapsulated within a polymer structure from which it is released by exposure to agents such as ultrasound, temperature, chemical agents, or degradation over time.

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Other agents can be combined with the biocidal compound and carrier, taking care that the compound is not completely neutralized, which can lead to loss of biocidal activity, especially activity against Gram negative bacteria. For example, a buffering agent can be added to protect against complete neutralization of the biocidal compound. Surfactants, colorings, and a variety of other materials can also be combined with the biocidal compound.

10

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to delivery systems for a biocidal and insecticidal phosphate ester compound. The compound is the subject of U.S. Serial No. 047,561 filed April 27, 1987 by Robert H. McIntosh entitled "Microbiocidal Composition and Method of Preparation Thereof". These compounds are normally viscous liquids.

The biocidal compound is incorporated onto or into a carrier material in order to provide a mechanism for continued release of the biocidal compound over an extended period of time following incorporation or application to another object or material. By utilizing the described carrier materials, one is able to obtain a sustained release over an extended period of time despite washing of the object or wearing away of the immediate surface. At the same time, selection of the appropriate carrier material ensures that the compound is released in a controlled fashion over a period of time. The phosphate ester-carrier mixture is also useful as a means by which the compound can be added to materials

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where the liquid phosphate ester causes unacceptable alteration of the viscosity or mechanical properties of the material.

Carrier materials include inert, porous
5 particulate materials, cationic resins, proteins having free amine functions, and polymeric microcapsules.

Examples of inert particulate materials are diatomaceous earth, attapulgite clays, colloidal
10 silicas, zeolite solids, and vermiculite. There are several forms of diatomaceous earth, including celite and a less porous form known as "silica flour". The phosphate ester-carrier composition can also be mixed into thermoplastic polymers such as polyesters and
15 extruded as films or fibers using mixing and extruding techniques known to those skilled in the art. The films and fibers can be fragmented for use as fillers or filter packing. Examples of useful polymers include polyolefins, polystyrenes, polyamines,
20 polyacrylics, polyamides, polyethers, and polyurethanes. Care must be exercised in the selection of the polymeric or particulate material to avoid complete neutralization of the charge on the phosphate ester.

25 Natural and synthetic polymers having an actual or incipient positive charge can be reacted with the phosphate ester. For example, the phosphate ester can be bound to naturally occurring polysaccharide and protein polymers such as acetylated 2-amino cellulose
30 (chitin), chitosan (the hydrolyzed form of chitin), gelatin, and collagen. The phosphate ester binds to the 2-amino position of the chitin. A microfibrillated form of chitin and chitosan, produced by passing solid slurries of these materials through a

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Manton-Gaulin homogenizer, obtained from Diacel, Japan, is effective as a carrier of the phosphate ester compound. Gelatin, a heterogeneous mixture of water soluble proteins of high average molecular weight, is prepared by hydrolysis of collagen. Gelatin forms a salt with the phosphate ester compound. Collagen reacts in a similar fashion with the phosphate ester compound. When either gelatin or collagen is mixed with the biocidal phosphate ester and heated, a film forms containing the phosphate compound. This film can be used as a biocidal coating for fibers of animal or plant origin, including wound bandages, tissues, and air filters.

The phosphate ester is microencapsulated for applications requiring more controlled release. Numerous methods and materials for microencapsulation or coacervation are known to those skilled in the art. In one method, small beads of the phosphate ester compound are prepared by simultaneously spraying polymer and phosphate derivatives through concentric nozzles. Alternatively, the phosphate ester is encapsulated by coacervation. Up to 50 % by weight of liquid phosphate ester is dispersed in a gelatin, guar gum or polymer solution and the polymer precipitated around the phosphate ester by addition of a weak acid.

The microencapsulated phosphate ester is released as a function of time, environment, wear, or exposure to a specific agent such as ultrasound, light, or a chemical compound.

Exposure to strong bases such as sodium or potassium hydroxide can completely neutralize the compound, thereby abolishing the anti-Gram negative bacterial activity of the phosphate ester compound. It is therefore desirable to protect the compound

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against exposure to strong basic materials. A preferred means for protecting the phosphate ester is to incorporate a buffering agent into the carrier material. Examples of acceptable buffering agents
5 include sodium phosphate/phosphoric acid, potassium biphthalate, potassium citrate, and sodium acetate/acetic acid, and sodium citrate/citric acid. The buffered solutions can be mixed with a carrier as described before and sprayed directly onto a surface
10 to inhibit or destroy bacteria and fungus. The buffer prevents inactivation of the phosphate ester by the salts in the surfaces which may leach out from the surface. For example, buffered solutions are preferred for use in applying the phosphate ester
15 compound to brick walls, cement bridges, outside cinder block foundations and other materials where mold prevention is desirable but inactivating salts may leach out of the surface material.

The phosphate ester can also be mixed with a
20 non-ionic detergent, wax, or oil before adsorption onto the carrier. These compounds are useful in protecting the antimicrobial agent as well as in delaying release.

The biocidal compound described in U.S.S.N.
25 047,561 filed April 27, 1987 is a phosphate ester and the salt thereof. In the preferred embodiment, the phosphate ester is partially neutralized with an organic substituted amine to produce an ammonium salt of a phosphoric acid. The phosphate esters can
30 instead be partially neutralized using zinc acetate, magnesium acetate, sodium hydroxide or potassium hydroxide (Group IA metals, Group IIA metals, and transition metals). Selection of the positive ion does affect biocidal activity, principally the anti-

-11-

Gram negative bactericidal activity, although the phosphate ester appears to be the primary source of biocidal activity. The biocidal activity is also a function of the relative ratio of mono-to di-alkyl substituted phosphoric acid ester and the charge on the phosphate molecule due to the available OH-groups.

In a preferred method, the biocidal phosphate ester is prepared by reacting 1 mole of phosphorous pentoxide with 3 moles of alcohol, most preferably 2-ethylhexanol, at a temperature of between about 60°C and 120°C. The phosphorous pentoxide is slowly added to the alcohol while the mixture is agitated. Completion of the reaction is determined by titration of the resulting acid with a solution of potassium or sodium hydroxide. The reaction products include dialkyl phosphoric acid and monoalkyl phosphoric acid.

Anti-microbiocidal activity is tested by plating a microorganism onto Trypticase Soy Nutrient Agar, or other appropriate media, punching 6 mm diameter, 5 mm deep holes into the agar, and applying 0.05 ml of each of the undiluted test compounds into the holes. The petri dish is examined for growth of the microorganisms after incubation for 24 hours at 30°C. The diameter of the clear area surrounding the hole containing the compound being tested is indicative of the degree of anti-microbiocidal activity.

To form the ammonium salt of the phosphate ester compound, one mole each of the reaction products of the phosphorous pentoxide and alcohol (assuming 50% monoalkyl and 50% dialkyl phosphoric acid is produced in the reaction) is partially neutralized with 1.3 moles of an amine such as bis(hydroxyethyl) cocoamine

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by heating the mixture at a temperature between 60°C and 120°C until the reaction is complete.

Metal salts of the phosphate ester are prepared by mixing a metal salt such as magnesium acetate or zinc acetate with an alkyl phosphate, such as 2-ethylhexyl phosphate (or (2-ethylhexyl)phosphoric acid according to IUPAC), warming to dissolve, and vacuum stripping off the acetic acid, then testing for activity.

For example, salts of an alkyl phosphate ester were prepared by mixing either a Group I metal, magnesium, or a transition metal, zinc, with an alkyl phosphate ester, then testing for antimicrobial activity, as follows.

- | | | |
|----|--|---------|
| 15 | 1. Magnesium (acetate) _{2.4} H ₂ O | 20 gram |
| | 2-ethyl-hexyl phosphate (Rockmart) | 53 gram |
| | 2. Zinc (acetate) _{2.2} H ₂ O | 15 gram |
| | 2-ethyl-hexyl phosphate (Rockmart) | 53 gram |

The process was the same for both products: mix the metal salt with the 2-ethylhexyl phosphate, warm to dissolve the metal acetate and after dissolution, vacuum strip off the acetic acid.

The resultant products are clear, colorless, viscous liquids.

The magnesium phosphate and zinc phosphate compounds were washed and evaluated for biocidal activity using the standard cup method test procedure:

A sterile nutrient agar solution was prepared. The nutrient agar was inoculated with a 24 hour culture of either Staphylococcus aureus (Gram positive) or Pseudomonas aeruginosa (Gram negative)

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organisms. The inoculated agar was poured into 100 x 15 mm sterile petri dishes and allowed to solidify at room temperature. After solidifying small reservoirs were punched for the compounds to be tested.

- 5 Magnesium phosphate was added to one well and zinc phosphate was added to another. The plates were then incubated 24 hours at 30°C and examined for zones of inhibition.

The zone of inhibition of Staphylococcus was 15 mm for the magnesium phosphate and 19 mm for the zinc phosphate. No inhibition of the Pseudomonas was observed, however, the results clearly demonstrate that Group II and transition metal salts of the alkyl phosphate esters have bactericidal activity.

- 15 Example I. Preparation of Biocidal Powders from Diatomaceous Earth using Ammonium Salts of Phosphoric Acid Esters.

A biocidal alkyl phosphate powder was prepared by reacting a fatty or hydroxy amine, bis(hydroxyethyl)cocoamine, with the phosphate esters to form the ammonium salt which was then mixed with diatomaceous earth.

- 33 grams of partially neutralized monophosphate ester and diphosphate ester prepared by reaction of P_2O_5 with 2-ethylhexanol followed by reaction with dimethylcocoamine were mixed with 33 grams of a less viscous predominantly monophosphate ester mixture and then added to 33 grams of celite (diatomaceous earth) obtained from the John Manville Corporation. This was stirred for 1 hour to yield a free flowing powder having 66% by weight active phosphate ester which is useful as an antimicrobial dusting powder. This powder was subsequently used in example II. Similar

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results were obtained by mixing 50 grams of esters with 50 grams of celite.

A biocidal alkyl phosphate powder was prepared by adding 50 grams of monoalkyl phosphoric acid to 50
5 grams of hexane. this solution was slurried with 50 grams of celite. The hexane was evaporated from the slurry with stirring to yield a free flowing powder containing 50% by weight of adsorbed phosphate ester.

These powders were tested for antimicrobial
10 activity and found to inhibit both Staphylococcus and Psuedomonas.

Example II. Preparation of an Anti-microbial Latex Paint.

90 grams of 66% phosphate ester - 33%
15 diatomaceous earth prepared in example I (equivalent to about 2 oz. of undiluted phosphate ester salt) was mixed into one gallon of latex interior housepaint and applied to the interior walls of a bedroom. In contrast to results obtained with latex paint in the
20 absence of the phosphate ester, the painted walls remained free of mildew for two years even in high humidity.

By adsorbing the phosphate ester onto the diatomaceous earth prior to addition to the paint,
25 there was only a slight change in the viscosity of the latex paint. When the same amount of compound was added directly to the latex paint, the paint underwent a pronounced change of viscosity and lost some of its smooth flow and spreading characteristics.

30 Example III. Biocidal Synthetic Polymeric Coatings.

One mole of mono 2-ethylhexyl phosphoric acid, a very active anti-microbiocidal agent, was partially neutralized with approximately 1 mole of

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dimethylaminoethyl methacrylate. The resulting ammonium salt can be added to a substrate such as nylon, polyester, or cloth for polymerization in the presence of a suitable catalyst (a peroxide such as potassium persulfate, dibenzoyl peroxide, methylethyl ketone peroxide, etc.) to produce a dimethylaminoethyl methacrylate polymer having the mono substituted phosphoric acid compound attached to it which is useful as a protective coating on fabric and fibers.

10 The more hydrophobic the matrix material, the longer lasting the biocidal activity.

Similarly, one mole of 2-ethyl hexyl phosphate ester was partially neutralized with 1 mole of dimethylaminoethyl methacrylate prepared by esterification of methacrylic acid with dimethylaminoethanol. The resulting ammonium salt of the phosphate ester can be added to a porous or fibrous substrate, cotton, in the presence of a catalyst and polymerized in situ to form a protective coating.

Example IV. Biocidal Natural Polymeric Coatings.

One gram of monophosphate ester can be added to a 3% solution of gelatin in water and also used as a protective coating for fabrics such as cotton or wool.

25 Similarly, 3 grams of biocidal phosphate ester can be mixed into a 3% gelatin solution in water and used to coat a glass wall type air filter for home furnace.

Example V. Biocidal Gelatin Microcapsules.

30 50 grams of monophosphate ester can be vigorously mixed into a 3% gelatin solution using a homogenizer. The dispersion is then neutralized with diethylethanolamine. As the pH approaches the isoelectric point of the gelatin, approximately 5.5,

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the gelatin precipitates around the phosphate ester forming droplets containing the phosphate ester within a gelatin shell. These solidify into microcapsules.

Examples of buffering agents which can be included with the phosphate ester within the microcapsule include 0.1 M of potassium biphthalate-HCl pH 2.8, 0.1 M primary potassium citrate pH 3.7, 0.1 M acetic acid-sodium acetate pH 4.6, 0.1 M secondary sodium pH 5.0.

10 Example VI. Biocidal Epoxy Matrices.

The biocidal properties of epoxy encapsulated monoalkyl amine phosphate ester/dialkyl amine phosphate ester, prepared by reacting two moles of the product of the reaction of P_2O_5 with 2-ethylhexanol with 1.3 moles of dimethylcocoamine, were significantly improved by adsorbing the phosphate ester salt to either celite diatomaceous earth from John Manville Co., United States or Silver Bond silica flour from Tammsco, Inc., Tams, IL, prior to incorporation into the epoxy. The phosphate ester salt - carrier is preferably mixed into the hardener or the mixture of the hardener and resin, rather than into the unpolymerized resin, to retain the maximum amount of biocidal activity.

25 The following mixtures were prepared using the phosphate ester salt-silica flour mixture and tested for biocidal activity:

		parts by weight		parts by weight
30	A. epoxy resin:	DER 331 56.7	DER 331	55.81
	diluent:	WC-8 5.0	DER 732	6.25
	defoamer:	Dehydran 0.3	Dehydran	0.3
	B. hardener:	Epotuf 27.3	Epotuf	26.95
	phosphate ester-carrier:	10.7		10.7

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DER 331 is a DGEBA epoxy resin, equivalent weight 182-190, obtained from Dow Chemical Co. DER 732 is a polyglycol diepoxide, equivalent weight 305-335, obtained from Dow Chemical Co. WC-8 is a C₁₂-C₁₄ alkylglycidyl ether, equivalent weight 280-300, obtained from Wilmington Chemical Co., Wilmington, DE. Dehydran 1208 is a defoamer sold by Henkel, Inc., Teaneck, NJ. Epotuf 37-606 is a polyamine epoxy aduct sold by Reichold Chemical Co., Inc., White Plains, NY.

The samples prepared from this formula were tested for biocidal activity and the activity compared with the activity for the phosphate ester salt - epoxy mixture alone, as described below. Significantly better results were obtained for the mixture with carrier than for the phosphate ester salt - epoxy mixture alone.

Preparation of epoxy coating for test:

Liquid epoxy material is poured into 100 mm diameter square plastic petri dishes to a depth of approximately 5 mm. One-half of the dishes contain epoxy plus phosphate ester, with or without carrier, (experimentals) and an equal number of dishes contain only epoxy (controls). Depth of epoxy has no effect on biocide activity at the epoxy surface.

After the epoxy material has cured, the experimentals and controls are scored in the center of the dish using a synthetic abrasive pad 2" in diameter mounted in a drill.

Epoxy dust is removed by washing with distilled water. Dishes are allowed to dry and are used in the test three days after epoxy dust removal. The epoxy surface is abraded for several reasons:

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1. Rough surface simulates in use effect of people walking constantly over a floor surface, and is a worst-case scenario for a coating.
- 5 2. Abraded surface provides attachment sites for microorganisms as would occur on a floor.
3. Diameter of the rough surface gives a surface area of 3.14 sq. in. (89.5mm²). This allows for more accurate calculations of organisms per sq. in. (mm²) on the test material.
- 10 4. By having a central, specified area on the epoxy, contact with the sides of the dish not covered with epoxy are avoided during inoculation and recovery operations, thus preventing the intrusion of organisms not in the test area.
- 15 5. In this test, a rough surface is also necessary to prevent "beading-up" of the water based inoculum, thus preventing alteration of the relationship of organisms per square inch during the period of testing.
- 20
- 25

Organism preparation and inoculation of plates:

1. Cultures are prepared from 24 hour nutrient broth cultures of bacterial organisms by standard laboratory methods using centrifugation and resuspension in 0.85% NaCl.
- 30 2. Samples are removed and diluted into a 45°C agar solution to yield a final

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count of organisms between 1×10^4 and 5×10^4 organisms/ml in a solution containing 0.85% saline and 0.3% agar (no organic nutrients).

- 5 3. Prewet abraded area of epoxy with 0.85% saline using a sterile cotton swab that has been dipped into sterile saline.
- 10 4. Pipette 0.1 ml of innoculum onto the center of the abraded area of the epoxy in the petri dishes.
5. Spread the inoculum over the entire abraded surface of the epoxy.
- 15 8. Following inoculation of all plates, immediately place plates top side down into a humidity chamber held at 18-20°C and a relative humidity in excess of 85%. Incubate for 30 hours and count viable organisms.

20	CFU:sample	control	% reduction
With carrier+:			
	<u>Staphylococcus</u> 0	1.0×10^6	100.0
	<u>Psuedomonas</u> 3.9×10^2	2.8×10^5	99.9
	<u>E. coli</u> 4.3×10^3	5.2×10^6	99.9
25	Without carrier*:		
	<u>Staphylococcus</u> 7.16×10^4	2.11×10^6	96.6
	<u>Psuedomonas</u> 5.29×10^4	8.7×10^4	39.2
	<u>E. coli</u> ND	ND	ND

30 + Sample prepare above from mixture containing WC-8 as the diluent.

* The same relative quantity of phosphate ester salt was incorporated into an epoxy formed by mixing

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the combination of DER 331, DER 732, Dehydran 1208 and phosphate ester salt with Epotuf 37-606.

The samples with carrier retained their activity after repeated washings and scarifications, unlike the
5 phosphate ester salt - epoxy mixture without carrier.

Modifications and variations of the claimed invention, biocidal phosphate ester-carrier delivery systems, will be obvious to those skilled in the art from the foregoing detailed description of the
10 invention. These modifications and variations are intended to come within the scope of the appended claims.

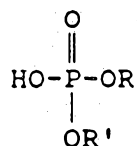
We claim:

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A biocidal composition comprising

(a) an inert carrier selected from the group consisting of diatomaceous earth, attapulgite clay, colloidal silica, zeolite, protein, polysaccharide, collagen, chitin, chitosan and gelatin; and

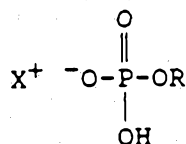
(b) a biocidally effective amount of a phosphate ester having the general formula:



wherein R and R' are selected from the group consisting of alkyl, aryl, aralkyl and al aryl groups, one or R or R' can be H, and

the phosphate ester is bound to the carrier.

2. The biocidal composition of claim 1 wherein the phosphate ester is a partially neutralized acid having the general formula

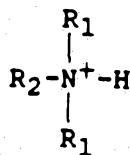


and X is selected from the group consisting of organic ions, Group IA metals, Group IIA metals and transition metals.

3. The biocidal composition of claim 2 wherein X⁺ is an ammonium ion.

4. The biocidal composition of claim 3 wherein the ammonium ion has the general formula





wherein R_1 is selected from the group consisting of an alkyl group of between 1 to 18 carbon atoms and a hydroxy alkyl group of from 2 to 18 carbon atoms; and

R_2 is an alkyl group of from 8 to 18 carbon atoms.

5. The biocidal composition of any preceding claim further comprising a buffering agent.
6. A biocidal composition according to any preceding claim, wherein the phosphate ester is microencapsulated in the carrier.
7. A biocidal composition according to claim 1 and substantially as hereinbefore described with reference to the Examples.
8. A method for providing an article with antimicrobial properties, the method comprising combining a biocidal-carrier composition according to any preceding claim with the article.
9. The method of claim 8 wherein the combination is formed by coating the carrier-biocidal composition on the article.
10. The method of claim 8 wherein the article is a paint and the combination is prepared by mixture of the carrier-biocidal composition with the paint.
11. A method for providing an article with antimicrobial properties according to claim 8 and substantially as

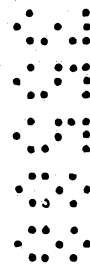


hereinbefore described with reference to the Examples.

12. An article provided with antimicrobial properties provided by the method of any one of claims 8 to 11.

DATED this 19th day of March, 1991.

INTERFACE RESEARCH CORPORATION
By Its Patent Attorneys
DAVIES & COLLISON



MTS

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US89/01955

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC (4): AOIN 25/10		
U.S. CL: 424/409		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
U.S.	106/15.05 ; 424/405, 408, 409; 523/122	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹		
Category [*]	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
A	US, A, 2,818,364 BIRUM 31 DECEMBER 1957 (SEE ENTIRE DOCUMENT)	1-21
A	US, A, 3,437,721 BARANAUCKAS 08 APRIL 1969 (SEE ENTIRE DOCUMENT)	1-21
A	US, A, 4,259,078 KIEBER 31 MARCH 1981 (SEE ENTIRE DOCUMENT)	1-21
A	JP, A, 50-157,531 SANKYO 19 DECEMBER 1975 (SEE ABSTRACT)	1-21
[*] Special categories of cited documents: ¹⁰ "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document 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 "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		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
17 JUNE 1989	25 JUL 1989	
International Searching Authority	Signature of Authorized Officer	
ISA/US	T. K. PAGE / <i>K. Page</i>	