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OPOSICION A:

☒ Patente de Invención

☐ Patente de Modelo de Utilidad

☐ Diseño Industrial

☐ Esquema de Trazado para Circuitos Integrados

☐ Marcas de Productos o Servicios

☐ Marca Colectiva

☐ Marca de Certificación

☐ Lema Comercial

2

SOLICITUD PUBLICADA

Número del expediente: 07 055.028 ✓

Solicitante: JOHNSON & JOHNSON CONSUMER COMPANIES, INC.

Apoderado: JIMENA ESCOBAR URIBE.

Título de la nueva creación o denominación del signo:
COMPOSICIONES Y MÉTODOS PARA TRATAR IRRITACIÓN Y EQUIPO DEL MISMO.

Gaceta: 596 de 30 de Septiembre de 2008, número de publicación 868.

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OPOSICION PRESENTADA POR:

OPOSITOR	Nombre: TECNOQUIMICAS S.A., Sociedad comercial organizada y existente a las leyes Colombianas, con domicilio y sede principal en la Ciudad de Cali Valle. Dirección: Calle 23 # 7-39 Cali - Valle Teléfono: 882 5555 Fax: 883 8859 E-mail: Domicilio: Cali – Valle	IDENTIFICACION C.C. ☐ NIT ☒ C.E. ☐ Otro ☐ Número: 890.300.466-5
REPRESENTANTE O APODERADO (74)	Nombre: José Luis Reyes Villamizar ✓ Dirección: Cra. 17 No. 88-23, Of. 205 Teléfono: (1) 621.26.31 E-mail: info@reyes-abogados.com Fax: (1) 621.25.42 Domicilio: Bogotá, D.C.	IDENTIFICACION C.C. ☒ NIT ☐ C.E. ☐ Otro ☐ Número: 79'152.473 de Usaquén TP 44655

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FUNDAMENTOS DE LA OPOSICION:

Causal: Incumplimiento de requisitos de patentabilidad (Título II, Capítulo I, Decisión 486 de 2000). Se violan los artículos 14, (las patentes de invención deben ser nuevas, tener nivel inventivo y ser susceptibles de aplicación industrial) 16 y 18 (una invención tiene nivel inventivo si no es obvia para una persona versada en la materia)). Artículo 30 (Reivindicaciones) y artículo 42 (oposiciones) de la Decisión 486 de la Comisión de la Comunidad Andina.

Justificación: Ver Anexo

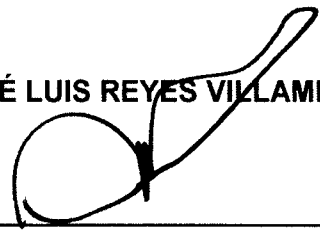
5 Comprobante de pago No. 08-101.249 (Oposición) Fecha Diciembre 29 de 2008
(Prórroga) Fecha _____

6 **Anexos:**

- ☒ Comprobante de pago de la tasa
- ☒ Poderes, si fuere el caso
- ☐ Pruebas de los fundamentos de la oposición
- ☐ Documentos que acrediten el legítimo interés, si fuere el caso
- ☒ Certificado de existencia y representación legal de las partes, cuando sean personas jurídicas
- ☒ Copia de la oposición para el traslado al solicitante.

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NOMBRE: JOSÉ LUIS REYES VILLAMIZAR

FIRMA: 

Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

E.

S.

D.

REF:

Expediente 07 055.028 ✓

TÍTULO SOLICITADO: COMPOSICIONES Y MÉTODOS PARA TRATAR
IRRITACIÓN Y EQUIPO DEL MISMO.

PUBLICACIÓN: Gaceta 596 de 30 de Septiembre de 2008, número de
publicación 868.

PRIORIDAD: US 60/632,151 de 01/12/2004

SOLICITANTE: JOHNSON & JOHNSON CONSUMER COMPANIES,
INC.

APODERADO: JIMENA ESCOBAR URIBE ✓

TRÁMITE: PRESENTACIÓN DE OPOSICION

✓
JOSÉ LUIS REYES VILLAMIZAR, mayor de edad, identificado como aparece al
pie de mi firma, abogado en ejercicio, titular de la tarjeta profesional número 44655
del Consejo Superior de la Judicatura, obrando en calidad de apoderado de la
sociedad **TECNOQUÍMICAS S.A.**, en ejercicio de lo dispuesto por el artículo 42 de
la Decisión 486 de 2000, muy respetuosamente me permito formular la siguiente

I. PETICIÓN

Sírvase negar el beneficio patentario a la solicitud contenida en el expediente **07 055.028**, por no cumplir con lo dispuesto por los artículos 14, 16, 18 y 20 literal d) de la Decisión 486 de 2000, con base en los fundamentos que se expondrán a continuación.

II. LEGÍTIMO INTERÉS

Asiste a **TECNOQUÍMICAS S.A.**, legítimo interés para presentar esta oposición, pues la eventual concesión de la solicitud restringiría injustificadamente el empleo de ciertas sustancias, derivados y procesos que a nuestro juicio carecen de nivel inventivo, en detrimento de sus legítimos intereses comerciales. De igual manera mis clientes están interesados, por su misma condición de industrias farmacéuticas, en evitar la concesión de privilegios de patente que incumplan los requisitos materiales de patentabilidad establecidos en las normas vigentes, y que supongan un riesgo para la libre competencia.

III. FUNDAMENTO DE LA OPOSICIÓN

La solicitud colombiana en trámite que reivindica un método para tratar una condición vaginal (infección) a través de una composición que contiene un principio activo (antiviral, antifúngico o antibiótico), un agente mejorador (anestésico local o antihistamínico), un ingrediente refrescante (alcoholes inferiores, mentol, alcanfor y azúcares como sorbitol) y un portador farmacéuticamente aceptable, a través de un dispositivo de aspersión de bomba invertida o de aerosol; incumple con los requisitos indispensables para otorgársele el privilegio de patente de invención tal y como se demuestra con los siguientes argumentos:

Para comenzar, todas las reivindicaciones de dicha solicitud colombiana en trámite incurren en una improcedencia directa de patentabilidad, en cuanto a que explícitamente se refieren a un tratamiento terapéutico, que involucra la aplicación de una formulación farmacéutica que contiene un principio activo (antiviral, antifúngico o antibiótico), un agente mejorador (anestésico local o antihistamínico), un ingrediente refrescante (alcoholes inferiores, mentol, alcanfor y azúcares como sorbitol) y un portador farmacéuticamente aceptable, a través de un dispositivo de aspersión de bomba invertida o de aerosol, para así tratar la sintomatología asociada a una infección vaginal; lo cual va en contra de lo expuesto por la decisión 486 de 2000 que explícitamente revela en su artículo 20 literal d) "*No serán patentables (...) los métodos terapéuticos o quirúrgicos para el*

tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales."

En segundo lugar y si lo anteriormente expuesto no fuese suficiente para no otorgársele el privilegio de patente de invención a dicha solicitud en trámite; existen también muchos documentos que exponen con anterioridad, información que contiene la esencia de lo reivindicado por la misma, y que por lo tanto demuestran la carencia de novedad y de nivel inventivo de la misma, veamos:

❖ La publicación internacional WO 00/56353 publicada el 28 de septiembre de 2000 revela:

1. A uro-genital condition treatment system comprising:
a carrier;
at least one polypeptide including an amino acid sequence selected from a group consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent of any of the foregoing; and
wherein the carrier carries the at least one polypeptide.

(...)

8. The uro-genital condition treatment system of claim 7 wherein a part of the applicator is for insertion into the vagina, urethra, or rectum.
9. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition is an infection, inflammation, or both.

(...)

25. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition includes vaginitis.

(...)

51. The method of claim 49 wherein the local application is achieved through a cream, an ointment, a balm, a gel, an aerosol foam, an aerosol spray, or a dissolvable pill.

❖ La publicación internacional WO 99/27922 publicada el 10 de Junio de 1999 revela:

1. The use of polyols for the preparation of a composition to be administered in the treatment or prophylaxis of mucosal yeast infection in mammals, comprising mixing at least one pharmacologically acceptable carrier with an amount of polyol sufficient to reduce or inhibit mucosal infection caused by yeasts such as *Candida s.p.* in said mammal.

2. The use according to claim 1 wherein the polyol is selected from the group consisting of xylitol, lactitol, sorbitol, mannitol and mixtures thereof, preferably xylitol.

(...)

7. The use according to any one of the preceding claims, wherein said mucosal yeast infection is a vaginal infection.

(...)

10. The use according to claim 9, wherein said composition is prepared in the form of an orally administrable preparation selected from the group comprising a liquid, a tablet, a pill, a chewing gum or tablet, a powder, a spray, a syrup, a sugar substitute, a candy or sweet, an ice-cream, a pet food, an animal feed, and the like, by mixing at least one pharmacologically acceptable carrier and an amount of xylitol sufficient to reduce or inhibit the infectious activity of yeasts on the mucosa of said mammal.

(...)

12. The use according to claim 10 or 11, wherein said composition additionally includes another antifungal drug effective against said yeast infection.

13. The use according to claim 9, wherein said composition is prepared in the form of a topically administrable preparation selected from the group comprising a liquid, a spray, an aerosol, a cream, a paste, a cement, an ointment, a jelly or gel, a lubricant, a plaster, a membrane, a mouth wash or rinse, a tooth paste, and eye drops, by mixing at least one topical carrier and an amount of xylitol sufficient to reduce or inhibit the infectious activity of yeasts on the mucosa of said mammal.

14. The use according to claim 7 or 13, wherein said composition is in a form suitable for vaginal yeast infection and xylitol is included in a cream, jelly, lubricant, or liquid or is applied onto the surface of a condom.

(...)

16. A device suitable for the treatment or prophylaxis of mucosal yeast infection in mammals, characterized in that it comprises a condom having polyol added thereto for administration of polyol into an orifice of the body, such as vagina.

❖ La publicación internacional WO 01/13956 publicada el 01 de Marzo de 2008 revela:

1. A composition comprising a lactic acid-producing bacterial species in a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal and Emu Oil.

(...)

10. The composition of claim 1, wherein said carrier is selected from a group comprising an emulsion, cream, lotion, gel, oil, ointment, suspension, aerosol spray, powder, aerosol powder, or semi-solid formulation.

(...)

17. The composition of claim 1, further comprising one or more anti-microbial agents selected from a group consisting of: a quaternary ammonium chloride, an iodine or iodifer compound, a phenolic compound, and an alcohol compound or tincture.

18. The composition of claim 1, further comprising one or more systemic anti-fungal compounds selected from a group consisting of: Amphotericin B, Dapsone, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, and Miconazole KI.

19. The composition of claim 1, further comprising one or more topical anti-fungal compounds selected from a group consisting of: Amphotericin B, Carbol-Fuchsin, Ciclopirox, Clotrimazole, Econazole, Haloprogin, Ketoconazole, Mafenide, Miconazole, Naftifine, Nystatin, Oxiconazole, Silver Sulfadiazine, Sulconazole, Terbinafine, Tioconazole, Tolnaftate, and Undecylenic acid.

20. The composition of claim 1, further comprising one or more vaginal anti-fungal compounds selected from a group consisting of: Butoconazole, Clotrimazole, Econazole, Gentian Violet, Miconazole, Nystatin, Terconazole, and Tioconazole.

Como se puede apreciar claramente, en estas anterioridades se revela la formulación de compuestos anti-infecciosos para la aplicación vaginal, a través de formulaciones tipo spray, aerosol y crema; así como la mención explícita del uso de polióles dentro de dicha formulación, específicamente el uso de sorbitol.

En el mismo sentido, y teniendo en cuenta que cualquier persona medianamente versada en la materia, reconoce que dentro la sintomatología de una infección

vaginal, especialmente por hongos, la comezón y/o el escozor son unos de los síntomas que resultan mas molestos; es entonces mas que obvia la asociación entre los agentes anti-infecciosos usados para dado caso y los agentes anestésicos locales o antihistamínicos, lo cual se puede confirmar a través de la publicación de diversos documentos. Dentro de algunos de estos documentos se pueden mencionar la patente europea EP 1206937 publicada el 22 de Mayo de 2002 en donde se exponen en el capitulo reivindicatorio la combinación de derivados de nitromidazol con dichos agentes antihistamínicos o anestésicos locales en el tratamiento de candidiasis vaginal. Por su parte la publicación internacional WO 03/032985 publicada el 24 de Abril de 2003 también menciona el tratamiento de infecciones fúngicas o bacteriales a nivel vaginal a través de la combinación de diversos agentes activos y el uso concomitante de anestésicos locales. Así mismo la patente americana US 4478822 publicada el 23 de octubre de 1984 revela nuevamente composiciones para aplicación vaginal que contienen diversos agentes anti-infecciosos en combinación con agentes antihistamínicos y/o anestésicos locales.

Para finalizar, y teniendo en cuenta que la solicitud colombiana reivindica también que la aspersión de dicha formulación farmacéutica se hace a través de dispositivos del tipo botella de aspersión de bomba invertida y/o una botella de aspersión de aerosol invertida; es relevante también mencionar que existen con anterioridad, una gran diversidad de documentos que revelan dispositivos con las mismas características técnicas, y muchos de estos implicados en la administración de fármacos, tal y como sucede en el capítulo reivindicatorio de la solicitud colombiana en tramite en cuestión. Dentro de algunos de estos documentos se pueden mencionar la patente americana US 2345854 publicada el 04 De Abril de 1944; la patente americana US 3043524 publicada el 10 de Julio de 1962; la patente europea EP 1222938 publicada el 17 de Julio de 2002; la patente americana US 6708846 publicada el 23 de marzo de 2004; la patente americana US 3818908 publicada el 25 de Junio de 1974 y la patente americana US 4702415 publicada el 27 de Octubre de 1987.

En conclusión, la solicitud colombiana en trámite carece absolutamente de todos los requisitos fundamentales para otorgársele el privilegio de patente de invención; primero que todo, porque incurre en una improcedencia directa de patentabilidad al reivindicar un método terapéutico, y en segundo lugar, y como ha quedado

demostrado, carece de novedad y de nivel inventivo, puesto que todos los aspectos esenciales que resumen la invención de dicha solicitud, se encuentran descritos con anterioridad en el mismo estado de la técnica.

Así las cosas, y con fundamento en los argumentos expuestos a lo largo del presente escrito, respetuosamente reitero la solicitud para que su despacho se abstenga de conceder el privilegio de patente solicitado, y ordene en consecuencia el archivo del expediente respectivo.

IV. FUNDAMENTOS DE DERECHO

Son fundamentos de derecho el Capítulo I, artículos 14, 16, 18 y 20 literal d) de (Requisitos de Patentabilidad) y el artículo 42 (Oposiciones) de la Decisión 486 de 2000.

V. PRUEBAS

Ruego que se tengan como tales, sin perjuicio de las que puedan presentarse al vencimiento de la prórroga solicitada, y de aquellas que el Despacho considere oficiosamente, las siguientes:

- ❖ Capítulos reivindicatorios de todos los documentos mencionados en el acápite de Fundamentos de la Oposición.

VI. ANEXOS

Para efectos del trámite correspondiente, me permito anexar al presente escrito los siguientes anexos

1. Certificado de existencia y representación legal de Tecnoquímicas S.A.
2. Poder para actuar.
3. Constancia de pago de las tasas de tramitación de oposición.
4. Copia para correr traslado al solicitante.
5. El mencionado en el acápite de pruebas.

VIII. NOTIFICACIONES

El suscrito recibirá notificaciones en la secretaría de su Despacho o en mi oficina localizada en la Carrera 17 No. 88-23, Oficina 207, Fax (1) 621.25.42 de esta ciudad. Tecnoquímicas S.A., las recibirá en la secretaría de su Despacho o en su sede localizada en la Calle 23 # 7-39, de la ciudad de Cali.

Señor Superintendente,



JOSÉ LUIS REYES VILLAMIZAR

C.C. 79'152.473 de Usaquén

T.P.A. 44.655 del C.S.J.



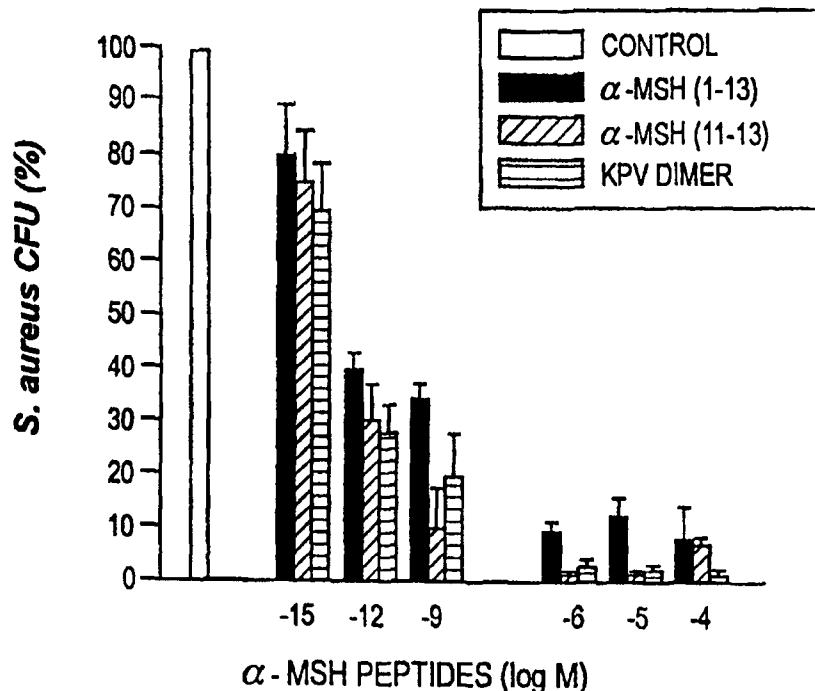
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 38/34, 38/06, 38/08, A61P 13/00, 15/00		A2	(11) International Publication Number: WO 00/56353
			(43) International Publication Date: 28 September 2000 (28.09.00)
(21) International Application Number: PCT/US00/07846		(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 23 March 2000 (23.03.00)			
(30) Priority Data: 60/126,233 24 March 1999 (24.03.99) US			
(71) Applicant (for all designated States except US): ZENGEN INC. [US/US]; Suite 980, 21800 Oxnard Street, Woodland Hills, CA 91367 (US).			
(72) Inventors; and (75) Inventors/Applicants (for US only): LIPTON, James [US/US]; 5800 Owensmouth Street #10, Woodland Hills, CA 91367 (US). CATANIA, Anna [IT/IT]; #15 Corsa Italia, I-20122 Milan (IT).		Published Without international search report and to be republished upon receipt of that report.	
(74) Agent: WISE, Michael; Lyon & Lyon LLP, 633 West Fifth Street, Los Angeles, CA 90071 (US).			

(54) Title: A URO-GENITAL CONDITION TREATMENT SYSTEM

(57) Abstract

The present invention is directed to a system for treating uro-genital conditions. One aspect of this invention involves the treatment system comprising one or more polypeptides with an amino acid sequence including KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), for treatment of uro-genital conditions. The one or more polypeptides can also be a dimer formed from any of the amino acid sequence above. Uro-genital conditions can include infections, inflammation, or both. In one preferred embodiment of the invention, the uro-genital condition includes infection and/or inflammation of the vagina, vulva, urinary tract, penis, and/or the rectum. In another preferred embodiment of the invention, the one or more polypeptides are dissolved in a carrier. In another preferred embodiment of the invention, the one or more polypeptides are associated with a tampon for preventing toxic shock syndrome. In another preferred embodiment, the one or more polypeptides are associated with a contraceptive for prevention of sexually transmitted diseases or infections. In another preferred embodiment, the one or more polypeptides are associated with a suppository for insertion into the vagina or rectum.



WHAT IS CLAIMED IS:

1. A uro-genital condition treatment system comprising:
a carrier;
at least one polypeptide including an amino acid sequence selected from a group
5 consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ.
ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent
of any of the foregoing; and
wherein the carrier carries the at least one polypeptide.
2. The uro-genital condition treatment system of claim 1 wherein the at least one
10 polypeptide includes a dimer formed from any amino acid sequence in the group in claim 1.
3. The uro-genital condition treatment system of claim 2 wherein the dimer is a KPV
dimer.
4. The uro-genital condition treatment system of claim 1 wherein the amino acid
sequence KPV (SEQ. ID. NO. 1), HFRWGKPV (SEQ. ID. NO. 3), or SYSMEHFRWGKPV
15 (SEQ. ID. NO. 4) is located at the C-terminal of the at least one polypeptide.
5. The uro-genital condition treatment system of claim 1 wherein the amino acid
sequence KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID.
NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), includes at least one amino acid in the D-
form.
- 20 6. The uro-genital condition treatment system of claim 1 wherein the at least one
polypeptide is N-acetylated or C-amidated or both.
7. The uro-genital condition treatment system of claim 1 further comprises an applicator
for applying the carrier to a site of the uro-genital condition.
8. The uro-genital condition treatment system of claim 7 wherein a part of the applicator
25 is for insertion into the vagina, urethra, or rectum.
9. The uro-genital condition treatment system of claim 1 wherein the uro-genital
condition is an infection, inflammation, or both.
10. The uro-genital condition treatment system of claim 1 wherein the uro-genital
condition includes the presence of bacteria or fungi in a uro-genital area.
- 30 11. The uro-genital condition treatment system of claim 1 wherein the uro-genital
condition includes the presence of a virus in a uro-genital area.
12. The uro-genital condition treatment system of claim 1 the uro-genital condition is
caused by a bacterial infection or a fungal infection or both.

13. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition is caused by a viral infection, bacterial infection, fungal infection, or any combination thereof.
14. The uro-genital condition treatment system of claim 10 wherein the bacteria is a gram-positive bacteria.
15. The uro-genital condition treatment system of claim 10 wherein the bacteria is from the genus of *Staphylococcus*.
16. The uro-genital condition treatment system of claim 10 wherein the bacteria is *Staphylococcus aureus*.
- 10 17. The uro-genital condition treatment system of claim 10 wherein the fungi is from the genus *Candida*.
18. The uro-genital condition treatment system of claim 10 wherein the fungi is *Candida albicans*.
19. The uro-genital condition treatment system of claim 11 wherein the virus is a HIV.
- 15 20. The uro-genital condition treatment system of claim 11 wherein the virus is HSV.
21. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition is located in a female reproductive cavity or on a genitalia or both.
22. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition is located in the urinary tract.
- 20 23. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition is located on a penis.
24. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition is located in a rectal cavity or on a rectal area or both.
25. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition includes vaginitis.
- 25 26. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition includes cystitis or urethritis.
27. The uro-genital condition treatment system of claim 1 wherein the uro-genital condition includes balanoposthitis.
- 30 28. The uro-genital condition treatment system of claim 1 wherein the carrier is a cream, an ointment, a balm, an aerosol foam, an aerosol spray, or a dissolvable pill.
29. A tampon comprising:
an absorbent material;

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at least one polypeptide including an amino acid sequence selected from the group consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent of any of the foregoing; and

5 wherein the absorbent material is associated with the at least one polypeptide.

30. The tampon of claim 29 wherein the at least one polypeptide includes a dimer formed from any amino acid sequence in the group in claim 29.

31. The tampon of claim 30 wherein the dimer is a KPV dimer.

32. The tampon of claim 29 wherein the amino acid sequence KPV (SEQ. ID. NO. 1),
10 HFRWGKPV (SEQ. ID. NO. 3), or SYSMEHFRWGKPV (SEQ. ID. NO. 4) is located at the C-terminal of the at least one polypeptide.

33. The tampon of claim 29 wherein the amino acid KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4) includes at least one amino acid in the D-form.

15 34. The tampon of claim 29 wherein the at least one polypeptide is N-acetylated or C-amidated or both.

35. A contraceptive comprising:

a barrier;

a carrier associated with the barrier;

20 at least one polypeptide including an amino acid sequence selected from the group consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent of any of the foregoing; and

wherein the carrier carries the at least one polypeptide.

25 36. The contraceptive of claim 35 wherein the at least one polypeptide includes a dimer formed from any amino acid sequence in the group in claim 35.

37. The contraceptive of claim 36 wherein the dimer is a KPV dimer.

38. The contraceptive of claim 35 wherein the amino acid KPV (SEQ. ID. NO. 1), HFRWGKPV (SEQ. ID. NO. 3), or SYSMEHFRWGKPV (SEQ. ID. NO. 4) is located at the
30 C-terminal of the at least one polypeptide.

39. The contraceptive of claim 35 wherein the amino acid sequence KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4) includes at least one amino acid in the D-form.

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40. The contraceptive of claim 35 wherein the at least one polypeptide is N-acetylated or C-amidated or both.
41. The contraceptive of claim 35 wherein the barrier is a condom, a diaphragm, or a sponge.
- 5 42. A suppository comprising:
a carrier;
at least one polypeptide including an amino acid sequence selected from the group consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent
10 of any of the foregoing; and
wherein the carrier carries the at least one polypeptide.
43. The suppository of claim 42 wherein the at least one polypeptide includes a dimer formed from any amino acid sequence in the group in claim 42.
44. The suppository of claim 43 wherein the dimer is a KPV dimer.
- 15 45. The suppository of claim 42 wherein the amino acid sequence KPV (SEQ. ID. NO. 1), HFRWGKPV (SEQ. ID. NO. 3), or SYSMEHFRWGKPV (SEQ. ID. NO. 4) is located at the C-terminal of the at least one polypeptide.
46. The contraceptive of claim 42 wherein the amino acid sequence KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV
20 (SEQ. ID. NO. 4) includes at least one amino acid in the D-form.
47. The suppository of claim 42 wherein the at least one polypeptide is N-acetylated or C-amidated or both.
48. A method of treating uro-genital condition comprising:
using at least one polypeptide including an amino acid sequence selected from the
25 group consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent of any of the foregoing.
49. The method of claim 49 further comprising:
locally applying the at least one polypeptide at a site of the uro-genital condition.
- 30 50. The method of claim 49 wherein the local application is achieved through a suppository, a tampon, or a contraceptive.
51. The method of claim 49 wherein the local application is achieved through a cream, an ointment, a balm, a gel, an aerosol foam, an aerosol spray, or a dissolvable pill.

52. The method of claim 48 wherein the at least one polypeptide includes a dimer formed from any amino acid sequence in the group in claim 48.
53. The method of claim 52 wherein the dimer is a KPV dimer.
54. The method of claim 48 wherein the amino acid sequence KPV (SEQ. ID. NO. 1),
5 HFRWGKPV (SEQ. ID. NO. 3), or SYSMEHFRWGKPV (SEQ. ID. NO. 4) is located at the C-terminal of the at least one polypeptide.
55. The method of claim 48 wherein the amino acid sequence KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4) includes at least one amino acid in the D-form.
- 10 56. The method of claim 48 wherein the at least one polypeptide is N-acetylated or C-amidated or both.
57. A method of preventing toxic shock syndrome comprising:
using at least one polypeptide including an amino acid sequence selected from the group consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV
15 (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent of any of the foregoing.
58. The method of claim 57 wherein the toxic shock syndrome is associated with toxic shock syndrome toxin-1 produced by *Staphylococcus aureus*.
59. The method of claim 57 further comprising:
20 locally applying the at least one polypeptide in the vagina.
60. The method of 59 wherein the local application is achieved through a tampon.
61. The method of 57 wherein the at least one polypeptide is associated with a tampon.
62. A method for preventing infection from sexually transmitted diseases comprising:
using a contraceptive together with at least one polypeptide including an amino acid
25 sequence selected from the group consisting KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV (SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent of any of the foregoing.
63. A method of claim 62 wherein the contraceptive is a condom, a diaphragm, or a sponge.
- 30 64. A method of claim 63 wherein at least one polypeptide is carried by a lubricant present on the condom.
65. A method of treating an antibiotic resistant microorganism comprising:
using at least one polypeptide including an amino acid sequence selected from the group consisting of KPV (SEQ. ID. NO. 1), MEHFRWG (SEQ. ID. NO. 2), HFRWGKPV

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(SEQ. ID. NO. 3), SYSMEHFRWGKPV (SEQ. ID. NO. 4), or a biologically functional equivalent of any of the foregoing.

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(21) International Application Number: PCT/FI98/00934 (22) International Filing Date: 1 December 1998 (01.12.98) (30) Priority Data: 974385 1 December 1997 (01.12.97) FI (71) Applicant (for all designated States except US): XYROFIN OY [FI/FI]; PI 213, FIN-48101 Kotka (FI). (72) Inventors; and (75) Inventors/Applicants (for US only): VARGAS MUNITA, Sergio Luis [CL/CL]; Infectious Diseases Division, Calvo Mackenna Hospital, Casilla 215, T Correo Tajamar, Providencia, Santiago (CL). PEARSON, Julita [GB/GB]; 219 Pickhurst Rise, West Wickham, Kent BR4 0QA (GB). VIRKKI, Markku, Tapio [FI/FI]; Laurilahdenkuja 1 C 6, FIN-02320 Espoo (FI). PEPPER, Tammy [GB/GB]; March House, 159 Oatlands Drive, Weybridge, Surrey KT13 9JZ (GB). SAUNDERS, David [GB/GB]; Springhill, 12 Compton Way, Farnham, Surrey GU10 1Q7 (GB). (74) Agent: BORENIUS & CO. OY AB; Kansakoulukuja 3, FIN-00100 Helsinki (FI).		(81) Designated States: AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: THE USE OF POLYOLS IN COMBATING YEAST INFECTION AND POLYOL PREPARATIONS FOR SAID USE		
(57) Abstract The invention relates to the use of polyols such as xylitol for the preparation of a composition to be administered in the treatment or prophylaxis of mucosal yeast infection in mammals, as well as to preparations for use in the systemic or topical therapeutic or prophylactic treatment of mucosal yeast infections. The invention relates specifically but not solely to the combating of infections caused by <i>Candida s.p.</i> in mucosa in connection with exocrine glands of the mammalian body.		

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Claims

1. The use of polyols for the preparation of a composition to be administered in the treatment or prophylaxis of mucosal yeast infection in mammals, comprising mixing at least one pharmacologically acceptable carrier with an amount of polyol sufficient to reduce or inhibit mucosal infection caused by yeasts such as *Candida s.p.* in said mammal.
2. The use according to claim 1 wherein the polyol is selected from the group consisting of xylitol, lactitol, sorbitol, mannitol and mixtures thereof, preferably xylitol.
3. The use according to claims 1 or 2, wherein said yeast is a *Candida s.p.* such as *Candida albicans*.
4. The use according to claim 1, 2 or 3, wherein said mucosal infection is an infection of the mucosa in connection with exocrine glands of the body of said mammal.
5. The use according to claim 1 or 2, wherein said mammal is selected from the group comprising human beings, mammalian pet animals such as cats and dogs, mammalian farm animals such as horses, cattle, pigs, and the like.
6. The use according to any one of the preceding claims, wherein said mucosal yeast infection is an oral infection, especially oral candidiasis.
7. The use according to any one of the preceding claims, wherein said mucosal yeast infection is a vaginal infection.
8. The use according to any one of the preceding claims, wherein said mucosal yeast infection is an udder infection.
9. The use according to any one of the preceding claims, wherein xylitol is incorporated into a pharmaceutical composition to be administered via systemic or topical administration.
10. The use according to claim 9, wherein said composition is prepared in the form of an orally administrable preparation selected from the group comprising a liquid, a tablet, a pill, a chewing gum or tablet, a powder, a spray, a syrup, a sugar substitute, a candy or sweet, an ice-cream, a pet food, an animal feed, and the like, by mixing at least one

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pharmacologically acceptable carrier and an amount of xylitol sufficient to reduce or inhibit the infectious activity of yeasts on the mucosa of said mammal.

11. The use according to claim 10, wherein said composition includes an amount of xylitol sufficient to provide an oral daily intake of about 0.05 to 1.0 g/kg of said mammal, preferably 0.1 to 0.8 g/kg of said mammal, most preferably about 0.2 to 0.5 g/kg of said mammal.

12. The use according to claim 10 or 11, wherein said composition additionally includes another antifungal drug effective against said yeast infection.

13. The use according to claim 9, wherein said composition is prepared in the form of a topically administrable preparation selected from the group comprising a liquid, a spray, an aerosol, a cream, a paste, a cement, an ointment, a jelly or gel, a lubricant, a plaster, a membrane, a mouth wash or rinse, a tooth paste, and eye drops, by mixing at least one topical carrier and an amount of xylitol sufficient to reduce or inhibit the infectious activity of yeasts on the mucosa of said mammal.

14. The use according to claim 7 or 13, wherein said composition is in a form suitable for vaginal yeast infection and xylitol is included in a cream, jelly, lubricant, or liquid or is applied onto the surface of a condom.

15. The use according to claim 8 or 14, wherein said composition is in a form suitable for udder yeast infection and xylitol is included in a spray, dip, or tissue.

16. A device suitable for the treatment or prophylaxis of mucosal yeast infection in mammals, characterized in that it comprises a condom having polyol added thereto for administration of polyol into an orifice of the body, such as vagina.

17. The device according to claim 16, wherein said polyol is xylitol.

18. A method for the therapeutic or prophylactic treatment of mammals suffering from or being subject to an increased risk of mucosal yeast infection, said method comprising administering xylitol to said mammal in an amount which is effective in reducing or inhibiting mucosal infections caused by yeasts such as *Candida s.p* in said mammal, or effective in enhancing the effect of other antifungal drugs used in the treatment of said infection.

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19. The method according to claim 18, wherein said xylitol is mixed with or replaced by another polyol.
20. The method according to claim 18, wherein said yeast is a *Candida s.p.* such as *Candida albicans*.
21. The method according to claim 19 or 20, wherein said mucosal infection is an infection of the mucosa in connection with exocrine glands of the body of said mammal.
22. The method according to claim 19, wherein said mammal is selected from the group comprising human beings, mammalian pet animals such as cats and dogs, mammalian farm animals such as horses, cattle, pigs, and the like.
23. The method according to claim 22, wherein said mammal is a human being suffering from AIDS.
24. The method according to claim 19, wherein said xylitol is administered by systemic or topical administration, alone or in combination with other antifungal drugs.
25. The method according to claim 24, wherein said xylitol is administered orally.
26. The method according to claim 24 or 25, wherein said xylitol is administered as a sugar substitute in the diet of said mammal.
27. The method according to claim 26, wherein said mucosal yeast infection is an oral infection, especially oral candidiasis.
28. The method according to claim 19, wherein said mucosal yeast infection is a vaginal infection.
29. The method according to claim 19, wherein said mucosal yeast infection is mastitis or an udder infection.
30. A composition for use in the therapeutic or prophylactic treatment of mammals suffering from or being subject to an increased risk of mucosal yeast infections, containing at least one pharmacologically acceptable carrier and an amount of xylitol sufficient to

reduce or inhibit mucosal infection caused by yeasts such as *Candida s.p.* in said mammal, or sufficient to enhance the effect of other antifungal drugs used in the treatment of said infection.

31. The composition according to claim 30, wherein said xylitol is mixed with or replaced by another polyol.

32. A pharmaceutical preparation for use in the systemic or topical therapeutic or prophylactic treatment of mucosal yeast infections, said preparation containing at least one pharmacologically acceptable carrier and an amount of polyol sufficient to reduce or inhibit mucosal infection caused by yeasts, such as *Candida s.p.* in said mammal, or sufficient to enhance the effect of other antifungal drugs used in the treatment of said infection.

33. The preparation according to claim 32, which is in the form of an orally administrable preparation selected from the group comprising a liquid, a tablet, a pill, a chewing gum or tablet, a powder, a lozenge, a spray, a syrup, a sugar substitute, a candy or sweet, an ice-cream, pet food, animal feed, and the like, by mixing at least one pharmacologically acceptable carrier and an amount of xylitol sufficient to reduce or inhibit the infectious activity of yeasts on the mucosa of said mammal.

34. The preparation according to claim 33, wherein said preparation includes an amount of xylitol sufficient to provide an oral daily intake of about 0.05 to 1.0 g/kg of said mammal, preferably 0.1 to 0.8 g/kg of said mammal, most preferably about 0.2 to 0.5 g/kg of said mammal.

35. The preparation according to claim 33 or 34, wherein said composition additionally includes another antifungal drug effective against said yeast infection.

36. The preparation according to claim 32, which is in the form of a topically administrable preparation selected from the group comprising a liquid, a spray, an aerosol, a cream, a paste, a cement, an ointment, a jelly or gel, a lubricant, a plaster, a membrane, a mouth wash or rinse, a tooth paste, and eye drops, by mixing at least one topical carrier and an amount of xylitol sufficient to reduce or inhibit the infectious activity of yeasts on the mucosa of said mammal.

37. The preparation according to claim 36, which is in a form suitable for reducing or

inhibiting vaginal yeast infection and xylitol is included in a cream, jelly, lubricant, or liquid or is applied onto the surface of a condom.

38. The preparation according to claim 36, which is in a form suitable for reducing or inhibiting udder yeast infection and xylitol is included in a spray, dip, or tissue.

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WHAT IS CLAIMED IS:

1. A composition comprising a lactic acid-producing bacterial species in a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal and Emu Oil.
- 5 2. The composition of claim 1, wherein said lactic acid-producing bacterial species is a *Bacillus* species selected from the group consisting of: *Bacillus subtilis*, *Bacillus uniflagellatus*, *Bacillus laterosporus*, *Bacillus laterosporus* BOD, *Bacillus megaterium*, *Bacillus polymyxa*, *Bacillus licheniformis*, *Bacillus pumilus*, and *Bacillus sterothermophilus*,
10 *Bacillus coagulans*, *Bacillus thermophilus*, *Bacillus mycoides*, *Bacillus cereus*, and *Bacillus circulans*.
3. The composition of claim 1, wherein said lactic acid-producing bacterial species is a member of the *Lactobacillus* genus selected from the group consisting of: *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus salivarius*, *Lactobacillus delbrukil*,
15 *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Lactobacillus gaserli*, *Lactobacillus jensenii* and *Lactobacillus sporogenes*.
4. The composition of claim 1, wherein said lactic acid-producing bacterial species is a member of the genus *Enterococcus* selected from the group consisting of: *Bacillus facium* and *Enterococcus thermophilus*.
5. The composition of claim 1, wherein said lactic acid-producing bacterial species is a
20 member of the *Bifidobacterium* genus selected from the group consisting of: *Bacillus longum*, *Bacillus infantis*, *Bacillus bifidus*, and *Bacillus bifidum*.
6. The composition of claim 1, wherein said lactic acid-producing bacterial species is a member of the genus *Pseudomonas* selected from a group consisting of: *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas lindbergii*, *Pseudomonas cepacia*,
25 *Pseudomonas florescenes*, and *Pseudomonas* 679-2.
7. The composition of claim 1, wherein said lactic acid-producing bacterial species is a member of the genus selected from a group consisting of: *Micromonospora*, *Sporolactobacillus*, *Micrococcus*, *Berkholderia*, and *Rhodococcus*.
8. The composition of claim 1, wherein said lactic acid-producing bacterial species is a
30 *Bacillus coagulans* strain.

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9. The composition of claim 1, wherein said lactic acid-producing bacterial stain is included in said composition in a form selected from a group consisting of: vegetative cells, a dried bacterial cell mass, a flowable concentrate, a stabilized gel, a stabilized paste, and spores.
- 5 10. The composition of claim 1, wherein said carrier is selected from a group comprising an emulsion, cream, lotion, gel, oil, ointment, suspension, aerosol spray, powder, aerosol powder, or semi-solid formulation.
11. The composition of claim 1, wherein the Emu Oil comprises approximately 0.5 % to approximately 99.9%, by weight of said composition.
- 10 12. The composition of claim 1, wherein the Emu Oil comprises approximately 10% to approximately 75%, by weight of said composition.
13. The composition of claim 1, wherein the Emu Oil comprises approximately 25% to approximately 60%, by weight of said composition.
14. The composition of claim 1, wherein the concentration of the lactic acid-producing
15 bacteria ranges from approximately 1% to approximately 90%, by weight of said composition.
15. The composition of claim 1, wherein the concentration of the lactic acid-producing bacteria ranges from approximately 10% to approximately 75%, by weight of said composition.
16. The composition of claim 1, further comprising one or more compounds selected from
20 a group consisting of: dimethyl sulfoxide (DMSO), methylsulfonylmethane (MSM), and Lignisul MSM.
17. The composition of claim 1, further comprising one or more anti-microbial agents selected from a group consisting of: a quaternary ammonium chloride, an iodine or iodifer compound, a phenolic compound, and an alcohol compound or tincture.
- 25 18. The composition of claim 1, further comprising one or more systemic anti-fungal compounds selected from a group consisting of: Amphotericin B, Dapsone, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, and Miconazole KI.

19. The composition of claim 1, further comprising one or more topical anti-fungal compounds selected from a group consisting of: Amphotericin B, Carbol-Fuchsin, Ciclopirox, Clotrimzole, Econazole, Haloprogin, Ketoconazole, Mafenide, Miconazole, Naftifine, Nystatin, Oxiconazole, Silver Sulfadiazine, Sulconazole, Terbinafine, Tioconazole, Tolnaftate, and Undecylenic acid.
20. The composition of claim 1, further comprising one or more vaginal anti-fungal compounds selected from a group consisting of: Butoconazole, Clotrimazole, Econazole, Gentian Violet, Miconazole, Nystatin, Terconazole, and Tioconazole.
21. A composition comprising an extracellular product of a lactic acid-producing bacterial species in a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal and Emu Oil.
22. The composition of claim 21, wherein said extracellular product is a hydrophilic supernatant or filtrate of a culture of a lactic acid-producing bacterial strain fractionated using a method selected from the group consisting of sub-micron filtration, ion exchange chromatography, and High Performance Liquid Chromatography (HPLC).
23. The composition of claim 21, wherein said extracellular product is derived from a culture of *Bacillus coagulans*.
24. The composition of claim 21, wherein said extracellular product is derived from a culture of a *Pseudomonas lindbergii*.
25. The composition of claim 21, wherein said carrier is selected from a group comprising an emulsion, cream, lotion, gel, oil, ointment, suspension, aerosol spray, powder, aerosol powder, or semi-solid formulation.
26. The composition of claim 21, wherein the Emu Oil comprises approximately 0.5 % to approximately 99.9%, by weight of said composition.
27. The composition of claim 21, wherein the Emu Oil comprises approximately 10% to approximately 75%, by weight of said composition.
28. The composition of claim 21, wherein the Emu Oil comprises approximately 25% to approximately 60%, by weight of said composition.

29. The composition of claim 21, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 1% to approximately 90%, by weight of said composition.
30. The composition of claim 21, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 10% to approximately 75%, by weight of said composition.
31. The composition of claim 21, further comprising one or more compounds selected from a group consisting of: dimethyl sulfoxide (DMSO), methylsulfonylmethane (MSM), and Lignisul MSM.
32. The composition of claim 21, further comprising one or more anti-microbial agents selected from a group consisting of: a quaternary ammonium chloride, an iodine or iodifer compound, a phenolic compound, and an alcohol compound or tincture.
33. The composition of claim 21, further comprising one or more systemic anti-fungal compounds selected from a group consisting of: Amphotericin B, Dapsone, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, and Miconazole KI.
34. The composition of claim 21, further comprising one or more topical anti-fungal compounds selected from a group consisting of: Amphotericin B, Carbol-Fuchsin, Ciclopirox, Clotrimazole, Econazole, Haloprogin, Ketoconazole, Mafenide, Miconazole, Naftifine, Nystatin, Oxiconazole, Silver Sulfadiazine, Sulconazole, Terbinafine, Tioconazole, Tolnaftate, and Undecylenic acid.
35. The composition of claim 21, further comprising one or more vaginal anti-fungal compounds selected from a group consisting of: Butoconazole, Clotrimazole, Econazole, Gentian Violet, Miconazole, Nystatin, Terconazole, and Tioconazole.
36. A composition comprising a lactic acid-producing bacterial species, an extracellular product of a lactic acid-producing bacterial species, a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal, and Emu Oil.

37. The composition of claim 36, wherein said lactic acid-producing bacterial species is a member of the genus selected from a group consisting of: the *Bacillus* genus, the *Lactobacillus* genus, the *Enterococcus* genus, the *Bifidiobacterium* genus, the *Pseudomonas* genus, the *Micromonospora* genus, the *Sporolactobacillus* genus, the *Micrococcus* genus, the *Berkholderia* genus, and the *Rhodococcus* genus.
38. The composition of claim 36, wherein said lactic acid-producing species is *Bacillus coagulans*.
39. The composition of claim 36, wherein said lactic acid-producing bacterial stain is included in said composition in a form selected from a group consisting of: vegetative cells, a dried bacterial cell mass, a flowable concentrate, a stabilized gel, a stabilized paste, and spores.
40. The composition of claim 36, wherein said extracellular product is a hydrophilic supernatant or filtrate of a culture of a lactic acid-producing bacterial strain fractionated using a method selected from the group consisting of sub-micron filtration, ion exchange chromatography, and High Performance Liquid Chromatography (HPLC).
41. The composition of claim 36, wherein said extracellular product is derived from a culture of *Bacillus coagulans*.
42. The composition of claim 36, wherein said extracellular product is derived from a culture of *Pseudomonas lindbergii*.
43. The composition of claim 36, wherein said carrier is selected from a group comprising an emulsion, cream, lotion, gel, oil, ointment, suspension, aerosol spray, powder, aerosol powder, or semi-solid formulation.
44. The composition of claim 36, wherein the Emu Oil comprises approximately 0.5 % to approximately 99.9%, by weight of said composition.
45. The composition of claim 36, wherein the Emu Oil comprises approximately 10% to approximately 75%, by weight of said composition.
46. The composition of claim 36, wherein the Emu Oil comprises approximately 25% to approximately 60%, by weight of said composition.
47. The composition of claim 36, wherein the concentration of the lactic acid-producing bacteria ranges from approximately 1% to approximately 90%, by weight of said composition.

48. The composition of claim 36, wherein the concentration of the lactic acid-producing bacteria ranges from approximately 10% to approximately 75%, by weight of said composition.
49. The composition of claim 36, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 1% to approximately 90%, by weight of said composition.
50. The composition of claim 36, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 10% to approximately 75%, by weight of said composition.
51. The composition of claim 36, further comprising one or more compounds selected from a group consisting of: dimethyl sulfoxide (DMSO), methylsulfonylmethane (MSM), and Lignisul MSM.
52. The composition of claim 36, further comprising one or more anti-microbial agents selected from a group consisting of: a quaternary ammonium chloride, an iodine or iodifer compound, a phenolic compound, and an alcohol compound or tincture.
53. The composition of claim 36, further comprising one or more systemic anti-fungal compounds selected from a group consisting of: Amphotericin B, Dapsone, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, and Miconazole KI.
54. The composition of claim 36, further comprising one or more topical anti-fungal compounds selected from a group consisting of: Amphotericin B, Carbol-Fuchsin, Ciclopirox, Clotrimazole, Econazole, Haloprogin, Ketoconazole, Mafenide, Miconazole, Naftifine, Nystatin, Oxiconazole, Silver Sulfadiazine, Sulconazole, Terbinafine, Tioconazole, Tolnaftate, and Undecylenic acid.
55. The composition of claim 36, further comprising one or more vaginal anti-fungal compounds selected from a group consisting of: Butoconazole, Clotrimazole, Econazole, Gentian Violet, Miconazole, Nystatin, Terconazole, and Tioconazole.

56. A method of preventing bacterial, yeast, fungal or viral infection comprising the topical application, to the skin or a mucous membrane of a mammal, a lactic acid-producing bacterial species in a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal and Emu Oil; and allowing said lactic acid-producing bacterial species and Emu Oil to contact the skin or mucous membrane for sufficient time to inhibit growth of bacteria, yeast, fungus or virus.

57. The method of claim 56, wherein said lactic acid-producing bacterial species is a *Bacillus* species selected from the group consisting of: *Bacillus subtilis*, *Bacillus uniflagellatus*, *Bacillus laterosporus*, *Bacillus laterosporus* BOD, *Bacillus megaterium*,
10 *Bacillus polymyxa*, *Bacillus licheniformis*, *Bacillus pumilus*, and *Bacillus stercorophilus*, *Bacillus coagulans*, *Bacillus thermophilus*, *Bacillus mycoides*, *Bacillus cereus*, and *Bacillus circulans*.

58. The method of claim 56, wherein said lactic acid-producing bacterial species is a member of the *Lactobacillus* genus selected from the group consisting of: *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus salivarius*, *Lactobacillus delbrueckii*,
15 *Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Lactobacillus gasei*, *Lactobacillus jensenii* and *Lactobacillus sporogenes*.

59. The method of claim 56, wherein said lactic acid-producing bacterial species is a member of the genus *Enterococcus* selected from the group consisting of: *Bacillus facium* and *Enterococcus thermophilus*.
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60. The method of claim 56, wherein said lactic acid-producing bacterial species is a member of the *Bifidobacterium* genus selected from the group consisting of: *Bacillus longum*, *Bacillus infantis*, *Bacillus bifidus*, and *Bacillus bifidum*.

61. The method of claim 56, wherein said lactic acid-producing bacterial species is a member of the genus *Pseudomonas* selected from a group consisting of: *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas lindbergii*, *Pseudomonas cepacia*,
25 *Pseudomonas fluorescens*, and *Pseudomonas 679-2*.

62. The method of claim 56, wherein said lactic acid-producing bacterial species is a member of the genus selected from a group consisting of: *Micromonospora*,
30 *Sporolactobacillus*, *Micrococcus*, *Berkholderia*, and *Rhodococcus*.

63. The method of claim 56, wherein said lactic acid-producing bacterial stain is included in said composition in a form selected from a group consisting of: vegetative cells, a dried bacterial cell mass, a flowable concentrate, a stabilized gel, a stabilized paste, and spores.
64. The method of claim 56, wherein said lactic acid-producing bacterial species is a
5 *Bacillus coagulans* strain.
65. The method of claim 56, wherein said carrier is selected from a group comprising an emulsion, cream, lotion, gel, oil, ointment, suspension, aerosol spray, powder, aerosol powder, or semi-solid formulation.
66. The method of claim 56, wherein the Emu Oil comprises approximately 0.5 % to
10 approximately 99.9%, by weight of said composition.
67. The method of claim 56, wherein the Emu Oil comprises approximately 10% to approximately 75%, by weight of said composition.
68. The method of claim 56, wherein the Emu Oil comprises approximately 25% to approximately 60%, by weight of said composition.
- 15 69. The method of claim 56, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 1% to approximately 90%, by weight of said composition.
70. The method of claim 56, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 10% to approximately 75%, by
20 weight of said composition.
71. The method of claim 56, wherein said composition further comprises one or more compounds selected from a group consisting of: dimethyl sulfoxide (DMSO), methylsulfonylmethane (MSM), and Lignisul MSM.
72. The method of claim 56, wherein said composition further comprises one or more anti-
25 microbial agents selected from a group consisting of: a quaternary ammonium chloride, an iodine or iodifer compound, a phenolic compound, and an alcohol compound or tincture.
73. The method of claim 56, wherein said composition further comprises one or more systemic anti-fungal compounds selected from a group consisting of: Amphotericin B, Dapsone, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, and Miconazole
30 KI.

74. The method of claim 56, wherein said composition further comprises one or more topical anti-fungal compounds selected from a group consisting of: Amphotericin B, Carbol-Fuchsin, Ciclopirox, Clotrimzole, Econazole, Haloprogin, Ketoconazole, Mafenide, Miconazole, Naftifine, Nystatin, Oxiconazole, Silver Sulfadiazine, Sulconazole, Terbinafine, Tioconazole, Tolnaftate, and Undecylenic acid.
75. The method of claim 56, wherein said composition further comprises one or more vaginal anti-fungal compounds selected from a group consisting of: Butoconazole, Clotrimazole, Econazole, Gentian Violet, Miconazole, Nystatin, Terconazole, and Tioconazole.
76. The method of claim 56, wherein the step of allowing the lactic acid-producing bacteria to contact the skin or mucous membrane inhibits growth of one or more microbes selected from the group consisting of: *Staphylococcus* species, *Pseudomonas* species, *Clostridium* species, *Escherichia coli*, *Proteus* species, *Klebsiella* species, *Gardnereia vaginails*, *Proponbacterium acnes*, *Aeromonas hydrophia*, *Candida* species, *Trichophyton* species, *Aspergillus* species, *Acremonium* species, *Scopulariopsis* species, Herpes simplex I, Herpes simplex II, and Herpes zoster.
77. A method of preventing bacterial, yeast, fungal or viral infection comprising the topical application, to the skin or a mucous membrane of a mammal, an extracellular product of a lactic acid-producing bacterial species in a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal and Emu Oil; and allowing said extracellular product and Emu Oil to contact the skin or mucous membrane for sufficient time to inhibit growth of bacteria, yeast, fungus, or virus.
78. The method of claim 77, wherein said extracellular product is a hydrophilic supernatant or filtrate of a culture of a lactic acid-producing bacterial strain fractionated using a method selected from the group consisting of sub-micron filtration, ion exchange chromatography, and High Performance Liquid Chromatography (HPLC).
79. The composition of claim 77, wherein said extracellular product is derived from a culture of *Bacillus coagulans*.
80. The composition of claim 77, wherein said extracellular product is derived from a culture of a *Pseudomonas lindbergii*.

81. The method of claim 77, wherein said carrier is selected from a group comprising an emulsion, cream, lotion, gel, oil, ointment, suspension, aerosol spray, powder, aerosol powder, or semi-solid formulation.
82. The method of claim 77, wherein the Emu Oil comprises approximately 0.5 % to
5 approximately 99.9%, by weight of said composition.
83. The method of claim 77, wherein the Emu Oil comprises approximately 10% to approximately 75%, by weight of said composition.
84. The method of claim 77, wherein the Emu Oil comprises approximately 25% to approximately 60%, by weight of said composition.
- 10 85. The method of claim 77, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 1% to approximately 90%, by weight of said composition.
86. The method of claim 77, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 10% to approximately 75%, by
15 weight of said composition.
87. The method of claim 77, further comprising one or more compounds selected from a group consisting of: dimethyl sulfoxide (DMSO), methylsulfonylmethane (MSM), and Lignisul MSM.
88. The method of claim 77, further comprising one or more anti-microbial agents selected
20 from a group consisting of: a quaternary ammonium chloride, an iodine or iodifer compound, a phenolic compound, and an alcohol compound or tincture.
89. The method of claim 77, further comprising one or more systemic anti-fungal compounds selected from a group consisting of: Amphotericin B, Dapsone, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, and Miconazole KI.

90. The method of claim 77, further comprising one or more topical anti-fungal compounds selected from a group consisting of: Amphotericin B, Carbol-Fuchsin, Ciclopirox, Clotrimzole, Econazole, Haloprogin, Ketoconazole, Mafenide, Miconazole, Naftifine, Nystatin, Oxiconazole, Silver Sulfadiazine, Sulconazole, Terbinafine, Tioconazole, Tolnaftate, and Undecylenic acid.

91. The method of claim 77, further comprising one or more vaginal anti-fungal compounds selected from a group consisting of: Butoconazole, Clotrimazole, Econazole, Gentian Violet, Miconazole, Nystatin, Terconazole, and Tioconazole.

92. The method of claim 77, wherein the step of allowing the extracellular product of the lactic acid-producing bacteria to contact the skin or mucous membrane inhibits growth of one or more microbes selected from the group consisting of: *Staphylococcus* species, *Pseudomonas* species, *Clostridium* species, *Escherichia coli*, *Proteus* species, *Klebsiella* species, *Gardnerella vaginalis*, *Propionibacterium acnes*, *Aeromonas hydrophila*, *Candida* species, *Trichophyton* species, *Aspergillus* species, *Acremonium* species, *Scopulariopsis* species, Herpes simplex I, Herpes simplex II, and Herpes zoster.

93. A method of preventing bacterial, yeast, fungal or viral infection comprising the topical application, to the skin or a mucous membrane of a mammal, a lactic acid-producing bacterial species, an extracellular product of a lactic acid-producing bacterial in a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal and Emu Oil; and allowing said lactic acid-producing bacteria, extracellular product, and Emu Oil to contact the skin or mucous membrane for sufficient time to inhibit growth of bacteria, yeast, fungus or virus.

94. The method of claim 93, wherein said lactic acid-producing bacterial species is a member of the genus selected from a group consisting of: the *Bacillus* genus, the *Lactobacillus* genus, the *Enterococcus* genus, the *Bifidobacterium* genus, the *Pseudomonas* genus, the *Micromonospora* genus, the *Sporolactobacillus* genus, the *Micrococcus* genus, the *Berkholderia* genus, and the *Rhodococcus* genus.

95. The method of claim 93, wherein said lactic acid-producing species is *Bacillus coagulans*.

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(H2)

96. The method of claim 93, wherein said lactic acid-producing bacterial stain is included in a form selected from a group consisting of: vegetative cells, a dried bacterial cell mass, a flowable concentrate, a stabilized gel, a stabilized paste, and spores.
97. The method of claim 93, wherein said extracellular product is a hydrophilic
5 supernatant or filtrate of a culture of a lactic acid-producing bacterial strain fractionated using a method selected from the group consisting of sub-micron filtration, ion exchange chromatography, and High Performance Liquid Chromatography (HPLC).
98. The composition of claim 93, wherein said extracellular product is derived from a culture of *Bacillus coagulans*.
- 10 99. The composition of claim 93, wherein said extracellular product is derived from a culture of a *Pseudomonas lindbergii*.
100. The method of claim 93, wherein said carrier is selected from a group comprising an emulsion, cream, lotion, gel, oil, ointment, suspension, aerosol spray, powder, aerosol powder, or semi-solid formulation.
- 15 101. The method of claim 93, wherein the Emu Oil comprises approximately 0.5 % to approximately 99.9%, by weight of said composition.
102. The method of claim 93, wherein the Emu Oil comprises approximately 10% to approximately 75%, by weight of said composition.
103. The method of claim 93, wherein the Emu Oil comprises approximately 25% to
20 approximately 60%, by weight of said composition.
104. The method of claim 93, wherein the concentration of the lactic acid-producing bacteria ranges from approximately 1% to approximately 90%, by weight of said composition.
105. The method of claim 93, wherein the concentration of the lactic acid-producing bacteria ranges from approximately 10% to approximately 75%, by weight of said
25 composition.
106. The method of claim 93, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 1% to approximately 90%, by weight of said composition.

107. The method of claim 93, wherein the concentration of the lactic acid-producing bacterial extracellular product ranges from approximately 10% to approximately 75%, by weight of said composition.
108. The method of claim 93, further comprising one or more compounds selected from a group consisting of: dimethyl sulfoxide (DMSO), methylsulfonylmethane (MSM), and Lignisul MSM.
109. The method of claim 93, further comprising one or more anti-microbial agents selected from a group consisting of: a quaternary ammonium chloride, an iodine or iodifer compound, a phenolic compound, and an alcohol compound or tincture.
110. The method of claim 93, further comprising one or more systemic anti-fungal compounds selected from a group consisting of: Amphotericin B, Dapsone, Fluconazole, Flucytosine, Griseofulvin, Itraconazole, Ketoconazole, and Miconazole KI.
111. The method of claim 93, further comprising one or more topical anti-fungal compounds selected from a group consisting of: Amphotericin B, Carbol-Fuchsin, Ciclopirox, Clotrimazole, Econazole, Haloprogin, Ketoconazole, Mafenide, Miconazole, Naftifine, Nystatin, Oxiconazole, Silver Sulfadiazine, Sulconazole, Terbinafine, Tioconazole, Tolnaftate, and Undecylenic acid.
112. The method of claim 93, further comprising one or more vaginal anti-fungal compounds selected from a group consisting of: Butoconazole, Clotrimazole, Econazole, Gentian Violet, Miconazole, Nystatin, Terconazole, and Tioconazole.
113. The method of claim 93, wherein the step of allowing the extracellular product of the lactic acid-producing bacteria to contact the skin or mucous membrane inhibits growth of one or more microbes selected from the group consisting of: *Staphylococcus* species, *Pseudomonas* species, *Clostridium* species, *Escherichia coli*, *Proteus* species, *Klebsiella* species, *Gardnereia vaginails*, *Propionbacterium acnes*, *Aeromonas hydrophilia*, *Candida* species, *Trichophyton* species, *Aspergillus* species, *Acremonium* species, *Scopulariopsis* species, Herpes simplex I, Herpes simplex II, and Herpes zoster.

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114. An article of manufacture comprising a flexible article and an effective amount of a lactic acid-producing bacterial species in a pharmaceutically-acceptable carrier which is suitable for topical application to skin or a mucous membrane of a mammal and Emu Oil, applied to said flexible article, wherein said flexible article is intended to be worn by or
5 attached to skin or a mucous membrane of a mammal so as to allow the indigenous anti-microbial activity of the extracellular product derived from the lactic acid-producing bacterial species to occur adjacent to, or on the skin or mucous membrane.

115. The article of manufacture of claim 114, wherein said lactic acid-producing bacterial species is a member of the genus selected from a group consisting of: the *Bacillus* genus, the
10 *Lactobacillus* genus, the *Enterococcus* genus, the *Bifidiobacterium* genus, the *Pseudomonas* genus, the *Micromonospora* genus, the *Sporolactobacillus* genus, the *Micrococcus* genus, the *Berkholderia* genus, and the *Rhodococcus* genus.

116. The article of manufacture of claim 114, wherein said lactic acid-producing bacterial species is a *Bacillus coagulans* strain.

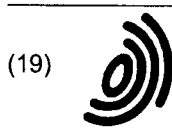
15 117. The article of manufacture of claim 114, wherein said article of manufacture is selected from the group consisting of: a diaper, a pliable material for wiping skin or a mucous membrane, a dermal patch, adhesive tape, an absorbent pad, a tampon, a feminine hygiene napkin, and an article of clothing.

118. The article of manufacture of claim 114, wherein the applying step comprises
20 impregnating said composition into a fibrous or non-fibrous solid matrix.

119. The article of manufacture of claim 114, further comprising an extracellular product derived from a hydrophilic supernatant or filtrate of a culture of a lactic acid-producing bacterial strain fractionated using a method selected from the group consisting of sub-micron filtration, ion exchange chromatography, and High Performance Liquid Chromatography
25 (HPLC).

120. The article of manufacture of claim 119, wherein said extracellular product is derived from a culture of *Bacillus coagulans*.

121. The article of manufacture of claim 119, wherein said extracellular product is derived from a culture of a *Pseudomonas lindbergii*.



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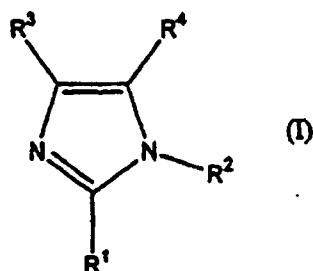
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(54) **NITROIMIDAZOLE EXTERNAL PREPARATIONS FOR DERMATOSIS**

(57) An external preparation for skin disease which comprises a nitroimidazole derivative represented by the following formula (I):



wherein R¹, R³ and R⁴ may be the same or different and represent a hydrogen atom, a nitro group, a lower alkyl group, a substituted lower alkyl group, a lower alkenyl group, or a substituted lower alkenyl group; and R² represents a hydrogen atom, a lower alkyl group, a substituted lower alkyl group and a lower alkenyl group or a substituted lower alkenyl group, provided that any one of R¹, R³ and R⁴ is a nitro group.

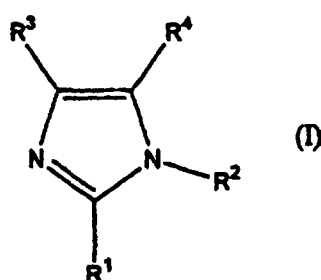
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[0833] The external preparations of the present invention exhibited no changes in appearance or pH, and did not exhibit any significant changes in content or viscosity.

[0834] Thus, the external preparations provided by the present invention were clearly determined to be pharmacologically stable.

Claims

1. An external preparation for therapeutic or prophylactic treatment, or amelioration of skin disease which comprises a nitroimidazole derivative represented by the following formula (I), a pharmaceutically acceptable salt thereof, an ester thereof or other derivatives thereof as an active ingredient:



wherein R^1 , R^3 and R^4 may be the same or different and each independently represents a hydrogen atom, a nitro group, a lower alkyl group, a lower alkyl group substituted by 1 or more substituents which may be the same or different selected from Substituent group α and Substituent group β , a lower alkenyl group, or a lower alkenyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group α and the Substituent group β ; and R^2 represents a hydrogen atom, a lower alkyl group, a lower alkyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group α and the Substituent group β , a lower alkenyl group or a lower alkenyl group substituted by 1 or more substituents, which may be the same or different selected from the Substituent group α and the Substituent group β , provided that any one of R^1 , R^3 and R^4 is a nitro group, wherein.

The Substituent group α comprises

a lower alkyloxy group, a lower alkyloxy group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β , a lower alkylcarbonyloxy group, a lower alkylcarbonyloxy group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β , a lower alkylsulfonyl group, a lower alkylsulfonyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β , a cycloalkyl group, a cycloalkyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β , a heteroaryl group, a heteroaryl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β , an aryl group and an aryl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group β ; and

the Substituent group β comprises

a hydroxy group, a mercapto group, a halogen atom, an amino group, a lower alkylamino group, a lower alkyloxy group, a lower alkenyl group, a cyano group, a carboxy group, a carbamoyloxy group, a carboxamide group, a thiocarboxamide group and a morpholino group.

2. The external preparation according to Claim 1, wherein R^4 is a nitro group.
3. The external preparation according to Claim 2, wherein R^1 and R^2 are the same or different and represent a lower alkyl group, a lower alkyl group substituted by 1 or more substituents selected from the Substituent group α and the Substituent group β , a lower alkenyl group, or a lower alkenyl group substituted by 1 or more substituents which may be the same or different selected from the Substituent group α and the Substituent group β , and R^3 is a hydrogen atom.
4. The external preparation according to Claim 3, wherein the Substituent group α is a lower alkyloxy group and the Substituent group β is a hydroxy group, an amino group, a halogen atom, a cycloalkyl group, a heteroaryl group

or an aryl group.

5. The external preparation according to Claim 4, wherein the Substituent group β is a hydroxy group, an amino group, a halogen atom or a heteroaryl group.
6. The external preparation according to Claim 5, wherein R^1 is a lower alkyl group.
7. The external preparation according to any one of Claims 5 and 6, wherein R^2 is a lower alkyl group substituted by a hydroxy group.
8. The external preparation according to Claim 4, which comprises 2-(2-methyl-5-nitroimidazole-1-yl)ethanol (general name: metronidazole), a pharmaceutically acceptable salt thereof, an ester thereof or other derivatives thereof as an active ingredient.
9. The external preparation according to Claim 3, wherein the Substituent group α is a lower alkylsulfonyl group or a lower alkylsulfonyl group substituted by substituents which may be the same or different selected from the Substituent group β and the Substituent group β is a hydroxy group, a halogen atom, an amino group, a lower alkylamino group, a lower alkyloxy group, a lower alkenyl group, a cyano group, a carboxy group, a cycloalkyl group or an aryl group.
10. The external preparation according to Claim 9, wherein R^1 is a lower alkyl group or lower alkyl group substituted by substituents which may be the same or different selected from the Substituent group β .
11. The external preparation according to Claim 9 or 10, wherein R^2 is a lower alkylsulfonyl group or a lower alkyl group substituted by a lower alkylsulfonyl group substituted by substituents which may be the same or different selected from the Substituent group β .
12. The external preparation according to Claim 9, which comprises 1-(2-ethylsulfonyl-ethyl)-2-methyl-5-nitroimidazole (general name: tinidazole) or a pharmaceutically acceptable salt thereof as an active ingredient.
13. The external preparation which comprises at least one compound of the nitroimidazole derivatives as defined in any one of Claims 1 to 12 and at least one medicine selected from the group consisting of an antimycotic agent, antibacterial agent, sulfa, immunosuppressant, antiinflammatory agent, antibiotic, antiviral agent, metabolic antagonist, antihistamine, tissue repair promoter, vitamin, antiallergic, local anesthetic, hair agent and steroid being administered simultaneously or separately with an interval.
14. The external preparation according to Claim 13, wherein the antimycotic agent, the antibacterial agent, the sulfa, the immunosuppressant, the antiinflammatory agent, the antibiotic, the antiviral agent, the metabolic antagonist, the antihistamine, the tissue repair promoter, the vitamin, the antiallergic, the local anesthetic, the hair agent or the steroids is used with a concentration at which the agent itself does not demonstrate any pharmacological effect.
15. The external preparation according to any one of Claims 1 to 14, which further comprises crotamiton.
16. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is atopic dermatitis.
17. The external preparation according to Claim 16, wherein the skin disease is facial atopic dermatitis.
18. The external preparation according to Claim 16 or 17, wherein the skin disease is infant atopic dermatitis.
19. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is blotches, pigmentation or scars of the skin.
20. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is psoriasis.
21. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is hircus, body odor or osmidrosis.
22. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is contact dermatitis,

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plant dermatitis or insect bites.

23. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is dermal pruritis or drug rash.

24. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is chilblain.

25. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is erythroderma.

26. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is tinea.

27. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is suppurative skin disease.

28. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is pressure sore.

29. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is wound.

30. The external preparation according to any one of Claims 1 to 15, wherein the skin disease is palmoplantar pustulosis, lichen planus, lichen nitidus, pityriasis rubra pilaris, pityriasis rosea, erythema (including polymorphic exudative erythema, erythema nodosum and Darier's erythema annulare centrifugum), discoid lupus erythematosus, drug rash and toxic rash, alopecia areata, burns (including scars and keloids), pemphigus, Dühring dermatitis herpetiformis (including pemphigoid), seborrheic dermatitis, dermal stomatitis, Candidiasis (including interdigital erosion, intertrigo, dermal Candidiasis, infantile parasitic erythema, perionychia and vaginal Candidiasis) or tinea versicolor.

31. The external preparation according to any one of Claims 1 to 30, wherein the form is selected from cream, lotion, shampoo, gel, rinse, face lotion wash, milky lotion, paste, shaving cream, foundation, cologne, pack, ointment, patch, semi-solid, solid or liquid.

32. The external preparation according to any one of Claims 1 to 31, wherein a concentration of the nitroimidazole derivative is 1.5 to 10 % by weight based on the amount of the preparation.

33. Use of the nitroimidazole derivative as claimed in any one of Claims 1 to 12 for production of an external preparation used for therapeutic or prophylactic treatment of atopic dermatitis.

34. Use of the nitroimidazole derivative as claimed in any one of Claims 1 to 12 for production of an external preparation used for amelioration of bloches, pigmentation or scars.

35. Use of the nitroimidazole derivative as claimed in any one of Claims 1 to 12 for production of an external preparation used for therapeutic or prophylactic treatment of psoriasis.

36. Use of the nitroimidazole derivative as claimed in any one of Claims 1 to 12 for production of an external preparation used for therapeutic or prophylactic treatment of hircus, body odor or osmidrosis.

37. A therapeutic or prophylactic treatment of atopic dermatitis utilizing the external preparation as claimed in any one of Claims 1 to 15.

38. Amelioration of bloches, pigmentation or scars utilizing the external preparation as claimed in any one of Claims 1 to 15.

39. A therapeutic or prophylactic treatment of psoriasis utilizing the external preparation as claimed in any one of Claims 1 to 15.

40. A therapeutic or prophylactic treatment of hircus, body odor or osmidrosis utilizing the external preparation as claimed in any one of Claims 1 to 15.

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(54) Title: NOVEL METHODS OF TREATING LOCAL FUNGAL AND BACTERIAL INFECTIONS

(57) Abstract: This invention relates to novel compositions, methods of use, regimens and kits for treating local fungal and bacterial infections that are susceptible to treatment administered either locally or topically and systemically. The methods of this invention relate to ways in which to relieve symptoms of such infections in an unexpectedly shorter timespan than with conventional treatment with greater predictability than those methods currently known.

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WHAT IS CLAIMED IS:

1. A method of treating a local fungal or bacterial infection comprising oral administration of an effective amount of anti-infective agent and
5 concurrent local administration of an external topical composition comprising an effective amount of a topical relief agent to ameliorate local symptoms.
2. A method of treating a local fungal infection comprising oral administration of an antifungal-effective amount of an antifungal agent and concurrent
10 local administration of an external topical composition comprising an antifungal agent
3. A method of treating a vaginal fungal infection comprising oral administration of an antifungal-effective amount of an antifungal agent
15 and concurrent vulvar administration of an external topical composition comprising an antifungal agent.
4. A method of treating a vaginal fungal infection comprising oral administration of fluconazole and concurrent vulvar administration of an external topical composition comprising fluconazole.
- 20 5. A method of treating a vaginal fungal infection comprising oral administration of fluconazole in an amount of from about 75 to about 150 mg/day for one to three days and concurrent vulvar administration of an external topical composition comprising an antifungal agent selected from the group consisting of miconazole nitrate, fluconazole, terconazole,
25 butoconazole, clotrimazole, and combinations thereof.
6. A method of treating a vaginal fungal infection comprising oral administration of fluconazole in an amount of from about 75 to about 150 mg/day and concurrent vulvar administration of an external topical composition comprising an anti-inflammatory agent.
- 30 7. A method of treating a vaginal fungal infection comprising oral administration of fluconazole in an amount of from about 125 to about 150 mg and concurrent vulvar administration of an external topical composition comprising an emollient agent.

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8. A method of treating a vaginal bacterial infection comprising oral administration of metronidazole in an amount of from about 500 single oral dose and concurrent vulvar administration of an external topical composition comprising 0.75% metronidazole gel.
- 5 9. A method of treating a local viral infection comprising oral administration of acyclovir (Zovirax), famcyclovir (Famvir), valcyclovir (Valtrex) in a daily dosage of from about 250 mg to about 2000 mg/day and concurrent local administration of an external topical composition comprising emollient or local anesthetic ingredients.
- 10 10. A kit comprising an oral dosage form of fluconazole and an external topical composition.
11. An applicator containing an external topical composition comprising stick, wipe, sanitary pad, pantyliner, wash, spray and roll-on.
12. A method of treating a topical infection comprising oral administration of an effective amount of anti-infective agent and concurrent local administration of an external topical composition comprising an effective amount of a topical relief agent to ameliorate local symptoms.
- 15 13. A method according to claim 12 wherein said oral administration comprises administering a composition comprising fluconazole and said topical composition comprises miconazole nitrate.
- 20 14. A method of treating onychomycosis comprising oral administration of an effective amount of anti-fungal agent and concurrent local administration of an external composition to a nail affected by onychomycosis comprising an effective amount of an anti-fungal agent to ameliorate local symptoms.
- 25 15. A method of treating a local bacterial infection comprising oral administration of an effective amount of anti-infective agent and concurrent local administration of an external topical composition comprising an effective amount of a topical relief agent to ameliorate local symptoms.
- 30 16. A method according to claim 14 wherein said anti-fungal agent is fluconazole.

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United States Patent [19]
Haslam et al.

[11] **Patent Number:** 4,478,822
[45] **Date of Patent:** Oct. 23, 1984

[54] **DRUG DELIVERY SYSTEM UTILIZING
THERMOSETTING GELS**

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[21] **Appl. No.:** 495,239

[22] **Filed:** May 16, 1983

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A61K 31/135; A61K 31/54; A61K 31/415;
A61K 31/435; A61K 31/19; A61K 31/66

[52] **U.S. Cl.** 424/78; 424/285;
424/300; 424/85; 424/309; 424/311; 424/94;
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424/116; 424/324; 424/326; 424/177; 424/330;
424/343; 424/180; 424/181; 424/209; 424/211;
424/220; 424/221; 424/224; 424/230; 424/238;
424/243; 424/246; 424/248.51; 424/251;
424/253; 424/254; 424/256; 424/258; 424/263;
424/265; 424/267; 424/270; 424/271; 424/273
P; 424/273 R; 424/274; 424/275; 424/283

[58] **Field of Search** 424/78, 85, 94, 177,
424/180, 181, 209, 211, 220, 221, 224, 230, 238,
243, 246, 248.51, 251, 253, 254, 256, 258, 263,
265, 267, 270, 271, 273 P, 273 R, 274, 275, 283,
285, 300, 309, 311, 313, 317, 321, 322, 324, 326,
330, 343

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T. L. Whateley.

Primary Examiner—Douglas W. Robinson
Attorney, Agent, or Firm—Manfred Polk; Michael C.
Sudol, Jr.

[57] **ABSTRACT**

This invention relates to a unique drug delivery system
for delivering drugs to a body cavity. The drug delivery
system comprises a medicament and a polymer such
that the drug delivery system is a liquid at room tempera-
ture but forms a semi-solid or gel at the body tempera-
ture in the body cavity.

55 Claims, 1 Drawing Figure

EXAMPLE 6

Sodium acetate	2%
Tetronic ® 1307	21%
Benzalkonium chloride	0.01%
pH adjusted with HCl to 5	
sufficient purified water to	100%
gel-sol transition temperature	25° C.

EXAMPLE 7

	Solution 1	Solution 2
Timolol maleate	0.68%	0.68%
Tetronic ® 1307	22%	27%
pH adjusted with HCl to	4	4
sufficient purified water	100%	100%
gel-sol transition temperature	30° C.	26° C.

If the pharmaceutical compositions of Example 1-7 were compared with similar compositions but without the polymer, it would be expected that the compositions of Examples 1-7 would result in greater sustained concentrations of the drug at the site of administration.

Following the procedure of Examples 1-7 one can use an appropriate amount of the polymers listed below in place of the Tetronic ®1307 or Tetronic ®1508 polymer used in Examples 1-7.

Tetronic 1107

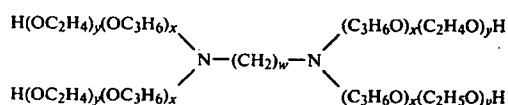
Tetronic 908

Tetronic 707

Following the procedure of Examples 1-7 one can use an appropriate amount of the drugs previously enumerated in this application.

What is claimed is:

1. An aqueous pharmaceutical composition for rectal, urethral, nasal, vaginal, optical or oral in the buccal pouch administration to a body cavity to treat a condition requiring pharmacological treatment comprising
 - a. 10% to 50% by weight of a polymer of the formula:



wherein w is an integer of from 2-6 containing approximately 40% to 80% poly(oxyethylene) and approximately 20 to 60% poly(oxypropylene) and having a molecular weight of 7,000 to 50,000; and x and y are any integers within the above constraints; and

- b. a pharmacologically effective amount of drug selected from the group consisting of anti-bacterial substances, antihistamines and decongestants, anti-inflammatories, anti-parasitics, antiviral, local anesthetics, antifungal, amebicidal, or trichomonocidal agents, analgesics, antiarthritics, antiasthmatics, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, and muscle relaxants and anti-protozoals; and
- c. a pharmaceutically acceptable acid or base being in sufficient quantity to adjust the pH of the composition

tion to range from 2 to 9 and wherein the composition is liquid at about room temperature or below.

2. The composition of claim 1 wherein the polymer is one wherein w is 2.

3. The composition of claim 1 wherein the polymer is Tetronic ®1307.

4. The composition of claim 1 wherein the gel-sol transition temperature of the composition is room temperature or below and said composition is liquid at this temperature.

5. The composition of claim 1 wherein the antibacterial substances are selected from the group consisting of beta-lactam antibiotics, tetracyclines, chloramphenicol, neomycin, gramicidin, bacitracin, sulfonamides, aminoglycoside antibiotics, tobramycin, nitrofurazone, nalidixic acid and analogs and the antimicrobial combination of fludalanine/pentizidone.

6. The composition of claim 1 wherein the antihistaminics and decongestants are selected from the group consisting of perilamine, chlorpheniramine, tetrahydrozoline and antazoline.

7. The composition of claim 1 wherein the anti-inflammatory drugs are selected from the group consisting of cortisone, hydrocortisone, betamethasone, dexamethasone, fluocortolone, prednisolone, triamcinolone, indomethacin, sulindac and its salts and corresponding sulfide.

8. A composition of claim 1 wherein the antiparasitic compound is ivermectin.

9. The composition of claim 1 wherein the antiviral effective compounds are selected from the group consisting of acyclovir and interferon.

10. A composition of claim 1 wherein the local anesthetics are selected from the group consisting of benzocaine, lidocaine and procaine.

11. The composition of claim 1 wherein the antifungal, antiprotozoal, amebicidal or trichomonocidal agent is selected from the group consisting of polyoxyethylene nonylphenol, alkylaryl sulfonate, oxyquinoline sulfate, miconazole nitrate, sulfanilamide, condicidin, sulfisoxazole, nystatin, clotrimazole, metronidazole, chloramphenicol, chloroquine, trimethoprim or sulfamethoxazole.

12. The composition of claim 1 wherein the analgesic drug is selected from the group consisting of diflunisal, aspirin or acetaminophen.

13. The composition of claim 1 wherein the antiarthritics are selected from the group consisting of phenylbutazone, indomethacin, sulindac, dexamethasone, ibuprofen, allopurinol, oxyphenbutazone or probenecid.

14. The composition of claim 1 wherein the antiasthma drugs are selected from the group consisting of theophylline, ephedrine, beclomethasone dipropionate and epinephrine.

15. The composition of claim 1 wherein the anticoagulants are selected from the group consisting of heparin, bishydroxycoumarin, and warfarin.

16. The composition of claim 1 wherein the anticonvulsants are selected from the group consisting of diphenylhydantoin and diazepam.

17. The composition of claim 1 wherein the antidepressants are selected from the group consisting of amitriptyline, chlordiazepoxide, perphenazine, protriptyline, imipramine and doxepin.

18. The composition of claim 1 wherein the antidiabetics are selected from the group consisting of insulin, tolbutamide, tolazamide, acetohexamide and chlorpropamide.

19. The composition of claim 1 wherein the antineoplastics are selected from the group consisting of adriamycin, fluorouracil, methotrexate and asparaginase.

20. The composition of claim 1 wherein the antipsychotics are selected from the group consisting of prochlorperazine lithium carbonate, lithium citrate, thioridazine, molindone, fluphenazine, trifluoperazine, perphenazine, amitriptyline and triflupromazine.

21. The composition of claim 1 wherein the antihypertensives are selected from the group consisting of spironolactone, methyl dopa, hydralazine, clonidine, chlorothiazide, deserpidine, timolol, propranolol, metoprolol, prazosin hydrochloride and reserpine.

22. The composition of claim 1 wherein the muscle relaxants are selected from the group consisting of melphalan, danbrolene, cyclobenzoprine, methocarbamol and diazepam.

23. The composition of claim 1 which includes a buffering agent or salt of from 0 to 5% by weight of the composition.

24. The composition of claim 23 wherein the buffering agent or salt is selected from the group consisting of alkali or alkali earth carbonates, chlorides, sulfates, phosphates, bicarbonates, citrates, borates, acetates and succinates.

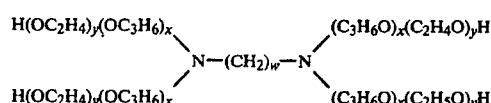
25. The composition of claim 1 which includes from 0.001% to 5% by weight of the composition of a preservative.

26. The composition of claim 25 wherein the preservatives are selected from the group consisting of sodium bisulfite, sodium thiosulfate, ascorbate, benzalkonium chloride, chlorobutanol, thimerosal, phenylmercuric borate, parabens, benzylalcohol and phenylethanol.

27. The composition of claim 1 wherein the acid or base is selected from the group consisting of hydrochloric acid or sodium hydroxide.

28. A method of treating a condition requiring pharmacological treatment which comprises administering rectal, urethral, nasal, vaginal, optical or oral in the buccal pouch to a body cavity a liquid drug delivery device comprising:

a. 10% to 50% by weight of a polymer of the formula



wherein w is an integer of from 2 to 6 containing approximately 40% to 80% poly(oxyethylene) and approximately 20-60% poly(oxypropylene) and having a molecular weight of 7,000 to 50,000; and x and y are any integers within the above constraints; and

b. a pharmacologically effective amount of drug selected from the group consisting of antibacterial substances, antihistamines and decongestants, anti-inflammatories, antiparasitics, antivirals, local anesthetics, antifungal, amebicidal, or trichomonocidal agents, analgesics, antiarthritics, antiasthmatics, anticoagulants, anticonvulsants, antidepressants, antidiabetics, antineoplastics, antipsychotics, antihypertensives, muscle relaxants and antiprotozoals; and

c. a pharmaceutically acceptable acid or base being in sufficient quantity to adjust the pH of the composition

tion to range from 2 to 9 and wherein the composition is liquid at about room temperature or below.

29. A method of treatment according to claim 28 wherein the polymer is one wherein w is 2.

30. A method of treatment according to claim 23 wherein the polymer is Tetronic®1307.

31. A method of treatment according to claim 28 wherein the gel-sol transition temperature of the composition is room temperature or below and said composition is liquid at this temperature.

32. A method of treatment of claim 28 wherein said pharmaceutical composition is administered rectally, urethrally, nasally, vaginally, otically or orally within the buccal pouch.

33. A method of treatment according to claim 28 wherein the antibacterial substances are selected from the group consisting of beta-lactam antibiotics, tetracyclines, chloroamphenicol, neomycin, gramicidin, bacitracin, sulfonamides, aminoglycoside antibiotics, tobramycin, nitrofurazone, nalidixic acid and analogs and the antimicrobial combination of fludalanine/pentizidone.

34. A method of treatment according to claim 28 wherein the antihistaminics and decongestants are selected from the group consisting of perilamine, chlorpheniramine, tetrahydrozoline and antazoline.

35. A method of treatment according to claim 28 wherein the anti-inflammatory drugs are selected from the group consisting of cortisone, hydrocortisone, betamethasone, dexamethasone, fluocortolone, prednisolone, triamcinalone, sulindac and its salts and corresponding sulfide.

36. A method of treatment of claim 28 wherein the antiparasitic compound is ivermectin.

37. A method of treatment according to claim 28 wherein the antiviral effective compounds are selected from the group consisting of acyclovir and interferon.

38. A method of treatment according to claim 28 wherein the local anesthetics are selected from the group consisting of benzocaine, lidocaine and procaine.

39. A method of treatment according to claim 28 wherein the antifungal, antiprotozoal, amebicidal or trichomonocidal agent is selected from the group consisting of polyoxyethylene nonylphenol, alkylaryl sulfonate, oxyquinoline sulfate, miconazole nitrate, sulfonamide, condicidin, sulfisoxazole, nystatin, clotrimazole, metronidazole, chloramphenicol, chloroquine, trimethoprim or sulfamethoxazole.

40. A method of treatment according to claim 28 wherein the analgesic drug is selected from the group consisting of diflunisal, aspirin or acetaminophen.

41. A method of treatment according to claim 28 wherein the antiarthritics are selected from the group consisting of phenylbutazone, indomethacin, sulindac and its salts and corresponding sulfide, dexamethasone, ibuprofen, allopurinol, oxyphenbutazone or probenecid.

42. A method of treatment according to claim 28 wherein the antiasthma drugs are selected from the group consisting of theophylline, ephedrine, beclomethasone dipropionate and epinephrine.

43. A method of treatment according to claim 28 wherein the anticoagulants are selected from the group consisting of heparin, bishydroxycoumarin, and warfarin.

44. A method of treatment according to claim 28 wherein the anticonvulsants are selected from the group consisting of diphenylhydantoin and diazepam.

45. A method of treatment according to claim 28 wherein the antidepressants are selected from the group

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consisting of amitriptyline, chlordiazepoxide perphenazine, protriptyline, imipramine and doxepin.

46. A method of treatment according to claim 28 wherein the antidiabetics are selected from the group consisting of insulin, tolbutamide, tolazamide, acetohexamide and chlorpropamide.

47. A method of treatment according to claim 28 wherein the antineoplastics are selected from the group consisting of adriamycin, flurouracil, methotrexate and asparaginase.

48. A method of treatment according to claim 28 wherein the antipsychotics are selected from the group consisting of prochlorperazine lithium carbonate, lithium citrate, thioridazine, molindone, fluphenazine, trifluoperazine, perphenazine, amitriptyline and triflupromazine.

49. A method of treatment according to claim 28 wherein the antihypertensives are selected from the group consisting of spironolactone, methyldopa, hydralazine, clonidine, chlorothiazide, deserpidine, timolol, propranolol, metoprolol, prazosin hydrochloride and reserpine.

50. A method of treatment according to claim 28 wherein the muscle relaxants are selected from the

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group consisting of melphalan, danbrolene, cyclobenzaprine, methocarbamol and diazepam.

51. A method of treatment according to claim 28 wherein the composition includes a buffering agent or salt of from 0% to 5% by weight of the composition.

52. A method of treatment according to claim 51 wherein the buffering agent or salt is selected from the group consisting of alkali or alkali earth carbonates, chlorides, sulfates, phosphates, bicarbonates, citrates, borates, acetates and succinates.

53. A method of treatment according to claim 28 wherein the composition includes from 0.001% to 5% by weight of the composition of a preservative.

54. A method of treatment according to claim 53 wherein the preservatives are selected from the group consisting of sodium bisulfite, sodium thiosulfate, ascorbate, benzalkonium chloride, chlorobutanol, thimerosal, phenylmercuric borate, parabens, benzylalcohol and phenylethanol.

55. A method of treatment according to claim 28 wherein the acid or base is selected from the group consisting of hydrochloric acid or sodium hydroxide.

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UNITED STATES PATENT OFFICE

2,345,854

POCKET SPRAY DEVICE

Samuel L. Margolies, Brooklyn, N. Y.

Application September 10, 1940, Serial No. 356,151

1 Claim. (Cl. 299—89)

This invention relates to pocket spray devices and more particularly relates to atomizers and spray devices for perfumes, cosmetics, medicinals and the like, having parts which can be fitted into approximately the size of an ordinary fountain pen or pencil, and thus when carried will simulate a pen or pencil both in size and in shape.

It has previously been proposed to provide spray devices which allegedly can be carried in the pocket of the user, but such devices have either been bulky, and thus inconvenient to carry, or, even if of small enough size to render carriage convenient, have been leaky and thus impractical for the purpose intended.

It is an object of this invention to provide a pocket spray device which may conveniently be fitted within an outside casing of substantially the size and shape of an ordinary fountain pen.

It is a further object of this invention to provide a spray device having a combination of parts which will produce a finely divided spray of the material stored in the device, which parts may be mounted within a casing substantially the size and shape of an ordinary fountain pen.

It is an object of this invention to provide a pocket spray device having the liquid containing portion and the air containing portion completely separable so that the two parts may be carried separately and may be replaced individually so that loss or destruction of one part will not necessitate discarding the other part.

It is a further object of the invention to provide such pocket spray device or atomizer which will be completely leak-proof when not in use.

It is a further object of the invention to provide a pocket spray device which may be simply and conveniently operated.

Further objects and advantages will appear from the following description and the drawings appended thereto in which

Figure 1 is a longitudinal section of a spray device embodying the principles of this invention;

Figure 2 is a longitudinal section of a modified form of spray device;

Figure 3 is a section taken on the line 3—3 of Fig. 1;

Figure 4 is a section similar to Fig. 1 of a modified form of spray device;

Figure 5 is a section similar to Fig. 1 of a further modification; and

Figure 6 is an enlarged sectional view of a part of Figure 5.

Referring particularly now to Figure 1, a construction is shown having an outside casing 11 which is generally cylindrical in shape and is preferably constructed approximately the size of a customary pocket pen or pencil. The casing 11 consists preferably of the top cap 12 which is hinged at 13 to swing open and which contains

the gasket 14 which may be of rubber or any other convenient insulating material. The cap may be held in closed position by any convenient means such as the snap catch shown which includes the resilient finger 9 which snaps over boss 16. The casing 11 also includes the upper cylindrical portion 15, lower portion 16 which may be connected to portion 15 as by threads 17, and the bottom member 18. If desired the clip member 19 may be provided for convenience in carrying.

Near the bottom of the upper portion 15 of the casing 11 is provided the closure member 21 which is threaded into the member 15 and provides a liquid seal at this point in the casing. The top portion of the casing 15 is provided with the closure member 22 which is also threaded into the interior of the casing 15 providing a liquid seal. The casing 15 and the top and bottom closures 21 and 22 define the liquid containing compartment 25. Threaded plug 26 screws into the closure member 22 and may be removed for refilling the liquid reservoir. The tube 27 is inserted into the liquid reservoir, its lower end terminating in the lower portion of the reservoir in the curved portion 28, and its upper end extending through the closure member 22 and terminating substantially flush with the top of the cap. The curved portion 28 of the tube 27 insures that no leakage will occur out of the top of the tube when the atomizer is not in use, as no matter what position the reservoir is placed in, no leakage will occur if no air is allowed to enter compartment 25. In addition the rubber gasket 14 doubly insures the absence of leakage.

To provide for atomizing the liquid in the container 25 the piston 30 is mounted within the lower wall 16 of the container 11. The piston is secured to the plunger 31 which extends downwardly through the bottom member 18 of the outside casing, and is provided at its end with the thumb piece 32. The spring 33 tends to draw the piston inwardly and preferably is provided with just sufficient strength to hold the piston, plunger and finger piece in position inside of the casing 16 when the device is not in use.

The piston includes the cup member 35 and cup member 34 which may be of leather placed back to back. The member 34 mounts the valve member 36. The valve plate 38 is limited in its upward movement by fingers 37 and the hair spring 39 tends to push the valve plate 38 downward. Port 40 is provided extending through the members 36, 34, and 33.

The tube 45 is provided extending from closure member 21 through the liquid containing chamber 25 and terminating in an outwardly turned portion 46 which is directed over the top end of the tube 27. The curved air connection 47 is provided near the top of the tube 45 to permit air to enter the liquid compartment 25 to com-

pensate for the removal of liquid so that a vacuum will not obtain within the chamber 25, thus preventing the removal of liquid. The curved member 47 insures that no leakage will take place through this air vent no matter the position of the device, and the gasket 14 further insures from undesired leakage.

The operation of the device is simple. The plunger 31 is drawn down, the valve plate 38 moving up against the annular flange 37 and permitting air to pass. The plunger 31 is then pushed up and valve plate 38 seals the port 40, thus sending air at high velocity through the tube 45, which in passing over the end of the tube 27 draws liquid from the liquid chamber 25 according to atomizer principles. The displacement of liquid in the chamber 25 is compensated for by reintroduction of air through the tube 47 and the device will operate smoothly and continuously, the liquid being atomized in a fine spray which may be sprayed in any desired direction by the operator.

In Figure 2 is shown a construction of atomizer which is adapted to be confined in a tube of the same cross sectional diameter, but which may conveniently be reduced in longitudinal dimension. No further description of the liquid chamber and atomizing means is necessary, reference being made to Fig. 1 for this construction. The construction for producing the blast of air at the opening of the tube 45, however, includes the cylindrical member 50 in which is confined the piston 30 as shown. The plunger 31 is secured to a cylindrical member 51 of a diameter adapted to fit snugly over the cylindrical member 50 in sliding substantially air tight relationship. Spring 52 tends to retract the plunger 31 and has just sufficient strength to hold the same in retracted position. The device may conveniently be operated by up and down movement of the outside cylinder 51.

An alternate construction is illustrated in Fig. 4 wherein the plunger 31 and cap 32 will be located at the top of the construction comparable to the top of a fountain pen when the device is in non-operative position. The construction is similar in operation and construction to that shown in Fig. 1 and differs only in modified location of parts. Thus the casing 60 which is comparable to the upper portion 15 of the casing 11 of Fig. 1, is exteriorly threaded at its top. The casing 61, comparable to the portion 16 in Fig. 1 and in the rest position of the device inverted over the top of casing 60, is provided with the interiorly threaded portion 64 into which the threaded portion of the casing 60 is screwed. The gasket 65 seals the liquid and air openings of the tubes 45 and 27. The lower portion of casing 60 is exteriorly threaded at 67.

To place the device in operative position the casing 61 is unscrewed from the top of casing 60, inverted and screwed to the bottom portion at 67, whereupon the device operates in the manner described in connection with Fig. 1. The advantage of this construction lies in the fact that the plunger 31 with its cap 32 is thus kept away from the bottom of the user's pocket and further that the liquid and air openings are positively sealed within the casing and do not depend to any extent whatsoever upon the presence of a hinged cap member, as shown in Fig. 1.

A modified construction of spray device is illustrated in Figs. 5 and 6 in which the means for producing a blast of air are the same as that described in connection with Figs. 1 and 4 and thus

require no further description. This construction, however, is particularly directed to a device which will permit spraying of liquids of greater specific gravity than those for which the constructions of Figs. 1 through 4 are especially adapted, and to this end the liquid reservoir 70 is provided, including the cylindrical casing 71, the top closure 72 having refill plug 73 and the bottom closure 74. Tube 75 is directly connected to the source of air. It has a descending portion 75a, an ascending portion 75b and a descending portion 75c which extends through the plate 74 and turns outwardly to the portion 76 of enlarged diameter. The enlarged portion 76 contains a screw 77 adapted to revolve freely in the portion 76.

The portion 75b of the tube 75 contains holes 78 and 79 one of which will always be below the liquid level, except when the liquid in the reservoir is substantially exhausted, and one of which will always be in the air space above the liquid level. These holes serve a combined purpose. Air entering through tube 75 will, in the position of the spray device shown in Fig. 5, blow out of hole 79 displacing some of the liquid into the tube 75. In the event that the removal of liquid from the liquid container is insufficiently compensated for so that a vacuum is formed, air will also escape from 79 and permit continuous removal of the liquid, thus providing an even delivery of spray from the portion 77. The two holes 78 and 79 further insure that the device will operate in any position in which it is held.

The cap 80 hinged at 81 is similar to the cap 12 of Fig. 1, the gasket 82 being adjusted to accommodate the open portion of the screw spray device. The reservoir 70 may be refilled by removing it from the piston containing portion 84 and unscrewing the plug 73.

It will be observed that in all forms of the invention the liquid containing portion forms a complete leakproof unit which may be carried separately from the piston containing portion. Either portion may be replaced if lost or destroyed thus saving the expense of obtaining an entire new device.

While I have illustrated and described in detail certain preferred forms of my invention, it is to be understood that changes may be made therein and the invention embodied in other structures. I do not, therefore, desire to limit myself to the specific constructions illustrated, but intend to cover my invention broadly in whatever form its principle may be utilized.

I claim:

A pocket atomizer comprising a pair of members separably connected end to end, the first of said members having storage means for storage of liquid, the second of said members having air compressing means including a piston, a plunger to operate said piston, said plunger having a cap, said cap comprising a cylindrical member snugly slidable over said second member to actuate said piston, means in said first member to conduct air compressed by said air compressing means under high velocity to the end of said first member remote from the connective end of said member, a tube in communication with the lower portion of said storage means and mounted in atomizing relation to said air conducting means at the end of said first member remote from its connected end, said air conducting means having communication with said liquid storage means in the upper part thereof.

SAMUEL L. MARGOLIES.

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3,043,524

METERING SPRAYER DEVICE

Sonia Boris, née Jokelson, Paris, France, assignor to Societe Technique de Pulverisation (par abreviation STEP), Pantin, France, a company of France

Filed Nov. 8, 1960, Ser. No. 68,047

Claims priority, application France Nov. 10, 1959

10 Claims. (Cl. 239-350)

This invention relates to an improved sprayer device having means for metering the quantity of material sprayed at each actuation of the device.

Conventional sprayer devices generally comprise a container for a store of material, e.g. liquid, to be sprayed, another container containing a store of gas under pressure, a jet or spray-nozzle such as a Venturi nozzle, and a manually-operable valve member, usually in the form of a spring pressed, finger-actuated, plunger, actuation of which connects the gas container with the spray nozzle for discharging therethrough a jet of the gas with minute droplets of liquid entrained therewith.

The quantity of spray discharged in such a device at each actuation of the valve member depends on the length of time the valve member remains actuated since throughout such time the delivery of gas to the spray nozzle remains established. This precludes the possibility of accurately metering the quantity of spray discharged. An object of the invention therefore is to provide a sprayer device in which such metering is made possible with a high degree of accuracy. Another object is to provide a sprayer device having two different modes of operation, in one (conventional or continuous) mode the device acting to discharge spray for so long as the valve member remains actuated, while in the other or metering mode the device acts to discharge a limited metered amount of spray per actuation of the valve member, means being provided for easily switching from one to the other mode of operation.

Basically the sprayer device of the invention may be characterized in that it includes a metering chamber adapted to be alternately placed in communication with the gas container or with the spray nozzle. When the chamber communicates with the gas container it is filled with an amount of gas at the high pressure existing in the container. On thereafter being placed in communication with the nozzle, the said amount of gas entrapped in the metering chamber is discharged through the nozzle entraining liquid droplets therewith in the usual way in the form of spray, the quantity of spray thus discharged being strictly limited or metered in accordance with the metering chamber volume.

A sprayer device according to the invention may be either of the type using a conventional dipper tube adapted for use in normal position i.e. with the liquid container held upright, or of the type adapted for use in inverted position of the liquid container, and wherein the liquid is delivered to the nozzle by gravity or by the suction created in said nozzle by the discharge of gas therethrough.

In one specific embodiment of the invention the metering chamber is provided as an e.g. annular recess formed in a spool-like valve member formed integrally with an actuating plunger or push-button, and slidable in a valve bore into which discharge two axially-spaced passages respectively connected with the spray nozzle and the gas reservoir, the spacing between the points at which said conduits open into the valve bore being greater than the axial length of the metering chamber, whereby only one or the other of said passages can at any time be effectively connected with the chamber, depending on the position of the valve member.

The metering chamber may be formed with an extension

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in the form of a longitudinally extending groove, so that by imparting to the valve spool a rotational displacement to position such groove in register with that one of said passages connected to the gas store, a continuous communication may be established between the gas reservoir and the nozzle, whereupon the sprayer device will operate in the conventional mode to discharge a jet of spray as long as the valve member remains in actuated position.

Preferably, the valve member or spool is arranged simultaneously to operate a cutoff valve element adapted to cut off the connection from the liquid container (or dipper tube) to the spray nozzle in the position of the valve member in which the chamber communicates with the gas container, and establish such connection in the alternate position of the valve member. Spring means may be provided for urging the valve member to said first position. The said cut-off valve may be operated from the valve member by way of a lost-motion connection or the like, to ensure that the connection from the liquid container to the spray nozzle is effectively established at the time the connection from the metering chamber to the spray nozzle is established, this arrangement being of especial advantage in sprayer constructions where a dipper tube is included.

Exemplary embodiments of the invention will now be described for purposes of illustration but not of limitation with reference to the accompanying drawings, wherein:

FIG. 1 is an axial cross sectional view of a first sprayer construction according to the invention, using an inverted liquid container, shown in its inverted position of use;

FIG. 2 is an end view from the bottom of FIG. 1;

FIG. 3 shows a portion of the sprayer of FIG. 1 in the operated position of the valve member;

FIG. 4 shows a portion of the sprayer of FIG. 1 in the operated position of the valve member, but with the valve member being set to the continuous-spray mode of operation;

FIG. 5 is an axial cross sectional view of another sprayer according to the invention embodying an upright liquid container and dipper tube.

As shown in FIG. 1, the sprayer device comprises a body 1 threadedly connected with the neck 2a of a container 2 containing a store of liquid to be sprayed, through a sealing gasket 3.

Slidably mounted in a blind axial bore 4 of body 1 is a valve member or spool 5 which projects beyond the lower end of the body to provide an actuating plunger or button 6. The valve spool is formed with an annular recess providing a metering chamber 7 which is adapted to communicate either with a passage or port 8 connected with the inlet end of a conventional Venturi-type spray nozzle, or with a passage or port 10 communicating at its other end with the interior of a container or reservoir 11 for compressed gas, e.g. air. The spacing between ports 8 and 10 is greater than the axial length of chamber 7, so that the chamber cannot communicate with both ports at the same time. A passage 12 connects the throat section of Venturi spray nozzle 9 with the bottom opening of the liquid container 2, which opening however is normally sealed by a cut-off valve head 13 secured to the end of a rod 14 coaxially and integrally projecting from the valve member 5. A spring 15 acting between an inner end surface of bore 4 and a shoulder of valve member 5 urges the valve member and valve head to an idle position in which the metering chamber 7 communicates with gas-reservoir port 10 but not with the nozzle 9, and wherein cut-off valve head 13 seals the liquid-container orifice.

In a side of valve member 5 is a longitudinal groove 20 one end of which connects with metering chamber 7, and the valve member 5 can be selectively rotated about

its axis to either of two angular positions in one of which (as shown in FIGS. 1 and 3) the groove 20 is positioned out of register with port 10, and in the other of which (FIG. 4) the groove 20 registers with port 10. For this purpose a centrally perforated disk 16 is slidably but non-rotatably keyed to an outer end portion of valve member 5 by means of an inward projection 16a of perforated disk 16 slidably projecting into a keyway 17 formed in the valve member 5 (in the portion thereof constituting the push-button 6). Disk 16 is formed with an arcuate slot 19 through which extends a screw 18 threaded into a tapped hole formed in the bottom end of body 1. Thus the valve member and disk can be bodily rotated together between a "continuous-spray" position in which groove 20 registers with port 10, which position is indicated by means of an index mark 21 (FIG. 2) on the disk registering with an index mark "C" on the sprayer body, and a "metered-spray" position in which groove 20 is displaced out of register with port 10, this position being indicated by index mark 21 registering with an index mark "D" on the sprayer body.

The sprayer device operates as follows: It is first assumed that the indexing disk 16 and valve member have been rotated to the "D" position so that the sprayer operates in the "metered-spray" mode. Normally owing to the action of spring 15 the valve member is positioned as in FIG. 1 so that metering chamber 7 communicates with gas passage 10 only and valve head 13 seals the liquid-container orifice. Metering chamber 7 therefore contains a certain volume of gas at the relatively high pressure obtaining in reservoir 11.

With the sprayer held in the inverted position shown, if the push-button 6 is depressed to displace the valve member 6 upwardly, as shown in FIG. 3, valve head 13 uncovers the liquid container orifice so that liquid can now flow through conduit 12 to the throat of nozzle 9. Simultaneously valve member 5 is moved to disconnect the metering chamber 7 from the gas passage 10 and connect the chamber with nozzle passage 8, whereby the metered volume of gas entrapped in chamber 7 is discharged through the spray nozzle 9, carrying with it an amount of liquid in finely divided form to produce a jet of spray. It will thus be evident that the quantity of spray discharged is strictly limited and metered in accordance with the volume of metering chamber 7.

If now the valve member 5 and disk 16 are rotated by action on button 6 so as to bring index 21 to the "D" setting, groove 20 is brought into register with gas port 10 (FIG. 4). In this condition, depression of button 6 will bring metering chamber 7 into communication with nozzle port 8, as before, but the communication of the chamber 7 with gas port 10 will not be discontinued owing to the presence of groove 20. Gas is now enabled to flow continuously from gas reservoir 11 to spray nozzle 20 and the sprayer operates in the so-called "continuous-spray" mode.

In the embodiment of FIG. 5, the sprayer body has a dipper tube 22 depending therefrom into the liquid reservoir. The connection between the upper end of the dipper tube and the passage 12 leading to the throat of Venturi nozzle 9 is normally sealed by a cutoff valve head 23 provided at the end of a rod 24 slidably extending through an axial perforation in valve member 5 and carrying at its upper end a stop 25 movable in an axial recess 26 of the push-button 6 portion of valve member 5. A relatively weak spring 27 acts between an end face of valve member 5 and a shoulder of cutoff valve shank 24 to urge the stop 25 into engagement with the valve member 5.

The operation of this embodiment is generally similar to that previously described except for the lost-motion connection provided from valve member 5 to cutoff valve head 23 through the shank 24. Thus, on depression of button 6 valve head 23 is first unseated to connect the dipper tube 22 with conduit 12 until the movement of valve head 23 and shank 24 is arrested by engagement

with the top of the dipper tube, whereupon further depression of button 6 compresses weak spring 27, and then establishes communication from the metering chamber to the nozzle inlet port as previously described. Releasing the button 6 will first cause upward movement of valve member 5 to disconnect the metering chamber from the nozzle port, and only thereafter will actuate the cutoff valve 23 to seal the dipper tube orifice, after the valve member 5 has engaged the stop 25 to raise the shank 24.

It will be understood that various modifications may be made in the constructions illustrated and described, as by including certain features of one construction in the other construction, or other changes.

What I claim is:

1. A sprayer device comprising a spray nozzle, a container for gas under pressure having an outlet for the latter, a container for material to be sprayed having an outlet for the latter extending to said nozzle, means defining a metering chamber and being movable between a first position, in which only said outlet for gas under pressure opens into said metering chamber, and a second position, in which said metering chamber communicates with said nozzle, and actuating means for selectively disposing said means defining a metering chamber in said first and second positions thereof so that, when in said first position, a metered quantity of gas under pressure determined by the volume of said metering chamber enters the latter from said container for the gas and, when moved to said second position, the metered quantity of gas under pressure escapes from said metering chamber through said nozzle along with material to be sprayed from said container for such material.

2. A sprayer device as in claim 1; further comprising a valve for closing said outlet for the material to be sprayed, said valve being movable with said means defining a metering chamber to close and open said outlet for the material to be sprayed in said first and second positions, respectively, of the means defining a metering chamber.

3. A sprayer device comprising a body having a bore therein with first and second passages extending from said bore at axially spaced apart locations along the latter, a first container for gas under pressure having an outlet communicating with said first passage, a spray nozzle carried by said body and communicating with said second passage, a plunger slidable in said bore and having a recess in the surface of the plunger to define a metering chamber, the axial extent of said recess on the plunger being less than the axial distance along said bore between said first and second passages so that said chamber can only alternatively communicate with said first and second passages, a second container for material to be sprayed, conduit means extending from said second container to said nozzle, and means for displacing said plunger axially from a first position, where said metering chamber communicates with said first passage to receive a metered quantity of gas under pressure from said first container determined by the volume of said chamber, to a second position, where said chamber communicates with said second passage for discharging said metered quantity of gas under pressure through said nozzle along with material to be sprayed reaching said nozzle from said second container by way of said conduit means.

4. A sprayer device as in claim 3; wherein said spray nozzle is of the venturi type having a throat at which said conduit means opens while said second passage opens axially into the venturi type spray nozzle so that the discharge of the metered quantity of gas under pressure through said nozzle induces the flow of material to be sprayed from said second container through said conduit means to said nozzle for atomizing by said gas.

5. A sprayer device as in claim 3; wherein said conduit means has a valve seat interposed therein between said second container and nozzle; and further comprising a

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valve movable with said plunger to engage said valve seat and close said conduit means when said plunger is in said first position, and to move away from said valve seat and thereby open said conduit means when said plunger is moved to said second position.

6. A sprayer device as in claim 5; wherein said valve is axially aligned with said plunger and fixed relative to the latter.

7. A sprayer device as in claim 5; wherein said valve is axially aligned with said plunger, and lost-motion connection means is provided between said valve and said plunger to unseat and seat said valve during a portion of the movement of said plunger from and to said first position.

8. A sprayer device as in claim 3; wherein said recess extends annularly around said plunger and the latter further has a second recess of limited angular extent extending axially from the first mentioned recess in the direction opposed to the axial movement of said plunger from said first position to said second position; and wherein said plunger is turnable in said bore to selectively angularly space and register said second recess with respect to said first passage so that, when said plunger is

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in said second position, registration of said second recess with said first passage, permits gas under pressure to flow from said first passage and through said second and first recesses and said second passage to said spray nozzle for continuous spraying from the latter of material reaching the nozzle from said second container.

9. A sprayer device as in claim 3; wherein said second container for the material to be sprayed is inverted and carried by said body above said nozzle.

10. A sprayer device as in claim 3; wherein said second container for the material to be sprayed is suspended from said body below said nozzle, and said conduit means includes a dipper tube depending from said body into said second container.

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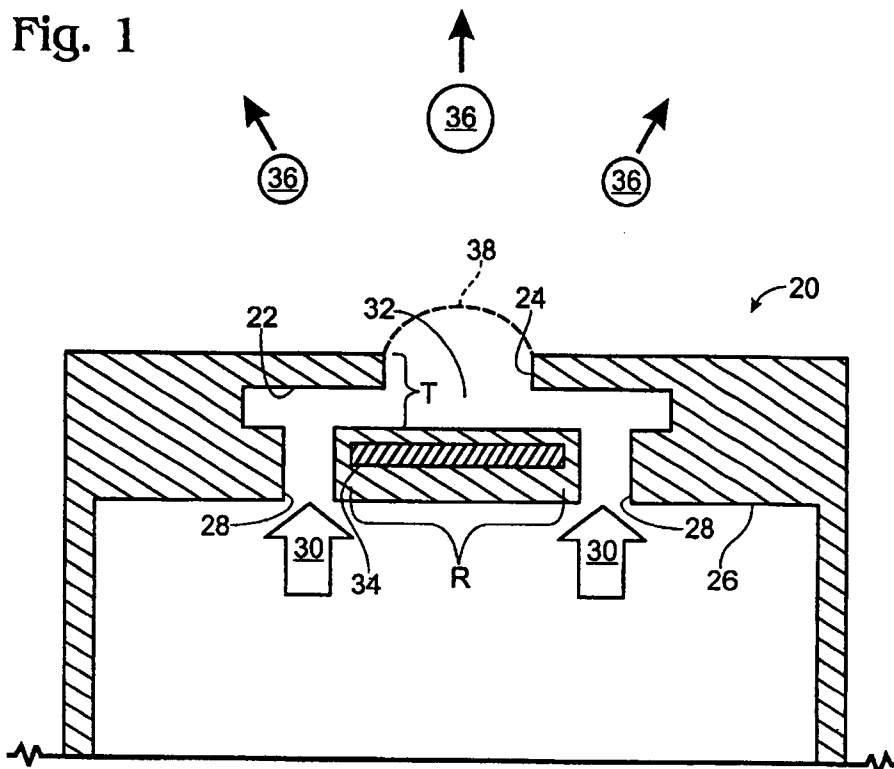
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(54) **Thermal generation of droplets for aerosol**

(57) A thermal-type drop generator (20) having a geometry that is configured so that the ejection of liquid from the chamber (33) has the effect of separating the ejected volume into a number of small droplets. The relationship between the thickness of the liquid chamber

and the area of the heat transducer (35) used to eject the liquid is controlled to provide the separating aspect so that the resultant droplets (36) have very small volumes, in the range of tens of femtoliters. Such small droplets are readily entrained in an aerosol and especially useful for pulmonary delivery of medicinal fluid.



that the liquid in the supply is directed to the drop generator head 72 that carries the multiple drop generators as described above in connection with Fig. 2. Preferably, the conduit and drop generator head are primed (as by applying suction to the orifices in the head) upon manufacture or by the user before the inhaler is operated to eject drops as described next.

[0055] The above-mentioned flex circuit 60 may be bonded, for example, to the inhaler 71 in a correspondingly shaped recess 61 in the body 68. That circuit connects the heat transducers of the drop generators with suitable conditioned control signals from a controller 52, which is part of the inhaler control system 81. The control system 81 includes the controller 52 that is provided with a power supply 79 and operator switch 77. The controller is an integrated circuit that responds to the switch signal by directing to the head 72 controlled current pulses for firing the drop generators as required. It will be appreciated that the control system can be configured in any of a number of ways and, most preferably, integrated with the body of the inhaler.

[0056] The drop generator head 72 is preferably located at the mouthpiece 69 of the inhaler. The recess 61 or other mechanisms may be used for providing an air stream during inhalation so that the droplets become entrained in the air.

[0057] It will be appreciated that the control system 81 and arrangement of the drop generator head 72 (that is, so that the droplets produced by the head 72 are immediately propelled into the surrounding air) provides for both precise metering of the amount of droplets ejected and of the amount of liquid expelled, as well as the generation of suitably small droplets. That is, the expulsion of the liquid from the chamber need not be accompanied with other mechanisms for reducing the volume of ejected liquid to suitably small droplets.

[0058] Even though the foregoing description has focused on the production of droplets suitable for aerosol delivery of the droplets to the alveoli, it will be appreciated that such small droplets can be generated for other applications. The drop generators of the present invention could be incorporated with supplies of liquids suitable for scent delivery, dispensing precisely controlled amounts of pesticides, paints, fuels, etc.

[0059] Thus, having here described preferred embodiments of the present invention, it is anticipated that other modifications may be made thereto within the scope of the invention by individuals skilled in the art. Thus, although preferred and alternative embodiments of the present invention have been described, it will be appreciated that the spirit and scope of the invention is not limited to those embodiments, but extend to the various modifications and equivalents as defined in the appended claims.

Claims

1. A drop generator (20), comprising:

a substrate (40) having a heat transducer (35) carried on an upper surface (56) of the substrate, the heat transducer being a substantially planar member having an area;
an orifice member (48) attached to the substrate and having an outer surface (49) through which is formed an orifice (25), the orifice member defining a chamber (33) that is adjacent to the heat transducer and is in fluid communication with the orifice and with an inlet (54) in the substrate for conducting liquid through the inlet and into the chamber;

wherein a chamber thickness is a dimension extending from the upper surface to the outer surface; and

wherein a ratio of the chamber thickness to the square root of the transducer area is less than about 0.75.

2. The drop generator (20) of claim 1 wherein the ratio is less than 0.50.

3. The drop generator (20) of claim 1 wherein the ratio is about 0.35.

4. The drop generator (20) of claim 1 wherein the orifice member (48) has at least two orifices (125) extending from the chamber (33) to open through the outer surface (49) of the orifice member (48) thereby to permit liquid to be propelled through the orifices from the chamber.

5. The drop generator (20) of claim 4 wherein the heat transducer (35) in the chamber (33) is a unitary member.

6. A method of generating droplets, comprising the steps of:

providing a supply of liquid;
filling chambers (33) with some of the liquid;
and
instantaneously heating the liquid in the chambers by an amount sufficient to produce a vapor bubble in each chamber for
propelling from each chamber droplets (36) of the liquid wherein each droplet has a volume of less than 100 femtoliters.

7. The method of claim 6 including the step of propelling the liquid from each chamber (33) as a substantially single volume that separates into two or more droplets.

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8. The method of claim 7 including the step of instantaneously heating the liquid so that the liquid in the chamber (33) is propelled with a single instance of heating the liquid.

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9. The method of claim 7 further comprising the step of providing an orifice member (48) that has at least two orifices (125) extending from the chamber (33) to permit liquid to be propelled through the orifices from the chamber.

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10. The method of claim 7 further comprising the step of providing a single orifice (25) through which substantially all of the liquid in the chamber (33) is propelled.

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(54) **DISPENSER FOR FLOWABLE MEDIA**

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(58) **Field of Search** **222/82, 83, 83.5,**
222/326, 327, 321.6, 386

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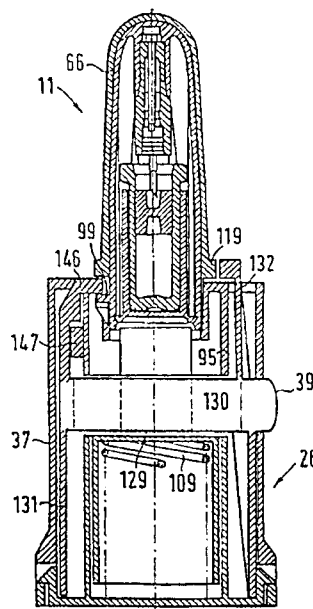
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(57) **ABSTRACT**

The invention relates to a dispenser, especially a disposable atomizer (25), with a dispenser unit (11). Said unit contains a media container (12) which also forms the pump chamber and which is sealed by a piston-type stopper (14). When activated, said piston-type stopper is punctured by a hollow needle (16). The outlet nozzle (20) surrounds the dispenser unit to a large extent. The dispenser unit (11) can be introduced into an activating unit (26). According to one configuration, this activating unit is pin-shaped with a loading chamber (29). The dispenser unit is held in place by an activating push rod (30) which can be longitudinally displaced when activated by turning (33) and is prestressed by a spring (36). The dispenser is activated by a trigger device (39). The dispenser unit (11) can also be changed after use.

15 Claims, 15 Drawing Sheets



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also FIG. 40), on which is shaped a fork 147 which is wedge-shaped at its two free ends and which is shown in FIG. 39a. As shown in FIG. 39, said fork 147 engages between the projection 95 of casing 37 and the locking lever 146 and presses the same outwards, so that the locking elements 99 are freed and the dispenser unit 11 can be removed. The projections 99 can correspond both to a bayonet and also simply to snap locking without turning into an operating position.

Following the release of the protective cap, which can only take place when the dispenser unit 11 has been inserted in the actuating unit 26, the bottom wedge-shaped member drops freely downwards. It is then no longer possible to fit said dispenser unit on an actuating unit.

FIG. 40 shows a construction with a tear-up tongue on the protective cap 66, but the arrangement of the actuating and release buttons 39 and 115 is the same as for FIG. 39.

FIG. 43 shows an actuating unit 26 with manual actuation by means of an actuating pusher 56, as shown in FIGS. 7 to 9. It projects a relatively long way and on it can be placed a lid 148, which contains a reserve holder 149 for two rechargeable replacement dispenser units 11. They can be jammed in or can also be inserted by means of the screw-bayonet connection with propeller blade-like locking elements 99. With the head of their protective caps 66 they engage in corresponding depressions in the actuating shoulder 44, so that even in the case of violent movements they remain in position.

Thus, this constitutes a different construction to the reserve holder for "replacement cartridges" or their functional parts already shown in FIGS. 2 and 8.

In the vicinity of the actuating shoulders a two-armed locking lever 150 is shaped onto the casing 37 and as a result of whose manufacture it can pivot in the direction of the arrow 151, i.e. counterclockwise. However, it is prevented from doing so by the flange 119 of the protective cap 66, so that it rests with its lower barrier surface 152 on an inner projection 153 of the actuating pusher and prevents an actuation before the protective cap is removed. On removing the protective cap 66, the locking lever 150 pivots counterclockwise into a position releasing actuation.

What is claimed is:

1. A dispenser for flowable media, for applying media to a person, comprising:

an exchangeable dispenser unit (11) operable for a limited number of application strokes, having
an outlet opening (19) in form of a spray nozzle,
at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19) said opening element (16) being spaced inwardly from the outlet opening (19) and
an outlet channel located between the media container (12) and the spray nozzle (19); and
said dispenser further comprising
an actuating unit (26) that is separable from the dispenser unit (11), and that is reusable,
the actuating unit (26) having functional parts at least contributing to actuation of the dispenser unit (11); and
wherein the dispenser unit (11) includes a wall apart from the media container that encloses the opening and closing elements to protect the medium within the dispenser from contamination.

2. The dispenser according to claim 1, wherein the media container (12) is at least partly located within the outlet piece (20) containing the spray nozzle (19).

3. A dispenser for flowable media, for applying media to a person, comprising:

an exchangeable dispenser unit (11) operable for a limited number of application strokes, having

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an outlet opening (19) in form of a spray nozzle,
at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19) said opening element (16) being spaced inwardly from the outlet opening (19), and

an outlet channel located between the media container (12) and the spray nozzle (19); and

said dispenser further comprising
an actuating unit (26) that is separable from the dispenser unit (11) and that is reusable,

the actuating unit (26) having functional parts at least contributing to actuation of the dispenser unit (11); and
wherein the dispenser unit (11) includes a wall apart from the media container that, encloses the opening and closing elements to protect the medium within the dispenser from contamination, and

wherein the media container (12) also forms a pump cylinder of a thrust piston pump, and wherein a closing element of the media container (12) is formed by a piston-type stopper being pierceable by an opening element including a hollow needle (16), and wherein a push rod (18) receives the hollow needle, the push rod having an end face (24) pressing onto the piston-type stopper (14) to perform a pump stroke, the push rod (18) being located in the outlet piece (20) containing the spray nozzle (19).

4. The dispenser according to claim 3, wherein a narrow sealing gap (120) is provided between a casing part (95) of the dispenser unit (11) and a reception sleeve (40) receiving the media container.

5. The dispenser according to claim 3, wherein the actuating unit (26) has a charging chamber in which the dispenser unit (11) can be inserted.

6. The dispenser according to claim 3, wherein the actuating unit comprises a tensionable and releasable actuating mechanism.

7. A dispenser for flowable media, for applying media to a person, comprising:

an exchangeable dispenser unit (11) operable for a limited number of application strokes, having

an outlet opening (19) in form of a spray nozzle,
at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19), and

an outlet channel located between the media container (12) and the spray nozzle (19); and

said dispenser further comprising
an actuating unit (26) that is separable from the dispenser unit (11) and that is reusable,

the actuating unit (26) having functional parts at least contributing to actuation of the dispenser unit (11); and
wherein the dispenser unit (11) encloses the opening and closing elements to protect the medium within the dispenser from contamination, and

further comprising actuating pressure point means for ensuring a minimum actuating force for the dispenser.

8. The dispenser according to claim 7, wherein the actuating pressure point means are provided by destructible material bridges (55).

9. A dispenser for flowable media, for applying media to a person, comprising:

an exchangeable dispenser unit (11) operable for a limited number of application strokes, having

an outlet opening (19) in form of a spray nozzle,
at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19), and

at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19), and

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an outlet channel located between the media container (12) and the spray nozzle (19); and
said dispenser further comprising
an actuating unit (26) that is separable from the dispenser unit (11) and that is reusable,
the actuating unit (26) having functional parts at least contributing to actuation of the dispenser unit (11); and
wherein the dispenser unit (11) encloses the opening and closing elements to protect the medium within the dispenser from contamination, and
wherein the actuating unit (26) is shaped like a round cylinder, having one end face providing a recess with fixing means for the dispenser unit (11).
10. A dispenser for flowable media, for applying media to a person, comprising:
an exchangeable dispenser unit (11) operable for a limited number of application strokes, having
an outlet opening (19) in form of a spray nozzle,
at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19), and
an outlet channel located between the media container (12) and the spray nozzle (19); and
said dispenser further comprising
an actuating unit (26) that is separable from the dispenser unit (11) and that is reusable,
the actuating unit (26) having functional parts at least contributing to actuation of the dispenser unit (11); and
wherein the dispenser unit (11) encloses the opening and closing elements to protect the medium within the dispenser from contamination, and
wherein the actuating unit comprises a tensionable and releasable actuating mechanism, the actuating mechanism contains a release mechanism having a shape-variable ring (130), which has a release shape (B) closer to a circle shape than a blocking oval shape (N).
11. A dispenser for flowable media, for applying media to a person, comprising:
an exchangeable dispenser unit (11) operable for a limited number of application strokes, having
an outlet opening (19) in form of a spray nozzle,
at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19), and
an outlet channel located between the media container (12) and the spray nozzle (19); and

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said dispenser further comprising
an actuating unit (26) that is separable from the dispenser unit (11) and that is reusable,
the actuating unit (26) having functional parts at least contributing to actuation of the dispenser unit (11); and
wherein the dispenser unit (11) encloses the opening and closing elements to protect the medium within the dispenser from contamination, and
further comprising actuation blocking means for preventing undesired actuation of the dispenser (25).
12. The dispenser according to claim 11, wherein the blocking means cooperate with means (88, 89, 132, 133, 150) dependent on proper insertion of the dispenser unit (11) in the actuating unit (26).
13. The dispenser according to claim 11, wherein the blocking means contain a locking element (132, 150), which cooperates with the dispenser unit and with a release element (129).
14. The dispenser according to claim 11, wherein, for preventing actuation prior to the removal of a protective cap (66), the blocking means cooperate with a protective cap (66) for the dispenser unit (11).
15. A dispenser for flowable media, for applying media to a person, comprising:
an exchangeable dispenser unit (11) operable for a limited number of application strokes, having
an outlet opening (19) in form of a spray nozzle,
at least one closing and opening element (15, 16) located between a media container (12) and the outlet opening (19), and
an outlet channel located between the media container (12) and the spray nozzle (19); and
said dispenser further comprising
an actuating unit (26) that is separable from the dispenser unit (11) and that is reusable,
the actuating unit (26) having functional parts at least contributing to actuation of the dispenser unit (11); and
wherein the dispenser unit (11) encloses the opening and closing elements to protect the medium within the dispenser from contamination, and
further comprising a protective cap being prevented from being drawn off from the dispenser unit by locking means (85, 86) before the dispenser is ready to operate.

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United States Patent [19]
Phillips

[11] **3,818,908**
[45] **June 25, 1974**

- [54] **MEDICAMENT DISPENSER**
[75] Inventor: **Robert E. Phillips**, Studio City,
Calif.
[73] Assignee: **Riker Laboratories, Inc.**,
Northridge, Calif.
[22] Filed: **Aug. 7, 1972**
[21] Appl. No.: **278,538**

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Primary Examiner—Richard A. Gaudet
Assistant Examiner—Lee S. Cohen
Attorney, Agent, or Firm—Alexander, Sell, Steldt &
DeLaHunt

- [52] U.S. Cl. **128/173, 222/193, 239/350,**
128/208, 128/211
[51] Int. Cl. **A61m 11/00**
[58] Field of Search **128/173, 173.1, 194, 201,**
128/211, 208, 266, 222, 185, 186; 239/350,
345-349, 355, 308, 318, 338; 222/193, 136,
402.2, 335, 383-385

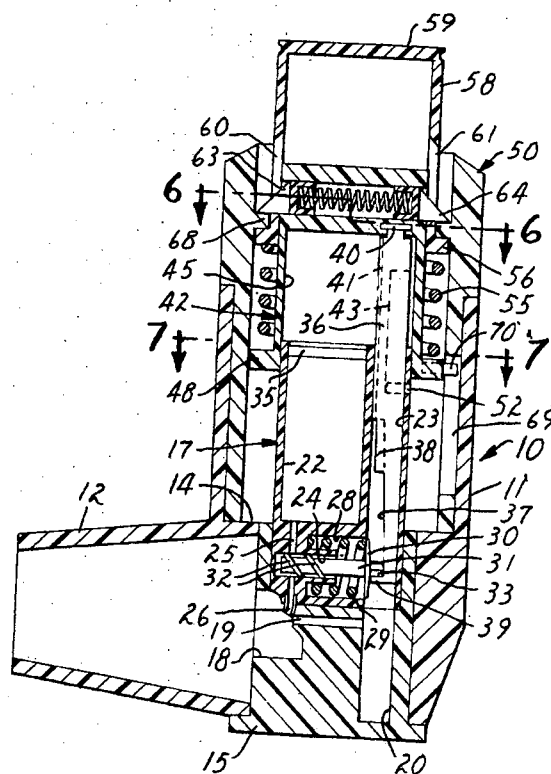
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[57] **ABSTRACT**

A dispenser for dispensing inhalable medicaments which dispenser dispenses the liquid medicaments in a mist by nebulizing a metered amount of the liquid. The liquid is metered by a rotary piston pump and a piston and cylinder arrangement within the dispenser compresses a small amount of air when a release mechanism is triggered to carry the dispensed liquid such that the patients will inhale a mist.

9 Claims, 7 Drawing Figures



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amount of the medicament is drawn into the cylinder 24 forward of the O ring 32. As the shell 58 is lifted the detents 63 and 64 are forced inwardly by rib 68 engaging their beveled edges and then are forced outwardly again to seat on the upper side of the rib 68 in the cap 50. Cam 39 again contacts the follower 33 to rotate the piston 31, turning the O rings 32 to a position cutting off communication between the pump and the inlet 25. The device is now positioned for a subsequent operation.

In an operative example, the air discharged from the passageway 19 to nebulize the liquid can be at pressures between 5 and 8 pounds per square inch at standard temperature and atmospheric pressure. The bore 45 of the shell 42 has a diameter of about 0.85 inch and it travels a total of 0.8 inch. The shell travels about 0.4 inch to release the spring and when released the pressure therein is about 8 pounds. The spring and the continued movement maintained by the operator then drives the shell 42. The amount of liquid dispensed may be about 5, 6, or 7 microliters, depending on pump capacity.

For preferred operation, a predetermined amount of air under a predetermined amount of pressure is directed at the discharged liquid. The predetermined amount of liquid is introduced into the air stream when the air is at its peak pressure.

Having thus described the invention with respect to a preferred embodiment, it will be understood that certain modifications can be made without departing from the spirit of this invention.

What is claimed is:

1. A dispenser for medicaments such that metered amounts of the medicament will be discharged in a state to be orally received during inhalation, said dispenser comprising:

a housing formed with a discharge passageway,
a reservoir for a quantity of liquid disposed in said housing,
metering pump means having an inlet communicating with said reservoir and an outlet communicating with said passageway for dispensing under pressure metered amounts of liquid from said reservoir,

operator means for operating said metering pump means to dispense said liquid from said outlet under pressure,

air compressing means within said housing for placing a volume of air under pressure and for directing said air under pressure toward said outlet, and
mechanical actuating means for actuating said operator means and said air compressing means whereby a metered amount of liquid is dispensed from said outlet and struck by said compressed air to be discharged with said air as a spray.

2. A dispenser according to claim 1 comprising resettable release means connected between said housing and said air compressing means for releasing said mechanical actuating means upon an operator applying pressure to said release means.

3. A dispenser according to claim 1 wherein said air compressing means comprises:

a hollow cylinder and a mating piston member, said cylinder and piston member being interfitted within said housing and mounted for relative movement, and

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a passageway leading from within said cylinder to a position adjacent said outlet.

4. A dispenser according to claim 3 wherein said mechanical actuating means comprises a helical compression spring disposed about the outer surface of said cylinder, said cylinder having a first position relative to said piston member wherein said compression spring is under compression and in which first position said cylinder is retained by said release means, and a second position relative to said piston wherein air has been driven from said cylinder by said spring compression being dissipated, and said operator means has actuated said metering pump means.

5. A dispenser according to claim 4 wherein said metering pump means is a rotary piston pump comprising means defining a cylindrical bore, a piston slidably received in said bore, spring means urging said piston out of said bore, passage means communicating with said bore to define said inlet and outlet and seal means on said piston for connecting the bore in fluid flow communication with said reservoir when said cylinder is in said first position and with said outlet when said cylinder is in said second position.

6. A dispenser according to claim 4 wherein resettable release means are provided for releasing said mechanical actuating means and comprises:

detent means supported by said cylinder,
shoulder means on said housing engageable by said detent means to hold said cylinder in said first position, and
manually actuatable means for compressing said compression spring with said cylinder in said first position and for unlocking said detent means and said shoulder means to allow movement of said cylinder to said second position.

7. A dispenser according to claim 1 wherein said metering pump means is a rotary piston pump comprising means defining a cylindrical bore, a piston slidably received in said bore, seal means on said piston connecting said bore with said inlet and then with said outlet upon operation of said actuating means, spring means urging said piston out of said bore, and passage means communicating with said bore to define said inlet and outlet.

8. A dispenser for an inhalation medicament comprising a tubular housing having a laterally projecting mouthpiece, a supply canister of medicament within said housing, means for metering a quantity of medicament for discharge upon actuation of an actuator on said dispenser, wherein the improvement comprises:

a rotary piston pump means for discharging a predetermined quantity of medicament from said canister and discharging the same from an outlet under pressure, and

means within said housing for providing a quantity of compressed air directed at said outlet and into said mouthpiece to carry said discharged medicament into said mouthpiece upon actuation of said actuator.

9. A dispenser according to claim 8 wherein said canister comprises:

a cylindrical shaped body member having an axially extending bore extending therethrough and a second bore forming a reservoir, said second bore extending toward one end, said body having a third bore extending generally diametrically and having

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passageways connecting said third bore to said reservoir and to said one end, and
said rotary piston pump means includes a piston slidably fitted in said third bore, said piston having means affording selective communication of said 5

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third bore with said reservoir and said one end, and a spring positioned about said piston urging it from said bore.

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[54] AEROSOL PRODUCING DEVICE

- [75] Inventor: Nathaniel Hughes, Palm Springs, Calif.
[73] Assignee: Vortran Corporation, Culver City, Calif.
[21] Appl. No.: 652,740
[22] Filed: Sep. 18, 1984

Related U.S. Application Data

- [63] Continuation-in-part of Ser. No. 555,703, Nov. 28, 1983, Pat. No. 4,635,857.
[51] Int. Cl.⁴ A61M 11/06
[52] U.S. Cl. 239/8; 128/200.18; 128/200.21; 239/11; 239/338; 239/370; 239/426; 239/434; 239/589.1; 261/78.2; 261/DIG. 65
[58] Field of Search 239/102, 338, 370, 590, 239/590.3, 590.5, DIG. 20, DIG. 23, 403, 426, 434, 8, 11, 461, 463, 589.1; 128/200.18, 200.21; DIG. 65, 78.2

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Primary Examiner—Andres Kashnikow

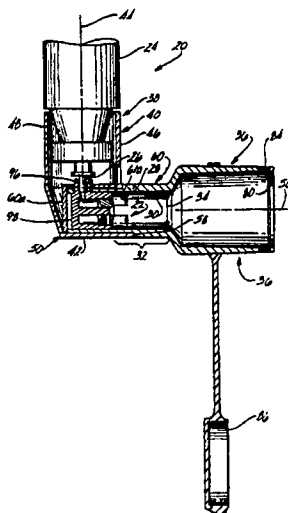
Assistant Examiner—Michael Forman

Attorney, Agent, or Firm—Christie, Parker & Hale

[57] ABSTRACT

An apparatus and method are disclosed for applying an active ingredient as an aerosol. A transducer (22) for creating an aerosol includes a propellant inlet (96) and a chamber defined by at least one chamber wall (128) confluent with the propellant inlet. A bluff body (112) is provided for creating at least one vortex (152) in the chamber when the propellant enters the propellant inlet in a supersonic flow condition. An orifice (118, 146) spaced apart from the bluff body and separated therefrom by the chamber wall is provided for creating an exiting vortex (154).

2 Claims, 15 Drawing Figures



The flow through the cylindrical apertures is substantially the same.

As the fluid exits the orifice 172, a vacuum is produced at the outlet of tube 192 due to the supersonic and vortical flow of the exiting vortex. Additionally, the sub-atmospheric pressure region in the vortex serves to produce flow of the fluid in container 194 through the tube 192. As the active ingredient leaves the tube 192, the fluid is effectively atomized by the action of the exiting vortex. The atomization of the active ingredient is substantially the same due to the action of the vortex as the atomization with the transducers previously described.

The propellant canister 188 may be a unit dose canister such as that described above with respect to FIG. 1 or may be a continuous flow canister providing output whenever the inlet tube 190 is depressed with respect to canister 188. In either case, the exiting vortex produced by the transducer 196 draws the active ingredient from container 194 as long as propellant is produced from canister 188. During continuous operation of canister 188, the active ingredient is drawn from flexible container 194 until fluid is no longer present in the container.

The manipulation of the resulting vortex may be carried out as desired. For example, the guide tube 196 may be provided with expansion chambers and resonant screens as discussed with respect to FIG. 1. Alternatively, if the active ingredient is to be applied directly from the transducer, the guide tube 196 may be omitted.

FIG. 14 shows an alternative embodiment of transducer 186 and the inlet tube 192 wherein the inlet tube is placed external to the transducer 186 adjacent the outer rim of the diverging conical portion 174. Substantially the same result can be obtained for atomizing the active ingredient with the inlet tube 192 located as shown in FIG. 14 as can be obtained with the arrangement provided in FIG. 13. The function and operation of the arrangement shown in FIG. 14 is otherwise the same as that described with respect to FIG. 13.

FIG. 15 shows an additional embodiment of transducer 186 and the inlet tube 192 wherein the inlet 192 has its terminal portion flush with the surface of conical portion 174. The structure and function of the transducer is otherwise the same as described with respect to FIGS. 13 and 14.

These transducers are particularly efficient at low liter flows of oxygen and are very much suited for general hospital use at these flows with the requisite advantages for low oxygen rate therapy cited earlier. This capability makes nebulizers built with these inventions uniquely operable with oxygen concentrators.

It should be noted that the above are preferred configurations but others are foreseeable. The described embodiments of the invention are only considered to be

preferred and illustrative of the inventive concept; the scope of the invention is not to be restricted to such embodiments. Various and numerous other arrangements may be devised by one skilled in the art without departing from the spirit and scope of the invention.

I claim:

1. A process for creating an aerosol characterized by the steps of:

providing a propellant to an inlet of a transducer; impacting the propellant on a bluff body to create at least one vortex;

feeding the at least one vortex to an aperture spaced apart from the bluff body;

producing a vortex through an orifice spaced apart from the bluff body and separated from the bluff body by a wall preventing flow of fluid along the bluff body to the orifice; and

incorporating an active ingredient into the propellant.

2. A transducer for creating an aerosol having an inlet and an outlet portions, the transducer characterized by:

a single inlet tube having a first central axis;

a transducer body having a second central axis and to which the tube is coupled and wherein the first central axis is normal to a plane containing the second central axis;

a bluff body extending from one end of the transducer body substantially to another end along the second central axis and comprising a groove in an end adjacent the other end of the transducer body extending from an interior surface portion of the bluff body to the end thereof; and

a cylindrical lens portion adapted to be positioned substantially within the other end of the transducer body and about the end of the bluff body, the lens portion comprising:

a first cylindrical aperture comprising an upstream portion and extending from an upstream portion of the lens portion to a downstream portion through the center of the lens portion for fitting the lens portion about the bluff body,

a first conically-shaped depression in the upstream portion converging downstream-wise to the upstream portion of the aperture,

a second conically-shaped depression in the downstream portion of the lens portion diverging downstream-wise from the downstream portion of the aperture,

a second cylindrical aperture extending from the first depression toward the second depression, and

a third cylindrical aperture extending from the second cylindrical aperture to the first cylindrical aperture.

* * * * *

AA 32867777
 NOTARIA TERCERA
 ENCOMENDAS



ESCRITURA NUMERO CUATRO MIL QUINIENTOS -
 TREINTA Y NUEVE (No.4.539) -----

En la ciudad de Cali, Capital del Depar-
 tamento del Valle del Cauca, República de
 Colombia, a los VEINTITRES (23) días -
 del mes de OCTUBRE del año DOS MIL UNO --

(2.001), ante mí, JORGE ENRIQUE CAICEDO ZAMORANO, Notario

TERCERO (3o.) del Círculo de Calles y Vías, Notario

30 DIC 2008
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 AGENCIA DE AUTENTICACION

compareció JUAN MANUEL BARBERI OSPINA mayor de edad, identificado con la cédula de ciudadanía número 14.949.561 de Cali, y dijo: ----

PRIMERO.- Que obra en su carácter de Representante Legal de en nombre y representación de TECNOQUIMICAS S.A. sociedad comercial organizada y existente conforme a las leyes colombianas, con domicilio y sede principal en Cali constituida mediante escritura pública número 2670 de la Notaría Segunda de Cali de fecha 12 de junio de 1957, reformada en distintas oportunidades, según consta en el certificado expedido por la Cámara de Comercio de Cali -----

SEGUNDO: Que en tal carácter, por este público instrumento, concede Poder Especial pero amplio y suficiente a JOSE LUIS REYES VILLAMIZAR, mayor de edad, vecino de Bogotá, identificado con C.C. # 79.152.473 de Bogotá, abogado en ejercicio, portador de la T.P 44655 del C.S. de la J., domiciliado en Bogotá, D.C., República de Colombia con dirección carrera 7 No. 88.23 oficina 205, de la misma ciudad, como su representante con poder especial, amplio y suficiente, para obtener la protección de nuestra propiedad industrial y contra la competencia desleal, a cuyo efecto lo autorizo, para que nos represente ante cualesquiera entidad o persona, ejerzan o no jurisdicción, especialmente ante las del orden administrativo, contencioso-administrativo y judicial, en todo lo concerniente a los siguientes asuntos: a) Obtención, formulación de observaciones y oposición a patentes de invención, modelos y dibujos industriales y el registro de licencias de uso de esos derechos; b) Las acciones de oposición, cancelación, nulidad, medidas cautelares, concesión de licencias y en general los procesos civiles, penales, administrativos o contencioso-administrativos relacionados con estos derechos u otros de diferente naturaleza; acciones y procesos que promovamos o se nos promuevan; y c) para

LUZ MERY CORREA
 ELABORACION DE ESCRITURAS
 Notaría 3ª de Cali

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 WILLY VALERIO
 NOTARIO EN COMISION
 Bogotá D.C. - Colombia

que en todos los asuntos arriba determinados, , tanto en los términos señalados por los artículos 42 y complementarios de la Decisión 486 de la Comunidad Andina como del artículo 70 del C.P.C pueda sustituir este mandato, transigir, conciliar, admitir los hechos del proceso, desistir, cancelar, recibir, renunciar, y ratificar los actos de agentes oficiosos y ceder a título gratuito y/o oneroso, licenciar, inscribir contratos de cesión y de licencia, inscripción de prendas, levantamiento de prendas, inscribir derechos de retención y en general todos los asuntos que se deban tramitar ante la Superintendencia de Industria y Comercio.-----

Leído el presente instrumento al otorgante, lo aprobó y en constancia firma conmigo el Notario de todo lo cual doy fe.-----

Se agregan comprobantes. Derechos \$30.000.00 Decreto 1681 de Septiembre 16 de 1996. Reformado mediante Resolución No.5839 de Diciembre 27 del año 2.000 y Decreto 1326 de Julio 06 del año 2.001. Se corrió en la hoja número AA 3286877. ENMENDADO "OCTUBRE" VALE.

Juan m. Barberi

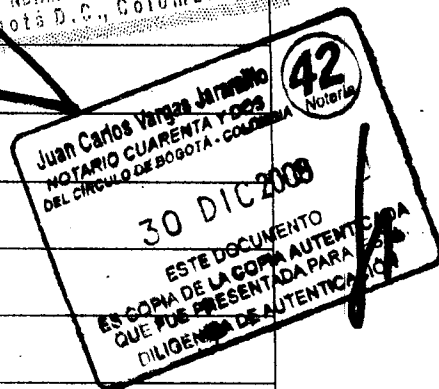
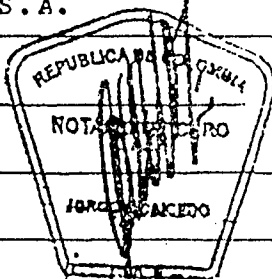
JUAN MANUEL BARBERI OSPINA

En rep. de TECNOQUIMICAS S.A.

Como Notario Veintitres de este Circulo
hago constar que esta fotocopia coincide
con su fotocopia auténtica que he tenido
a la vista.

113 AGO 2007

WILLY VALEK MORA
NOTARIO VEINTITRES
Bogotá D.C., Colombia



El Notario Tercero de Cali

Dr. JORGE ENRIQUE CAICEDO ZAMORANO



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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

Hora Certificado 11:23:52

Operacion : 02CP21027014

PAGINA No. 1

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CERTIFICA:

NOMBRE: TECNOQUIMICAS S.A.

SIGLA : TQ S.A.

DOMICILIO: CALI VALLE

DIRECCION COMERCIAL : ---C 23 7 39

DIRECCION NOTIFICACION JUDICIAL: ---C 23 7 39

CIUDAD: CALI

MATRICULA MERCANTIL NRO. 7049-4 FECHA MATRICULA : 01 DE JULIO DE 1957

AFILIADO

CERTIFICA:

NIT : 890300466-5

CERTIFICA:

QUE POR ESCRITURA NRO. 2670 DEL 12 DE JUNIO DE 1957 NOTARIA SEGUNDA DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 01 DE JULIO DE 1957 BAJO EL NRO. 16627 DEL LIBRO IX , SE CONSTITUYO LA SOCIEDAD DENOMINADA COMPANIAS TECNOQUIMICAS LIMITADA

CERTIFICA:

QUE POR ESCRITURA NRO. 8438 DEL 30 DE DICIEMBRE DE 1970 NOTARIA SEGUNDA DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 07 DE ENERO DE 1971 BAJO EL NRO. 42260 DEL LIBRO IX , LA SOCIEDAD SE TRANSFORMO DE SOCIEDAD LIMITADA EN SOCIEDAD EN COMANDITA POR ACCIONES BAJO EL NOMBRE DE COMPANIAS TECNOQUIMICAS LIMITADA COMANDITA POR ACCIONES (SIC) .

CERTIFICA:

QUE POR ESCRITURA NRO. 2139 DEL 21 DE ABRIL DE 1972 NOTARIA SEGUNDA DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 26 DE ABRIL DE 1972 BAJO EL NRO. 794 DEL LIBRO IX , LA SOCIEDAD CAMBIO SU NOMBRE DE COMPANIAS TECNOQUIMICAS LIMITADA COMANDITA POR ACCIONES (SIC) . POR EL DE TECNOQUIMICAS LIMITADA & CIA S.C. A. .

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

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Operacion : 02CP21027014 PAGINA No. 2

CERTIFICA:

QUE POR ESCRITURA NRO. 3255 DEL 30 DE AGOSTO DE 1983 NOTARIA DECIMA DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 31 DE AGOSTO DE 1983 BAJO EL NRO. 62343 DEL LIBRO IX ,LA SOCIEDAD SE TRANSFORMO DE SOCIEDAD EN COMANDITA POR ACCIONES EN SOCIEDAD AN?NIMA BAJO EL NOMBRE DE TECNOQUIMICAS S A .

CERTIFICA:

QUE POR ESCRITURA NRO. 5664 DEL 12 DE DICIEMBRE DE 2005 NOTARIA TERCERA DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 19 DE DICIEMBRE DE 2005 BAJO EL NRO. 14102 DEL LIBRO IX ,SE APROBO LA FUSION POR ABSORCION ENTRE (ABSORBENTE) TECNOQUIMICAS S.A. Y (ABSORBIDA (S)) DISTRIBUIDORA FARMACEUTICA CALOX COLOMBIANA S.A. - EN LIQUIDACION-, ORGANIZACION FARMACEUTICA AMERICANA S.A. OFA - EN LIQUIDACION- .

CERTIFICA:

QUE POR ESCRITURA NRO. 1675 DEL 08 DE MAYO DE 2008 NOTARIA TERCERA DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 16 DE MAYO DE 2008 BAJO EL NRO. 5362 DEL LIBRO IX , LA SOCIEDAD CAMBIO SU NOMBRE DE TECNOQUIMICAS S A . POR EL DE TECNOQUIMICAS S.A. . SIGLA: TQ S.A.

CERTIFICA:

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E.P. 1269	18/03/1986	NOTARIA	DECIMA	DE CALI	01/04/1986
83730 IX					
E.P. 5089	24/09/1986	NOTARIA	DECIMA	DE CALI	29/09/1986
87933 IX					
E.P. 7064	04/11/1987	NOTARIA	DECIMA	DE CALI	19/11/1987
2552 IX					
E.P. 7065	04/11/1987	NOTARIA	DECIMA	DE CALI	19/11/1987
2553 IX					
E.P. 5929	14/07/1989	NOTARIA	DECIMA	DE CALI	26/07/1989
20225 IX					
E.P. 8569	29/09/1989	NOTARIA	DECIMA	DE CALI	02/10/1989
22250 IX					
E.P. 10571	04/12/1992	NOTARIA	DECIMA	DE CALI	15/12/1992
60929 IX					
E.P. 10249	18/12/1995	NOTARIA	DECIMA	DE CALI	20/12/1995
10214 IX					
E.P. 2359	22/05/1997	NOTARIA	TERCERA	DE CALI	27/05/1997
3813 IX					
E.P. 2624	30/06/2000	NOTARIA	TERCERA	DE CALI	07/07/2000
4740 IX					
E.P. 3814	15/09/2000	NOTARIA	TERCERA	DE CALI	18/09/2000
6381 IX					
E.P. 3588	30/07/2004	NOTARIA	TERCERA	DE CALI	04/08/2004
8542 IX					
E.P. 2224	24/05/2006	NOTARIA	TERCERA	DE CALI	30/05/2006
6565 IX					
E.P. 1675	08/05/2008	NOTARIA	TERCERA	DE CALI	16/05/2008
5362 IX					

CERTIFICA:

VIGENCIA: 01 DE ENERO DEL AÑO 2057

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

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PAGINA No. 5

CERTIFICA:

OBJETO SOCIAL. LA SOCIEDAD TIENE POR OBJETO: A) LA FABRICACION, EL ENVASADO, LA IMPORTACION, LA EXPORTACION, LA VENTA Y DISTRIBUCION DE PRODUCTOS BIOLOGICOS Y QUIMICOS, MEDICAMENTOS O PRODUCTOS FARMACEUTICOS, PERFUMERIA O EFECTOS DE TOCADOR, PRODUCTOS VETERINARIOS, AGRICOLAS Y ALIMENTOS NATURALES Y/O PRODUCTOS DE CONSUMO POPULAR DE CUALQUIER NATURALEZA Y SERVICIOS EN GENERAL. B) INVERTIR EN SOCIEDADES O EMPRESAS DE CUALQUIER NATURALEZA O ESPECIE DE LA SOCIEDAD MERCANTIL, NACIONAL O EXTRANJERA, QUE TENGAN COMO ACTIVIDAD O NEGOCIO PROPIO DE SU OBJETO LA FABRICACION, DISTRIBUCION Y COMERCIO EN GENERAL DE PRODUCTOS BIOLOGICOS Y QUIMICOS, MEDICAMENTOS O PRODUCTOS FARMACEUTICOS, PERFUMERIA O EFECTOS DE TOCADOR, PRODUCTOS VETERINARIOS, AGRICOLAS, ALIMENTOS NATURALES Y/O PROCESADOS, PRODUCTOS DE CONSUMO POPULAR, SERVICIOS EN GENERAL O LA EXPLOTACION DE ESTABLECIMIENTOS DE COMERCIO DEDICADOS A DICHO GIRO. C) ADQUIRIR ACCIONES, CUOTAS SOCIALES, BONOS CEDULAS, TITULOS U OTROS VALORES EN COMPANIAS DE CUALQUIER NATURALEZA O TIPO LEGAL, DEDICADAS A LA EXPLOTACION DE CUALQUIER ACTIVIDAD ECONOMICA LICITA Y ENAJENARLAS. D) LA EXPLOTACION DEL NEGOCIO DE LA PUBLICIDAD Y EL ESTABLECIMIENTO DE OFICINAS DEDICADAS A ESTE NEGOCIO O A LA CREACION DE ORGANOS DE PUBLICIDAD HABLADOS O ESCRITOS. E) GARANTIZAR LAS OBLIGACIONES PROPIAS DE LOS ACCIONISTAS O DE TERCEROS. F) LA ADQUISICION DE BIENES MUEBLES, INMUEBLES Y DE TODA CLASE DE EQUIPO Y MAQUINARIA PARA SU ARRENDAMIENTO O PARA LA COMERCIALIZACION DE ELLOS. EN DESARROLLO DEL OBJETO SOCIAL PODRA OBTENER PRIVILEGIOS INDUSTRIALES, CONCESIONES, PATENTES DE INVENCION, DE MEJORAS O PROCEDIMIENTOS, MARCAS DE FABRICA O DE COMERCIO, YA SEA EN NOMBRE PROPIO O DE TERCEROS, OTORGAR A TERCEROS, DENTRO O FUERA DEL PAIS CONCESIONES O USOS DE EXPLOTACION SOBRE ESTOS DERECHOS, EJECUTAR TODA CLASE DE CONTRATOS DE COMPRAVENTA, DISTRIBUCION DE MATERIAS PRIMAS, DE PRODUCTOS SEMIELABORADOS O ELABORADOS EN EL MERCADO INTERNO O EN EL EXTERIOR Y EN GENERAL, LA CELEBRACION DE TODO ACTO O CONTRATO SOBRE BIENES MUEBLES O INMUEBLES DE COMERCIO, INDUSTRIALES O DE OTRA INDOLE QUE SE REFIERAN DIRECTAMENTE A LAS ACTIVIDADES QUE PERSIGUE LA SOCIEDAD.

CERTIFICA:

?RGANOS DE DIRECCI?N Y ADMINISTRACI?N. PARA LOS FINES DE SU DIRECCI?N, ADMINISTRACI?N Y REPRESENTACI?N, LA SOCIEDAD TIENE LOS SIGUIENTES ?RGANOS: A) ASAMBLEA GENERAL DE ACCIONISTAS. B) JUNTA DIRECTIVA. C) PRESIDENTE EJECUTIVO. D) TRES VICEPRESIDENTES EJECUTIVOS. E) VICEPRESIDENCIAS ADMINISTRATIVAS.

LA DIRECCI?N DE LA SOCIEDAD CORRESPONDE, EN PRIMER TERMINO A LA ASAMBLEA GENERAL DE ACCIONISTAS Y EN SEGUNDO LUGAR, A LA JUNTA DIRECTIVA COMO DELEGADA DE AQUELLA.

LA REPRESENTACI?N LEGAL DE LA SOCIEDAD Y LA GESTI?N DE LOS NEGOCIOS SOCIALES, ESTAR?N A CARGO DEL PRESIDENTE EJECUTIVO Y DE LOS TRES VICEPRESIDENTES

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PAGINA No. 6

EJECUTIVOS.

FUNCIONES DE LA ASAMBLEA DE ACCIONISTAS. ENTRE OTRAS LAS SIGUIENTES: 1) ACORDAR LA FUSI?N DE LA SOCIEDAD, SU TRANSFORMACI?N, LA ENAJENACI?N O EL ARRENDAMIENTO DE LA EMPRESA SOCIAL, LA DISOLUCI?N O LA PRORROGA Y CUALQUIER REFORMA, AMPLIACI?N MODIFICACI?N DEL CONTRATO SOCIAL. 9) AUTORIZAR LA ADQUISICI?N DE ACCIONES PROPIAS, CON SUJECI?N A LOS REQUISITOS ESTABLECIDOS POR LA LEY. 10) ADOPTAR EN GENERAL, TODAS LAS MEDIDAS QUE RECLAMEN EL CUMPLIMIENTO DE LOS ESTATUTOS O EL INTER?S DE LA SOCIEDAD.

LA JUNTA DIRECTIVA SE COMPONE DE SEIS (6) MIEMBROS PRINCIPALES O DIRECTORES, ELEGIDOS POR LA ASAMBLEA GENERAL DE ACCIONISTAS PARA PER?ODOS DE DOS A?OS, SIN PERJUICIO DE QUE PUEDAN SER REMOVIDOS LIBREMENTE POR LA ASAMBLEA O REELEGIDOS INDEFINIDAMENTE. SIMULT?NEAMENTE CON LA ELECCI?N DE LOS PRINCIPALES, LA ASAMBLEA ELEGIR? SEIS (6) SUPLENTE NUM?RICOS LOS CUALES, EN EL ORDEN DE DESIGNACI?N, REEMPLAZAR?N A LOS PRINCIPALES EN SUS FALTAS ABSOLUTAS, ACCIDENTALES O TEMPORALES.

EN LA JUNTA DIRECTIVA SE ENTIENDE DELEGADO EL MAS AMPLIO MANDATO PARA ADMINISTRAR LA SOCIEDAD Y POR CONSIGUIENTE, TENDR? ATRIBUCIONES SUFICIENTES PARA ORDENAR QUE SE EJECUTE O CELEBRE CUALQUIER ACTO O CONTRATO COMPRENDIDO DENTRO DEL OBJETO SOCIAL Y PARA ADOPTAR LAS DETERMINACIONES NECESARIAS EN ORDEN A QUE LA SOCIEDAD CUMPLA SUS FINES Y DE MANERA ESPECIAL, TENDR? LAS SIGUIENTES FUNCIONES ENTRE OTRAS: C) NOMBRAR Y REMOVER LIBREMENTE AL PRESIDENTE EJECUTIVO, A LOS VICEPRESIDENTES EJECUTIVOS Y A LOS VICEPRESIDENTES ADMINISTRATIVOS. E) DISPONER EL ESTABLECIMIENTO O LA CLAUSURA DE SUCURSALES O AGENCIAS, DENTRO O FUERA DEL DOMICILIO SOCIAL. F) FIJAR LAS POL?TICAS DE LA SOCIEDAD EN LOS DIFERENTES ORDENES DE SU ACTIVIDAD, ESPECIALMENTE EN MATERIA FINANCIERA, ECON?MICA Y LABORAL; APROBAR PLANES DE INVERSI?N Y DE PRODUCCI?N; DECIDIR SOBRE NUEVAS LINEAS DE PRODUCCI?N Y VENTA, ESTABLECER NORMAS GENERALES EN MATERIA DE PRECIOS Y DE VENTAS DE LOS PRODUCTOS ELABORADOS POR LA SOCIEDAD O DE LOS MATERIALES Y DEM?S ELEMENTOS EN QUE ELLA NEGOCIE Y DICTAR NORMAS Y REGLAMENTOS PARA LA ORGANIZACI?N Y EL FUNCIONAMIENTO DE TODAS LAS DEPENDENCIAS DE LA SOCIEDAD. G) DETERMINAR LA APLICACI?N QUE DEBA DARSE A LAS UTILIDADES QUE, CON EL CAR?CTER DE RESERVAS DE INVERSI?N, HAYAN SIDO APROPIADAS POR LA ASAMBLEA DE ACCIONISTAS. H) AUTORIZAR PREVIAMENTE LAS OPERACIONES QUE TENGAN POR OBJETO: 1) ADQUIRIR, HIPOTECAR Y EN CUALQUIER OTRA FORMA GRAVAR O LIMITAR EL DOMINIO DE BIENES RA?CES CUYA CUANT?A SEA SUPERIOR A \$100.000.000.00 MONEDA CORRIENTE; 2) CONSTITUIR PRENDA SOBRE BIENES SOCIALES O DARLOS EN ANTICRESIS PARA ACTOS O CONTRATOS CUYA CUANT?A SEA SUPERIOR A \$100.000.000.00 MONEDA CORRIENTE; 3) AUTORIZAR INVERSIONES EN BIENES DE CAPITAL O EFECTUAR REPARACIONES O MEJORAS DE LOS MISMOS, CUANDO UNAS U OTRAS IMPLIQUEN, EN CADA CASO, COSTOS O DESEMBOLSOS EN CUANT?A O SUPERIOR A CIENTO MIL D?LARES AMERICANOS (\$US100.000.00). 4) AUTORIZAR LOS CONTRATOS DE MUTUO QUE PUEDAN CELEBRAR LA SOCIEDAD LOS REPRESENTANTES LEGALES CUANDO SU CUANT?A SEA SUPERIOR A \$100.000.000.00 MONEDA LEGAL COLOMBIANA O A US\$300.000.00. L) AUTORIZAR AL REPRESENTANTE LEGAL PARA QUE SOLICITE, LLEGADO EL CASO, QUE SE ADMITA A LA COMPA??A A LA CELEBRACI?N DE CONCORDATO PREVENTIVO CON SUS ACREEDORES. M)

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CERTIFICADO NACIONAL

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PAGINA No. 7

SERVIR DE ?RGANO CONSULTIVO Y ASESOR DE LOS REPRESENTANTES DE LA COMPA??A.

LA ADMINISTRACI?N INMEDIATA DE LA COMPA??A, SU REPRESENTACI?N LEGAL Y LA GESTI?N DE LOS NEGOCIOS SOCIALES ESTAR?N A CARGO DEL PRESIDENTE EJECUTIVO Y DE LOS TRES VICEPRESIDENTES EJECUTIVOS, DESIGNADOS POR LA JUNTA DIRECTIVA PARA PERIODOS DE UN A?O, REELEGIBLES INDEFINIDAMENTE Y REMOVIBLES LIBREMENTE POR ELLA EN CUALQUIER TIEMPO, QUIENES COMO REPRESENTANTES LEGALES PODR?N ACTUAR CONJUNTA O SEPARADAMENTE CON IGUALDAD DE FUNCIONES Y CALIDADES. TODOS LOS EMPLEADOS DE LA COMPA??A CON EXCEPCI?N DE LOS DESIGNADOS POR LA ASAMBLEA DE ACCIONISTAS Y LOS DEPENDIENTES DEL REVISOR FISCAL, SI LOS HUBIERE, ESTAR?N SOMETIDOS EN EL DESEMPE?O DE SUS CARGOS A LOS REPRESENTANTES LEGALES.

LOS REPRESENTANTES LEGALES SON MANDATARIOS CON REPRESENTACI?N INVESTIDOS DE FUNCIONES EJECUTIVAS Y ADMINISTRATIVAS Y COMO TALES TIENEN A SU CARGO LA REPRESENTACI?N LEGAL DE LA COMPA??A, LA GESTI?N COMERCIAL Y FINANCIERA, LA RESPONSABILIDAD DE LA ACCI?N ADMINISTRATIVA, LA COORDINACI?N Y LA SUPERVISI?N GENERAL DE LA EMPRESA, LAS CUALES CUMPLIR?N CON ARREGLO A LAS NORMAS DE LOS ESTATUTOS Y A LAS DISPOSICIONES LEGALES Y CON SUJECI?N A LAS ORDENES E INSTRUCCIONES DE LA JUNTA DIRECTIVA.

COMO REPRESENTANTES LEGALES DE LA COMPA??A EN JUICIO Y FUERA DE JUICIO, LOS REPRESENTANTES TIENEN FACULTADES PARA EJECUTAR O CELEBRAR SIN OTRAS LIMITACIONES QUE LAS ESTABLECIDAS EN LOS ESTATUTOS EN CUANTO SE TRATE DE OPERACIONES QUE DEBAN SER PREVIAMENTE AUTORIZADAS POR LA JUNTA DIRECTIVA O POR LA ASAMBLEA DE ACCIONISTAS, TODOS LOS ACTOS O CONTRATOS COMPRENDIDOS DENTRO DEL OBJETO SOCIAL O QUE TENGAN CAR?CTER SIMPLEMENTE PREPARATORIO, ACCESORIO O COMPLEMENTARIO PARA LA REALIZACI?N DE LOS FINES QUE PERSIGUE LA SOCIEDAD Y LOS QUE SE RELACIONAN DIRECTAMENTE CON LA EXISTENCIA Y EL FUNCIONAMIENTO DE LA MISMA. LOS REPRESENTANTES QUEDAN INVESTIDOS DE PODERES ESPECIALES PARA TRANSIGIR, ARBITRAR Y COMPROMETER LOS NEGOCIOS SOCIALES; PROMOVER O COADYUVAR ACCIONES JUDICIALES, ADMINISTRATIVAS O CONTENCIOSO ADMINISTRATIVAS EN QUE LA COMPA??A TENGA INTER?S E INTERPONER TODOS LOS RECURSOS QUE SEAN PROCEDENTES CONFORME A LA LEY; DESISTIR DE LAS ACCIONES O RECURSOS QUE INTERPONGAN; NOVAR OBLIGACIONES O CR?DITOS; DAR O RECIBIR BIENES EN PAGO; CONSTITUIR APODERADOS JUDICIALES O EXTRAJUDICIALES, DELEGARLES FACULTADES REVOCAR MANDATOS Y SUSTITUCIONES.

PAR?GRAFO: LOS REPRESENTANTES LEGALES DE LA SOCIEDAD TIENEN AMPLIAS FACULTADES, SIN NINGUNA LIMITACI?N Y SIN REQUERIR AUTORIZACI?N PREVIA DE LA JUNTA DIRECTIVA, PARA ACTUAR EN NOMBRE DE LA SOCIEDAD EN LICITACIONES PUBLICAS, PRIVADAS O CUALQUIER OTRA MODALIDAD DE CONTRATACI?N, PRESENTAR PROPUESTAS, ACEPTAR ADJUDICACIONES Y CONTRATAR SIN LIMITACI?N DE CUANT?A ALGUNA ANTE LAS ENTIDADES PUBLICAS, EMPRESAS INDUSTRIALES Y COMERCIALES DEL ESTADO, SOCIEDADES DE ECONOM?A MIXTA, BIEN SEAN ELLAS DEL ORDEN NACIONAL, DISTRITAL, DEPARTAMENTAL O MUNICIPAL.

CERTIFICA:

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027 Hora Certificado 11:23:52

Operacion : 02CP21027014 PAGINA No. 8

DOCUMENTO: ACTA No. 393 DEL 20 DE ENERO DE 1993
ORIGEN: JUNTA DIRECTIVA
INSCRIPCION: 26 DE ENERO DE 1993 No. 62203 DEL LIBRO IX

FUE(ON) NOMBRADO(S) :

PRESIDENTE EJECUTIVO
FRANCISCO JOSE BARBERI OSPINA
C.C.14445880

VICEPRESIDENTE EJECUTIVO
JUAN MANUEL BARBERI OSPINA
C.C.14949561

VICEPRESIDENTE EJECUTIVO
JUAN BAUTISTA DE LOS RIOS GUTIERREZ
C.C.17108621

VICEPRESIDENTE EJECUTIVO
EMILIO SARDI APARICIO
C.C.14434582

CERTIFICA:

DOCUMENTO: ACTA No. 67 DEL 28 DE MARZO DE 2008
ORIGEN: ASAMBLEA DE ACCIONISTAS
INSCRIPCION: 16 DE MAYO DE 2008 No. 5363 DEL LIBRO IX

FUE(ON) _NOMBRADO(S)

JUNTA DIRECTIVA

PRINCIPALES

PRIMER RENGLON
FRANCISCO JOSE BARBERI OSPINA
C.C.14445880

SEGUNDO RENGLON
JUAN MANUEL BARBERI OSPINA
C.C.14949561

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PAGINA No. 9

TERCER RENGLON

EMILIO SARDI APARICIO
C.C.14434582

CUARTO RENGLON

ANTONIO JAIR RAMIREZ ECHAVE
C.C.16741040

QUINTO RENGLON

DIEGO HUMBERTO QUIJANO REISSNER
C.C.16615708

SEXTO RENGLON

ALONSO BOTERO PARDO
C.C.16830282

SUPLENTE

PRIMER RENGLON

VICTOR RICARDO ROSA GARCIA
C.C.6811102

SEGUNDO RENGLON

ERNESTO TRUJILLO PEREZ
C.C.14984104

TERCER RENGLON

ANA MARIA ALVAREZ ROBLEDO
C.C.31170896

CUARTO RENGLON

GUSTAVO ADOLFO SANCHEZ LESMES
C.C.16625960

QUINTO RENGLON

JORGE ENRIQUE ARIZA BERNAL
C.C.19494493

SEXTO RENGLON

MARTHA LUZ GONZALEZ TORRES
C.C.31854671

CERTIFICA:

DOCUMENTO: ACTA No. 59 DEL 31 DE MARZO DE 2003

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027 Hora Certificado 11:23:52

Operacion : 02CP21027014 PAGINA No. 10

ORIGEN: ASAMBLEA DE ACCIONISTAS

INSCRIPCION: 23 DE ABRIL DE 2003 No. 2845 DEL LIBRO IX

FUE(RON) NOMBRADO(S) :

REVISOR FISCAL

DELOITTE & TOUCHE LTDA D & T LTDA

NIT.860005813-4

CERTIFICA:

DOCUMENTO: DOCUMENTO PRIVADO DEL 26 DE AGOSTO DE 2004

ORIGEN: DELOITTE & TOUCHE LTDA D & T LTDA

INSCRIPCION: 30 DE AGOSTO DE 2004 No. 9417 DEL LIBRO IX

FUE(RON) NOMBRADO(S) :

REVISOR FISCAL PRINCIPAL

LUIS FERNANDO QUICENO BENAVIDES

C.C.6106227

CERTIFICA:

DOCUMENTO: DOCUMENTO PRIVADO DEL 24 DE SEPTIEMBRE DE 2008

ORIGEN: DELOITTE & TOUCHE LTDA D & T LTDA

INSCRIPCION: 26 DE SEPTIEMBRE DE 2008 No. 11100 DEL LIBRO IX

FUE(RON) NOMBRADO(S) :

REVISOR FISCAL SUPLENTE

PATRICIA GASCA BARRERA

C.C.38603726

CERTIFICA:

QUE POR ESCRITURA NRO. 5235 DEL 19 DE JULIO DE 1996 NOTARIA DECIMA DE CALI ,
INSCRITA EN LA CAMARA DE COMERCIO EL 25 DE JULIO DE 1996 BAJO EL NRO. 144 DEL
LIBRO V MEDIANTE LA CUAL SE LE CONCEDE PODER ESPECIAL, AMPLIO Y SUFICIENTE A
CARLOS ALBERTO QUINTERO, MAYOR DE EDAD, VECINO DE ESTA CIUDAD, IDENTIFICADO

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PAGINA No. 11

CON LA CEDULA DE CIUDADANIA NRO.

14.440.778 DE CALI, PARA QUE EN NOMBRE Y REPRESENTACION DE LA SOCIEDAD, CUYA PERSONERIA OSTENTA, EL REPRESENTANTE EN LOS SIGUIENTES ACTOS: A) PRESENTAR EN LA ADMINISTRACION DE IMPUESTOS Y ADUANAS NACIONALES O DEL ORGANISMO QUE HAGA SUS VECES Y FIRMAR EN REPRESENTACION DE LA SOCIEDAD, LAS DECLARACIONES DEL IMPUESTO SOBRE LA RENTA Y COMPLEMENTARIOS QUE CORRESPONDA A LA SOCIEDAD, Y TODAS LAS DEMAS DECLARACIONES QUE LA SOCIEDAD DEBA PRESENTAR ANTE DICHA ENTIDAD, TALES COMO LA DE VENTAS, RETENCION EN LA FUENTE, TIMBRE Y CUALESQUIER OTRA DECLARACION QUE POR LEY LA SOCIEDAD ESTE OBLIGADA A PRESENTAR.

B) PARA PRESENTAR Y SUSCRIBIR TODOS LOS DOCUMENTOS QUE OBLIGUEN A TECNOQUIMICAS S.A., COMO DECLARANTE DEL IMPUESTO DE INDUSTRIA Y COMERCIO Y EL COMPLEMENTARIO DE AVISOS Y TABLEROS EN LOS MUNICIPIOS EN QUE LA SOCIEDAD ESTE OBLIGADA AL PAGO DE LOS CITADOS IMPUESTOS, PUDIENDO IGUALMENTE NOTIFICARSE DE TODAS LAS ACTUACIONES, ACTOS, DILIGENCIAS O GESTIONES RELACIONADAS O QUE SE DERIVEN DE LOS MENCIONADOS TRIBUTOS. C) PARA PRESENTAR Y SUSCRIBIR TODOS LOS DOCUMENTOS QUE OBLIGUEN A TECNOQUIMICAS S.A. COMO DECLARANTE DEL IMPUESTO PREDIAL Y COMPLEMENTARIOS EN LOS MUNICIPIOS DONDE TENGA BIENES INMUEBLES, PUDIENDO IGUALMENTE NOTIFICARSE DE TODAS LAS ACTUACIONES, ACTOS, DILIGENCIAS O GESTIONES RELACIONADAS O QUE SE DERIVEN DEL CITADO IMPUESTO. D) PARA DAR RESPUESTA A LOS REQUERIMIENTOS ORDINARIOS Y A LAS SOLICITUDES DE INFORMACION EN RELACION CON LOS IMPUESTOS ADMINISTRADOS POR LA DIRECCION DE IMPUESTOS Y ADUANAS NACIONALES Y POR LAS DEPENDENCIAS MUNICIPALES QUE ADMINISTREN LOS IMPUESTOS DE CARACTER TERRITORIAL. E) Y EN GENERAL, PARA QUE ASUMA LA PERSONERIA EN NOMBRE DE TECNOQUIMICAS S.A., SIEMPRE QUE LO ESTIME CONVENIENTE, DE MANERA QUE EN NINGUN CASO LA SOCIEDAD QUEDE SIN REPRESENTACION EN LOS ASUNTOS RELACIONADOS CON LAS FACULTADES OTORGADAS.

CERTIFICA:

QUE POR ESCRITURA NRO. 307 DEL 31 DE ENERO DE 2002 NOTARIA TERCERA DE CALI, INSCRITA EN LA CAMARA DE COMERCIO EL 13 DE FEBRERO DE 2002 BAJO EL NRO. 298 DEL LIBRO V MEDIANTE LA CUAL SE LE CONCEDE PODER ESPECIAL, AMPLIO Y SUFICIENTE A JORGE ROBERTO OBANDO RODRIGUEZ, MAYOR DE EDAD, VECINO DE ESTA CIUDAD, IDENTIFICADO CON LA CEDULA DE CIUDADANIA NRO. 14.960.183 DE CALI, PARA QUE EN NOMBRE Y REPRESENTACION DE LA SOCIEDAD, CUYA PERSONERIA OSTENTA: 1o.) PROMUEVA O DESISTA DE ACCIONES ANTE CORPORACIONES, ENTIDADES O FUNCIONARIOS DEL ORDEN JUDICIAL O GUBERNATIVO, YA SEA EN PROCESOS, ACTUACIONES O ACTOS SIMPLES, DILIGENCIAS O GESTIONES EN QUE TECNOQUIMICAS S.A. TENGA INTERES COMO ACTOR, DEMANDANDO O TERCERO INTERVINIENTE EN RELACION CON LOS ASUNTOS DE CARACTER LABORAL, POLICIVO, PENAL O DE FISCALIA, EN QUE LA EMPRESA SEA PARTE ACTIVA O PASIVA, CON CAPACIDAD PARA NOTIFICARSE Y CONTESTAR Y HACERSE PARTE DE ELLOS EN NOMBRE DE TECNOQUIMICAS S.A. 2o.) SUSCRIBA Y DE POR TERMINADO LOS CONTRATOS DE TRABAJO DEL PERSONAL VINCULADO A LA EMPRESA. 3o.) CONSTITUYA APODERADOS EN DESARROLLO DE ESTA REPRESENTACION LABORAL, REVOQUE Y SUSTITUYA DICHOS PODERES CUANDO LO ESTIME PROCEDENTE. 4o.) TRANSIGA, CONCILIE, DESISTA Y COMPROMETA A LA EMPRESA EN TODOS LOS TRAMITES ADMINISTRATIVOS Y PROCESOS JUDICIALES, DE CARACTER LABORAL, POLICIVO, PENAL O DE FISCALIA EN LOS QUE LA EMPRESA SEA

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PAGINA No. 12

 PARTE DEMANDANTE, DEMANDADA O TERCERO INTERVINIENTE. PARAGRAFO. LA FACULTAD PARA TRANSIGIR O CONCILIAR SE LIMITA A LA SUMA DE QUINIENTOS (500) SALARIOS LEGALES MENSUALES. 5o.) OTORGUE PODERES Y CONSTITUYA MANDATARIOS PARA INICIAR LAS ACCIONES JUDICIALES DE CARACTER CIVIL, COMERCIAL Y PENAL TENDIENTES A LA RECUPERACION DE LOS CREDITOS A FAVOR DE LA SOCIEDAD, BIEN SEA REPRESENTADOS EN FACTURAS, CHEQUES, TITULOS VALORES O CUALQUIER OTRO DOCUMENTO REPRESENTATIVO DE CREDITO, HASTA POR SUMA EQUIVALENTE A QUINIENTOS (500) SALARIOS MINIMOS LEGALES MENSUALES, CON EXPRESAS FACULTADES PARA ASISTIR EN NOMBRE DE TECNOQUIMICAS S.A. A LAS AUDIENCIAS DE CONCILIACION QUE PROGRAMEN LOS JUZGADOS CIVILES MUNICIPALES Y DEL CIRCUITO, CON AUTORIZACION PARA TRANSIGIR, DESISTIR CONCILIAR O COMPROMETER A LA SOCIEDAD HASTA POR LA CUANTIA INDICADA. 6o. REPRESENTA A TECNOQUIMICAS S.A. DENTRO DE LOS TRAMITES DE CONCORDATOS, PROCESOS DE REESTRUCTURACION ECONOMICA PREVISTO EN LA LEY 550 DE 1999 Y LAS NORMAS QUE LA ADICIONEN O MODIFIQUEN Y LIQUIDACIONES OBLIGATORIAS QUE SE TRAMITEN ANTE LA SUPERINTENDENCIA DE SOCIEDADES O ANTE LAS ENTIDADES PERTINENTES CUANDO SE TRATE DE OTRA CLASE DE ACREEDORES O ANTE LOS JUZGADOS CIVILES, CON EXPRESAS FACULTADES PARA TRANSIGIR, DESISTIR, CONCILIAR O COMPROMETER, NOMBRAR APODERADOS, PRESENTAR LOS CREDITOS, APORTAR LAS PRUEBAS QUE ESTIME NECESARIAS, ASISTIR A LAS AUDIENCIAS PRELIMINARES Y DEFINITIVAS, ACORDAR FORMULAS DE PAGO, RECIBIR Y EN GENERAL PARA EJERCER TODAS AQUELLAS GESTIONES NECESARIAS PARA OBTENER EL RECONOCIMIENTO Y PAGO DE LOS CREDITOS PRESENTADOS. LAS FACULTADES AQUI ESTABLECIDAS ESTAN LIMITADAS PARA LOS CREDITOS HASTA POR CUANTIA DE QUINIENTOS (500) SALARIOS MINIMOS LEGALES MENSUALES. PARAGRAFO. IGUALMENTE QUEDA FACULTADO PARA ACEPTAR Y REPRESENTAR A TECNOQUIMICAS CUANDO LA EMPRESA SEA NOMBRADA EN JUNTA DE ACREEDORES O EN ORGANOS EQUIVALENTES O SIMILARES, EN LOS PROCESOS QUE TRAMITEN ANTE LA SUPERINTENDENCIA DE SOCIEDADES O ANTE LAS ENTIDADES PERTINENTES CUANDO SE TRATE DE OTRA CLASE DE DEUDORES. 7o.) REPRESENTA A TECNOQUIMICAS S.A. EN LOS PROCEDIMIENTOS DE CONCILIACION QUE LOS DEUDORES DE LA SOCIEDAD CONVOQUEN ANTE LAS ENTIDADES FACULTADAS PARA ELLO CON EL FIN OBTENER UN ACUERDO EN EL PAGO DE LAS ACREENCIAS, CON EXPRESAS FACULTADES PARA TRANSIGIR, DESISTIR, CONCILIAR O COMPROMETER Y RECIBIR, FACULTADES QUE SE LIMITAN HASTA POR LA SUMA DE QUINIENTOS (500) SALARIOS MINIMOS LEGALES MENSUALES. 8o.) REVISE LOS EXPEDIENTES DE LOS PROCESOS JUDICIALES DE CARACTER EJECUTIVO EN QUE LA SOCIEDAD SEA PARTE DEMANDANTE, EN TODO EL TERRITORIO NACIONAL, PARA LA RECUPERACION DE SUS ACREENCIAS. 9o.) APRUEBE Y SUSCRIBA ACUERDOS PRIVADOS DE PAGO Y CONCILIACIONES DE OBLIGACIONES A FAVOR DE TECNOQUIMICAS POR LA VENTA DE SUS PRODUCTOS HASTA POR LA SUMA DE (500) SALARIOS MINIMOS LEGALES MENSUALES.

CERTIFICA:

QUE POR ESCRITURA NRO. 4.202 DEL 31 DE MAYO DE 1995 NOTARIA DECIMA DE CALI, INSCRITA EN LA CAMARA DE COMERCIO EL 24 DE SEPTIEMBRE DE 2003 BAJO EL NRO. 134 DEL LIBRO V SE CONFIERE PODER ESPECIAL A ANTONIO JAIRO RAMIREZ ECHAVE, ABOGADO TITULADO Y EN EJERCICIO, CON TARJETA PROFESIONAL No. 58.401 DEL MINISTERIO DE JUSTICIA, IDENTIFICADO CON LA CEDULA DE CIUDADANIA NUMERO 16.741.040 DE CALI PARA QUE REPRESENTA A TECNOQUIMICAS S.A., EN LOS SIGUIENTES ACTOS: A)

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PAGINA No. 13

SOLICITAR Y ADELANTAR ANTE EL INSTITUTO COLOMBIANO AGROPECUARIO TODOS LOS
TRAMITES ATINENTES A LA OBTENCION DE LICENCIAS DE VENTA Y LICENCIAS DE
FUNCIONAMIENTO, RENOVACIONES, CERTIFICACIONES, AMPLIACIONES, INSCRIPCIONES Y
MODIFICACIONES EN GENERAL; B) TODOS LOS TRAMITES ANTE EL INVIMA ATINENTES A
LA OBTENCION DE REGISTRO SANITARIO, RENOVACION DEL MISMO, REFORMULACIONES,
ADICIONES DE NUESTRA LINEA DE PRODUCTOS, CAMBIOS DE TITULAR Y DE FABRICANTE,
CESIONES, CERTIFICACIONES DE FORMULA Y EXCLUSIVIDAD, MODIFICACIONES DE
FABRICAR Y VENDER A IMPORTAR Y VENDER Y VICEVERSA, E IGUALMENTE
CERTIFICACIONES SOBRE LA LINEA COMPLETA DE NUESTROS PRODUCTOS, A CUYO OBJETO
LO FACULTO PARA DAR ANTE DICHAS AUTORIDADES TODOS LOS PASOS NECESARIOS,
PRESENTAR SOLICITUDES, HACER DECLARACIONES, PAGAR DERECHOS, PROBAR
EXPLOTACIONES, SOLICITAR TESTIMONIOS, RECIBIR DOCUMENTOS, FORMULAR APELACIONES
Y RECLAMOS, DESISTIR Y PERCIBIR. ASI MISMO DICHO APODERADO ESTA AUTORIZADO
PARA HACER CUANTO FUERE NECESARIO ANTE LAS AUTORIDADES ADMINISTRATIVAS PARA
LOS FINES ARRIBA INDICADOS CON TODAS LAS DEMAS FACULTADES GENERALES Y
ESPECIALES QUE FUEREN NECESARIAS INCLUIDAS LAS DE SUSTITUIR Y DELEGAR EL
PRESENTE PODER SI LO ESTIMARE CONVENIENTE Y EN CASO NECESARIO REVOCAR DICHAS
SUSTITUCIONES. PUDIENDO ATENDER ASI MISMO LAS NOTIFICACIONES QUE DIRECTA O
INDIRECTAMENTE SE GENERE DE LOS ACTOS, ACTUACIONES, DILIGENCIAS O GESTIONES
QUE TENGAN RELACION DE CAUSALIDAD POR LOS SUSODICHOS TRAMITES Y 3) EN
GENERAL PARA QUE ASUMA LA PERSONERIA EN NOMBRE DE TECNOQUIMICAS S.A., SIEMPRE
QUE LO ESTIME CONVENIENTE, DE MANERA QUE EN NINGUN CASO QUEDE SIN LA DEBIDA
REPRESENTACION EN LA SALVAGUARDIA DE SUS DERECHOS Y OBLIGACIONES EN LOS
ASUNTOS CONCERNIENTES PARA LAS MATERIAS DE QUE TRATA ESTE PODER. ANTONIO
JAIRO RAMIREZ ECHAVE SE CENIRA RIGUROSAMENTE A LOS TERMINOS EXPRESADOS EN ESTE
MANDATO QUE SE OTORGA POR TERMINO INDEFINIDO Y CUALQUIER MODIFICACION O SU
REVOCATORIA SE HARA EXPRESAMENTE POR ESCRITURA PUBLICA.

CERTIFICA:

QUE POR ESCRITURA NRO. 6224 DEL 15 DE DICIEMBRE DE 2004 NOTARIA TERCERA DE
CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 17 DE ENERO DE 2005 BAJO EL NRO. 3
DEL LIBRO V MEDIANTE LA CUAL CONCEDE PODER ESPECIAL PERO AMPLIO Y SUFICIENTE
A DIEGO PEREZ MENDOZA MAYOR DE EDAD, VECINO DE BOGOTA, IDENTIFICADO CON CEDULA
DE CIUDADANIA NUMERO 16.820.530 DE CALI, COMO SU REPRESENTANTE CON PODER
ESPECIAL, AMPLIO Y SUFICIENTE, PARA REALIZAR TODOS LOS TRAMITES RELACIONADOS
CON EL PROCEDIMIENTO DE OTORGAMIENTO DE LICENCIA DE VENTA DE LOS PRODUCTOS
AGRICOLAS DE LA SOCIEDAD, CON FACULTAD PARA FIRMAR TODO TIPO DE DOCUMENTOS,
SOLICITUDES, REQUERIMIENTOS, MEMORIALES RESPUESTAS, ACLARACIONES BIEN SEA ANTE
EL INSTITUTO COLOMBIANO AGROPECUARIO ICA, MINISTERIO DEL MEDIO AMBIENTE,
MINISTERIO DE PROTECCION SOCIAL O ANTE LAS AUTORIDADES GUBERNAMENTALES
COMPETENTES EN LO RELACIONADO CON LOS TRAMITES QUE PERMITAN LA
COMERCIALIZACION DE ESE TIPO DE PRODUCTOS. LA FACULTAD TAMBIEN COMPRENDERA LA
DE NOTIFICARSE, RESPONDER E INTERPONER RECURSOS DE TODO TIPO DE ACTO
ADMINISTRATIVO. EL APODERADO SUSCRIBIRA TODOS LOS DOCUMENTOS Y REALIZAR TODOS
LOS ACTOS QUE OBLIGUEN A LA SOCIEDAD ANTE LAS AUTORIDADES MENCIONADAS,
PUDIENDO IGUALMENTE NOTIFICARSE DE TODAS LAS ACTUACIONES, ACTOS

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PAGINA No. 14

ADMINISTRATIVOS, DILIGENCIAS O GESTIONES RELACIONADAS O QUE SE DERIVEN DE DICHA ACTIVIDAD Y EN GENERAL, PARA QUE ASUMA LA PERSONERIA A NOMBRE DE TECNOQUIMICAS S.A., SIEMPRE QUE LO ESTIME CONVENIENTE, DE MANERA QUE EN NINGUN CASO QUEDE SIN LA DEBIDA REPRESENTACION EN LA SALVAGUARDIA DE SUS DERECHOS Y CUMPLIMIENTO DE OBLIGACIONES EN LOS ASUNTOS CONCERNIENTES PARA LAS MATERIAS DE QUE TRATA ESTE PODER. EL APODERADO SE CE?IRA RIGUROSAMENTE A LOS TERMINOS EXPRESADOS EN ESTE MANDATO QUE SE OTORGA POR TERMINO INDEFINIDO Y CUALQUIER MODIFICACION O REVOCATORIA SE HARA EXPRESAMENTE POR ESCRITURA PUBLICA.

CERTIFICA:

QUE POR ESCRITURA NRO. 4265 DEL 16 DE SEPTIEMBRE DE 2005 NOTARIA TERCERA DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 04 DE OCTUBRE DE 2005 BAJO EL NRO. 168 DEL LIBRO V EL SE?OR JUAN BAUTISTA DE LOS RIOS GUTIERREZ MAYOR DE EDAD, DOMICILIADO EN CALI, IDENTIFICADO CON LA CEDULA DE CIUDADANIA NUMERO 17108621 DE BOGOTA, QUIEN ACTUA EN SU CALIDAD DE REPRESENTANTE LEGAL DE TECNOQUIMICAS S. A. SOCIEDAD COMERCIAL ORGANIZADA Y EXISTENTE CONFORME A LAS LEYES COLOMBIANAS, CON DOMICILIO Y SEDE PRINCIPAL EN CALI. EN DICHA CONDICION CONFIERE PODER AMPLIO Y SUFICIENTE A LAS SIGUIENTES PERSONAS: CLAUDETTE VERNOT HERNANDEZ ABOGADA TITULADA Y EN EJERCICIO, IDENTIFICADA CON LA CEDULA DE CIUDADANIA No. 51722517 DE BOGOTA, PORTADORA DE LA TARJETA PROFESIONAL DE ABOGADO No. 57111 DEL C.S. DE LA J., ANDRES FELIPE ZAPATA OCAMPO, IDENTIFICADO CON LA CEDULA DE CIUDADANIA No. 79598546 DE BOGOTA, PORTADOR DE LA TARJETA PROFESIONAL DE ABOGADO No. 107240 DEL C.S. DE LA J. Y JUAN MANUEL SERRANO CASTILLO, IDENTIFICADO CON LA CEDULA DE CIUDADANIA No. 79875670 DE BOGOTA, PORTADOR DE LA TARJETA PROFESIONAL DE ABOGADO No. 124953 DE C.S. DE LA J., TODOS CON DOMICILIO EN LA CIUDAD DE BOGOTA, D.C., PARA QUE EN NOMBRE DE MI REPRESENTADA ACTUEN EN TODOS LOS ASUNTOS DE PROPIEDAD INTELECTUAL Y LOS DERIVADOS DE ELLA, CON FACULTAD PARA RECIBIR NOTIFICACIONES, NOMBRAR APODERADOS JUDICIALES O EXTRAJUDICIALES EN ESTOS ASUNTOS.

EL PRESENTE PODER SE CONFIERE PARA QUE LOS APODERADOS ACTUEN ANTE CUALQUIER PERSONA O AUTORIDAD ADMINISTRATIVA DEL ORDEN NACIONAL, DEPARTAMENTAL, DISTRITAL Y LOCAL; ANTE LAS AUTORIDADES CONTENCIOSO ADMINISTRATIVAS Y JUDICIALES, PARA OBTENER LA PROTECCION DE NUESTRA PROPIEDAD INTELECTUAL Y CONTRA LAS PRACTICAS RESTRICTIVAS DE LA COMPETENCIA Y LOS ASUNTOS DE COMPETENCIA DESLEAL, A CUYO EFECTO LA AUTORIZO, EN TODO LO CONCERNIENTE A LOS SIGUIENTES ASUNTOS: A) OBTENCION DE PATENTES DE INVENCION, DE MODELO DE UTILIDAD, ESQUEMAS DE TRAZADOS DE CIRCUITOS INTEGRADOS, DISE?OS INDUSTRIALES, EL REGISTRO DE MARCAS DE PRODUCTOS O SERVICIOS; LEMAS COMERCIALES; DEPOSITO DE NOMBRES Y ENSE?AS COMERCIALES, INDICACIONES GEOGRAFICAS; RENOVACION DE SIGNOS DISTINTIVOS, RENOVACIONES, AFECTACIONES AL REGISTRO, INSCRIPCION DE CONTRATOS, SOLICITUD Y RENOVACION DE NOMBRES DE DOMINIO; B) PRESENTACION DE OPOSICIONES AL REGISTRO DE MARCAS DE TERCERO, PRESENTACION DE ALEGATOS EN DEFENSA DE OPOSICIONES AL REGISTRO, ACCION DE CANCELACION, ACCION POR INFRACCION DE DERECHOS, REVOCATORIA DIRECTA, ACCION DE NULIDAD, ACCION DE NULIDAD Y RESTABLECIMIENTO DEL DERECHO, ACCION REIVINDICATORIA, ACCIONES DE TUTELA,

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PAGINA No. 15

POPULARES, DE GRUPO, DE CLASE; ACCIONES Y PROCESOS QUE PROMOVAMOS O SE NOS PROMUEVAN; C) AGOTAMIENTO DE LA VIA GUBERNATIVA, EJERCICIO DEL DERECHO DE PETICION ANTE CUALQUIER PERSONA O AUTORIDAD; D) SOLICITUD DE MEDIDAS CAUTELARES, PRESENTACION DE ACCIONES MEDIANTE PROCESOS CIVILES, PENALES, ADMINISTRATIVOS O CONTENCIOSO ADMINISTRATIVOS RELACIONADOS CON ESTOS DERECHOS U OTROS DE DIFERENTE NATURALEZA, MEDIDAS EN FRONTERA, ACCIONES Y PROCESOS QUE PROMOVAMOS O SE NOS PROMUEVAN; E) OBTENER Y TRAMITAR TODO LO RELACIONADO CON EL RECONOCIMIENTO DE DERECHOS DE AUTOR, DERECHOS CONEXOS Y NUEVAS TECNOLOGIAS Y SU PROTECCION LEGAL; F) SOLICITUD DE REGISTRO Y RENOVACION DE CONTRATOS DE TRANSFERENCIA DE TECNOLOGIA; G) OBTENER Y TRAMITAR TODO LO RELACIONADO CON LICENCIAS DE FUNCIONAMIENTO, REGISTROS SANITARIOS, AUTORIZACION DE CERTIFICADOS DE LIBRE VENTA, AUTORIZACION DE PUBLICIDAD ANTE EL MINISTERIO DE PROTECCION SOCIAL O EL INVIMA O ANTE CUALQUIER AUTORIDAD SANITARIA; H) OBTENCION DE CERTIFICADOS DE CARENCIA DE INFORMES POR TRAFICO DE ESTUPEFACIENTES. RENOVACIONES, AUTORIZACIONES EXTRAORDINARIAS ANTE LA DIRECCION NACIONAL DE ESTUPEFACIENTES O EL CONSEJO NACIONAL DE ESTUPEFACIENTES; I) SOLICITUD DE AUTORIZACIONES PARA PROMOCIONES, RIFAS Y JUEGOS ANTE ETESA O ANTE LAS AUTORIDADES COMPETENTES DEL ORDEN LOCAL, DISTRITAL O DEPARTAMENTAL; Y EN GENERAL CUALQUIERA OTRA PETICION ANTE LAS AUTORIDADES ADMINISTRATIVA, ASI COMO PARA NOTIFICARSE DE CUALQUIER PROVIDENCIA Y RENUNCIAR A TERMINOS. EN TODOS LOS ASUNTOS ARRIBA DETERMINADOS LA APODERADA QUEDA FACULTADA PARA SUSTITUIR TOTAL O PARCIALMENTE ESTE MANDATO, TRANSIGIR, CONCILIAR EXTRAJUDICIAL O JUDICIALMENTE, ADMITIR LOS HECHOS DEL PROCESO PERO NO PARA CONFESAR, DESISTIR, CANCELAR, RECIBIR, RENUNCIAR Y RATIFICAR LOS ACTOS DE AGENTES OFICIOSOS.

CERTIFICA:

QUE POR DOCUMENTO PRIVADO DEL 22 DE MAYO DE 2008 DE CALI, INSCRITA EN LA CAMARA DE COMERCIO EL 04 DE JUNIO DE 2008 BAJO EL NRO. 90 DEL LIBRO V Y MODIFICADO POR DOCUMENTO PRIVADO DE FECHA 18 DE JULIO DE 2008, INSCRITA EN LA CAMARA DE COMERCIO EL 08 DE AGOSTO DE 2008 BAJO EL NRO. 151 DEL LIBRO V, SE CONCEDE PODER ESPECIAL, AMPLIO Y SUFICIENTE A LOS SIGUIENTES FUNCIONARIOS DE LA EMPRESA:

1. ANA MAR?A ?LVAREZ R., CON C.C. 31.170.896 DE CALI Y JORGE ENRIQUE GIRALDO, CON C.C. 16.784.794 DE CALI, OBRARAN COMO APODERADOS ESPECIALES PARA EL DESARROLLO DE LAS SIGUIENTES FACULTADES:

A. SUSCRIBIR LOS CONTRATOS DE TRABAJO, SUS MODIFICACIONES Y DARLOS POR TERMINADO DEL PERSONAL VINCULADO O QUE SE VINCULE A TECNOQU?MICAS S.A.

B. SUSCRIBIR CONTRATOS DE APRENDIZAJE Y PASANTIAS ASI COMO SUS MODIFICACIONES Y ADICIONES.

C. SUSCRIBIR ACUERDOS CON LOS EMPLEADOS DE LA SOCIEDAD.

D. COMPARECER DIRECTAMENTE U OTORGAR PODER PARA ATENDER RECLAMACIONES Y

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PAGINA No. 16

PROCESOS DE ORDEN LABORAL BIEN SEA DE CAR?CTER ADMINISTRATIVO O JUDICIAL ANTE LAS OFICINAS REGIONALES DE TRABAJO, MINISTERIO DE LA PROTECCI?N SOCIAL Y ANTE CUALQUIER OTRA AUTORIDAD O ENTIDAD ANTE LA QUE SE INICIE Y TRAMITE PROCEDIMIENTOS DE CAR?CTER LABORAL O RELACIONADOS CON TEMAS DE LA SEGURIDAD SOCIAL.

E. FIRMAR TODOS LOS DOCUMENTOS Y ATENDER TODOS LOS TR?MITES ANTE LAS CAJAS DE COMPENSACI?N FAMILIAR, EMPRESAS PRESTADORAS DE SERVICIOS DE SALUD (EPS), FONDOS DE PENSIONES Y CESANT?AS, ADMINISTRADORA DE RIESGOS PROFESIONALES (ARP), INSTITUTO DE LOS SEGUROS SOCIALES (ISS). ESTA FACULTAD TAMBI?N COMPRENDE LA DESIGNACI?N DE APODERADOS.

F. ASISTIR EN NOMBRE DE LA SOCIEDAD A LAS AUDIENCIAS DE CONCILIACI?N, DECLARACIONES DE PARTE Y RENDICI?N DE TESTIMONIOS DENTRO DE LOS PROCESOS DE LA JURISDICCI?N LABORAL Y TR?MITES ADMINISTRATIVOS, CUANDO ELLO SEA REQUERIDO.

G. RESPONDER LAS DEMANDAS DE TUTELA DIRECTAMENTE O A TRAV?S DE APODERADO ESPECIAL.

H. SUSCRIBIR LOS CONTRATOS DE TODO TIPO CON ENTIDADES EDUCATIVAS DE TODO ORDEN, SIN LIMITACI?N DE CUANT?A.

I. SUSCRIBIR LOS DOCUMENTOS Y ESCRITURAS DE DONACI?N QUE SEAN AUTORIZADAS POR LA JUNTA DIRECTIVA, SIN LIMITACI?N ALGUNA.

J. SUSCRIBIR TODOS LOS CONTRATOS DE CONSTRUCCI?N, INSTALACI?N, SERVICIOS, REPARACIONES Y ADECUACIONES QUE SE REALICEN Y PRESTEN EN LA PLANTA Y SEDE ADMINISTRATIVA DE TECNOQU?MICAS S.A. LOCALIZADAS EN CALI, HASTA POR LA SUMA EQUIVALENTE A TRESCIENTOS (300) SALARIOS M?NIMOS LEGALES MENSUALES, DARLOS POR TERMINADO POR CUALQUIER CAUSA, PRESENTAR RECLAMOS ANTE LAS COMPA??AS ASEGURADORAS, EXIGIR EL PAGO DE MULTAS E INDEMNIZACIONES DE CUALQUIER TIPO QUE EST?N PACTADAS EN LOS RESPECTIVOS CONTRATOS Y EL CUMPLIMIENTO DE ELLOS.

K. ANTE EL MINISTERIO DEL MEDIO AMBIENTE Y ORGANISMOS DE CONTROL AMBIENTAL DEL ORDEN NACIONAL, DEPARTAMENTAL Y MUNICIPAL O DISTRITAL: FORMULAR SOLICITUDES, SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE REQUIERAN PRESENTAR, RENDIR DECLARACIONES, NOTIFICARSE DIRECTAMENTE O POR MEDIO DE APODERADO, EN TODOS LOS TR?MITES QUE LA SOCIEDAD TECNOQUIMICAS S.A. REQUIERA ADELANTAR ANTE LA ENTIDAD, AS? COMO DESIGNAR APODERADOS PARA INICIAR O RESPONDER PROCESOS DE CAR?CTER JUDICIAL O GUBERNATIVO.

L. SUSCRIBIR LOS CONTRATOS DE PRENDA SOBRE VEHICULOS DE PROPIEDAD DE TERCEROS PARA RESPALDAR LOS PRESTAMOS QUE LA EMPRESA OTORGUE Y TODO LOS DOCUMENTOS QUE SEAN REQUERIDOS PARA SU FORMALIZACI?N ANTE LAS SECRETARIAS DE TRANSITO Y/O MOVILIDAD DE LOS RESPECTIVOS MUNICIPIOS. ESTE PODER TAMBIEN COMPRENDE LA CANCELACION DE LAS PRENDAS Y LA FIRMA DE TODOS LOS DOCUMENTOS QUE SEAN REQUERIDOS PARA TAL FIN.

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PAGINA No. 17

M. FORMULAR PETICIONES RELACIONADAS CON LAS FACULTADES OTORGADAS ANTE CUALQUIER AUTORIDAD.

PAR?GRAFO I. EN LA ATENCI?N DE TODOS LOS ASUNTOS MENCIONADOS TENDR? LA FACULTAD DE DESIGNAR APODERADOS PARA INICIAR, RESPONDER REQUERIMIENTOS O DEMANDAS, O HACERSE PARTE EN PROCESOS DE CAR?CTER JUDICIAL, GUBERNATIVO, TRIBUNALES DE ARBITRAMIENTO Y RECLAMOS ANTE LAS COMPA??AS ASEGURADORAS.

PAR?GRAFO II. LOS APODERADOS EJERCER?N SUS FUNCIONES DE MANERA INDIVIDUAL Y SIN ORDEN DE PRELACI?N.

2. JORGE ENRIQUE ARIZA BERNAL, IDENTIFICADO CON LA C?DULA DE CIUDADAN?A NO. 19.494.493 DE BOGOT?, PARA EL EJERCICIO DE LAS SIGUIENTES FACULTADES:

A. ANTE EL MINISTERIO DEL MEDIO AMBIENTE: FORMULAR SOLICITUDES, SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE REQUIERAN PRESENTAR, RENDIR DECLARACIONES, NOTIFICARSE DIRECTAMENTE O POR MEDIO DE APODERADO, EN TODOS LOS TR?MITES QUE LA SOCIEDAD TECNOQU?MICAS S.A. REQUIERA ADELANTAR ANTE LA ENTIDAD, AS? COMO DESIGNAR APODERADOS PARA INICIAR O RESPONDER PROCESOS DE CAR?CTER JUDICIAL O GUBERNATIVO.

B. ANTE LA SUPERINTENDENCIA DE VIGILANCIA: FORMULAR SOLICITUDES, SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE REQUIERAN PRESENTAR, OTORGAR PODERES, RENDIR DECLARACIONES, ATENDER VISITAS, FIRMAR LAS ACTAS CORRESPONDIENTES Y NOTIFICARSE DIRECTAMENTE O POR MEDIO DE APODERADO, EN TODOS LOS TR?MITES QUE LA SOCIEDAD TECNOQU?MICAS S.A. REQUIERA ADELANTAR ANTE LA ENTIDAD, AS? COMO DESIGNAR APODERADOS PARA INICIAR O RESPONDER PROCESOS DE CAR?CTER JUDICIAL O GUBERNATIVO.

C. ANTE EL FONDO NACIONAL DE ESTUPEFACIENTES Y DIRECCI?N NACIONAL DE ESTUPEFACIENTES FORMULAR SOLICITUDES, SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE REQUIERAN PRESENTAR, RENDIR DECLARACIONES, NOTIFICARSE DIRECTAMENTE O POR MEDIO DE APODERADO, EN TODOS LOS TR?MITES QUE LA SOCIEDAD TECNOQU?MICAS S.A. REQUIERA ADELANTAR ANTE LAS CITADAS ENTIDADES, SUSCRIBIR LAS ACTAS DE VISITA, Y DESIGNAR APODERADOS PARA NOTIFICARSE DE ACTOS ADMINISTRATIVOS, INICIAR O RESPONDER PROCESOS DE CAR?CTER JUDICIAL O ADMINISTRATIVO DE CUALQUIER ORDEN.

D. EN TODO LO RELACIONADO CON LOS TR?MITES DE IMPORTACIONES Y EXPORTACIONES, SEG?N SE INDICA:

I. OTORGAR PODERES Y SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE PRESENTEN Y TRAMITEN ANTE LAS ADMINISTRACIONES DE ADUANAS DE LA DIRECCI?N DE IMPUESTOS Y ADUANAS - DIAN - AS? COMO RENDIR DECLARACIONES, ATENDER VISITAS E INSPECCIONES Y FIRMAS LAS CORRESPONDIENTES ACTAS ATENDER DIRECTAMENTE, CUANDO ELLO SEA REQUERIDO Y EN GENERAL OBRAR COMO APODERADO ESPECIAL ANTE LAS AUTORIDADES ADUANERAS EN TODAS LAS OPERACIONES RELACIONADAS CON EL COMERCIO EXTERIOR.

II. OTORGAR PODERES Y SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE PRESENTEN Y

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PAGINA No. 18

TRAMITEN ANTE LAS SOCIEDADES PORTUARIAS DE BUENAVENTURA, CARTAGENA Y BARRANQUILLA, AS? COMO RESPONDER Y ATENDER LOS TR?MITES DIRECTAMENTE O A TRAV?S DE APODERADOS.

III- OTORGAR PODERES ESPECIALES Y GENERALES, OTORGAR GARANT?AS Y SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE PRESENTEN Y TRAMITEN ANTE LAS NAVIERAS Y EMPRESAS ADMINISTRADORAS DE CONTENEDORES PARA EL MANEJO Y RETIRO DE ELLOS.

IV. OTORGAR PODERES ESPECIALES Y GENERALES A LAS SOCIEDADES DE INTERMEDIACI?N ADUANERA - SIA- Y SUSCRIBIR TODOS LOS DOCUMENTOS QUE SE PRESENTEN Y TRAMITEN DE ACUERDA CON LA NORMATIVIDAD LEGAL SOBRE LA MATERIA.

V. SUSCRIBIR LAS CARTAS DE ANTINARC?TICOS QUE SE PRESENTAN ANTE LA POLIC?A AEROPORTUARIA BIEN DIRECTAMENTE O AUTORIZANDO A LOS JEFES DE BODEGA DE YUMBO Y JAMUND? PARA ESE TR?MITE DOCUMENTOS DENTRO DE LOS TR?MITES DE EXPORTACIONES O REEMBARQUES DE MERCANC?AS, Y EN GENERAL ATENDER TODAS LAS DILIGENCIAS DIRECTAMENTE U OTORGAR PODER AUN TERCERO.

D. SUSCRIBIR CONTRATOS DE CONSTRUCCI?N Y DE OBRA QUE SE REALICEN Y PRESTEN EN LAS PLANTAS DE TECNOQU?MICAS S.A. LOCALIZADAS EN JAMUND?, YUMBO Y VILLA RICA (DEPARTAMENTO DEL CAUCA EN EL CONJUNTO INDUSTRIAL PARQUESUR) HASTA POR LA SUMA EQUIVALENTE A TRESCIENTOS (300) SALARIOS M?NIMOS LEGALES MENSUALES.

E. SUSCRIBIR CONTRATOS, SIN LIMITACI?N DE CUANT?A QUE TENGA QUE VER CON LA ADQUISICI?N DE EQUIPO Y MAQUINARIA, REPARACI?N, ADECUACI?N, INSTALACI?N, SERVICIOS T?CNICOS Y DE ASESOR?A.

E. SUSCRIBIR CONTRATOS DE FABRICACI?N CON TERCEROS BIEN SEA QUE TECNOQU?MICAS OBRE COMO FABRICANTE O COMO PROPIETARIO.

PARAGRAFO. EN LA ATENCI?N DE TODOS LOS ASUNTOS MENCIONADOS TENDR? LA FACULTAD DE DESIGNAR APODERADOS PARA INICIAR, RESPONDER REQUERIMIENTOS O DEMANDAS, O HACERSE PARTE EN PROCESOS DE CAR?CTER JUDICIAL O ADMINISTRATIVO DE CUALQUIER ORDEN.

3. MAR?A TERESA CA?ON DE GUZMAN, IDENTIFICADA CON LA C?DULA DE CIUDADAN?A NO. 31.238.104 DE CALI, CARLOS ARTURO PE?A NIETO IDENTIFICADO CON LA C?DULA DE CIUDADAN?A NO. 19.483.439 DE BOGOT? Y ?NGELA MAR?A CORREA CARDONA IDENTIFICADA CON LA C?DULA DE CIUDADAN?A NO. 66.835.555 DE CALI, LA PRIMERA COMO PRINCIPAL, EL SEGUNDO COMO PRIMER SUPLENTE Y LA TERCERA COMO SEGUNDA SUPLENTE, PARA QUE REPRESENTEN A TECNOQU?MICAS S.A. EN:

A. EN TODOS LOS ASUNTOS CAMBIARIOS, CON FACULTAD PARA FIRMAR DECLARACIONES DE CAMBIOS SEA POR CR?DITOS EN MONEDA EXTRANJERA, POR MOVIMIENTOS DE LA CUENTAS CORRIENTES DE COMPENSACI?N, IMPORTACIONES DE BIENES Y SERVICIOS, TRANSFERENCIAS Y OTROS CONCEPTOS, REGISTRO DE PR?STAMOS EN MONEDA EXTRANJERA OTORGADOS A LA EMPRESA EN SU CONDICI?N DE RESIDENTE Y TODOS AQUELLOS DOCUMENTOS, DECLARACIONES O RESPUESTAS A REQUERIMIENTOS QUE DEBAN HACERSE ANTE

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

Hora Certificado 11:23:52

Operacion : 02CP21027014

PAGINA No. 19

EL BANCO DE LA REPUBLICA U OTRAS ENTIDADES GUBERNAMENTALES RESPECTO DE OPERACIONES EN EL MERCADO CAMBIARIO.

LOS APODERADOS SUSCRIBIR?N TODOS LOS DOCUMENTOS Y REALIZAR TODOS LOS ACTOS QUE OBLIGUEN A LA SOCIEDAD ANTE LAS AUTORIDADES CAMBIARIAS, PUDIENDO IGUALMENTE NOTIFICARSE DE TODAS LAS ACTUACIONES, ACTOS ADMINISTRATIVOS, DILIGENCIAS O GESTIONES RELACIONADAS O QUE SE DERIVEN DE DICHA ACTIVIDAD Y EN GENERAL, PARA QUE ASUMAN LA PERSONER?A A NOMBRE DE TECNOQU?MICAS S.A., BIEN SEA DIRECTAMENTE O A TRAV?S DE APODERADO, SIEMPRE QUE LO ESTIMEN CONVENIENTE, DE MANERA QUE EN NING?N CASO QUEDE SIN LA DEBIDA REPRESENTACI?N EN LA SALVAGUARDIA DE SUS DERECHOS Y CUMPLIMIENTO DE OBLIGACIONES DE CAR?CTER CAMBIARIO Y EN LOS ASUNTOS CONCERNIENTES PARA LAS MATERIAS DE QUE TRATA ESTE PODER.

B. EN RELACI?N CON SECTOR FINANCIERO:

I. SUSCRIBIR LOS CONTRATOS DE CR?DITO Y LEASING CON LOS BANCOS, ENTIDADES FINANCIERAS, COMPA??AS DE FINANCIAMIENTO COMERCIAL, DE ACUERDO CON LOS CUPOS FIJADOS POR LA JUNTA DIRECTIVA, AS? COMO LOS PAGAR?S, LOS CONTRATOS DE GARANT?A PRENDAR?A E HIPOTECARIA, LA CONFIRMACI?N DE FORWARDS Y TODOS LOS DEM?S DOCUMENTOS QUE SEAN REQUERIDOS PARA LA CULMINACI?N Y FORMALIZACI?N DE ESTOS TR?MITES.

ESTAS FACULTADES IGUALMENTE APLICAN PARA TODOS LOS CR?DITOS QUE OTORQUE EL BANCO DE COMERCIO EXTERIOR DE COLOMBIA - BANCOLDEX.

II. SUSCRIBIR LOS FORMATOS Y CONTRATOS DE APERTURAS DE CUENTAS CORRIENTES, AHORROS, SERVICIOS DE BANCA VIRTUAL, LOS FORMATOS DE PROVEEDORES PARA PAGOS POR TRANSFERENCIA ELECTR?NICA Y LOS FORMULADOS ?NICOS DE CONOCIMIENTO DE PERSONA JUR?DICA QUE EXIGE EL SECTOR FINANCIERO.

III. SUSCRIBIR LAS LETRAS DE COBRANZA Y LAS CARTAS DE CR?DITO.

C. SOLICITAR TIDIS Y FIRMAR TODOS LOS DOCUMENTOS RELACIONADOS CON ESTE TR?MITE.

D. EN RELACI?N CON LA COMPA??AS ASEGURADORAS:

I. SUSCRIBIR DOCUMENTOS DE RECLAMACI?N Y OTORGAR PODERES PARA QUE COMPAREZCAN A LAS AUDIENCIAS DE RECLAMACIONES, AS? COMO LOS DOCUMENTOS DE TRANSACCI?N. ESTAS FACULTADES SE OTORGAN SIN LIMITACI?N DE CUANT?A.

II. SUSCRIBIR LAS CARTAS DE NO RECLAMACI?N A LAS COMPA??AS ASEGURADORAS POR OCURRENCIA DE SINIESTROS Y LAS RESPECTIVAS CONSTANCIAS.

III. SUSCRIBIR LOS DOCUMENTOS REQUERIDOS POR EL SISTEMA DE INFORMACI?N PARA LA PREVENCI?N DE LAVADO DE ACTIVOS (SIPLA).

E. FORMULAR PETICIONES RELACIONADAS CON LAS FACULTADES OTORGADAS.

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

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PAGINA No. 20

PAR?GRAFO 1. EN LA ATENCI?N DE TODOS LOS ASUNTOS MENCIONADOS TENDR? LA FACULTAD DE DESIGNAR APODERADOS PARA INICIAR, RESPONDER REQUERIMIENTOS O DEMANDAS, O HACERSE PARTE EN PROCESOS DE CAR?CTER JUDICIAL O GUBERNATIVO.

PAR?GRAFO II. LOS APODERADOS EJERCER?N SUS FUNCIONES DE MANERA INDIVIDUAL Y SIN ORDEN DE PRELACI?N.

4. ADRIANA JIM?NEZ MERA, IDENTIFICADA CON LA C.C. 31.174.077 DE PALMIRA, PARA EL DESARROLLO DE LAS SIGUIENTES FUNCIONES:

A. OTORGAR PODER Y CONSTITUIR MANDATARIOS PARA INICIAR LAS ACCIONES CIVILES, COMERCIALES Y PENALES TENDIENTES A LA RECUPERACI?N DE LA CARTERA, SIN LIMITACION DE CUANT?A, CON EXPRESAS FACULTADES PARA ASISTIR EN NOMBRE DE LA SOCIEDAD A LAS AUDIENCIAS DE CONCILIACI?N, CON AUTORIZACI?N PARA TRANSIGIR, DESISTIR, CONCILIAR O COMPROMETER A LA SOCIEDAD EN TODOS LOS PROCESOS, GESTIONES JUDICIALES, ADMINISTRATIVAS O RECLAMACIONES EXTRA PROCESO EN QUE INTERVENGA EN ASUNTOS RELACIONADOS CON LAS DEUDAS A FAVOR DE TECNOQU?MICAS S. A.

B. SUSCRIBIR LOS CONTRATOS DE ARRENDAMIENTO DE INMUEBLES, SU MODIFICACI?N Y O TERMINACI?N, INVENTARIOS Y ANEXOS PERTINENTES, BIEN SEA QUE LA SOCIEDAD OBRE COMO ARRENDADOR O ARRENDATARIO, SIN LIMITACI?N DE CUANT?A. ESTA FUNCI?N LA PODR? EJERCER DIRECTAMENTE O MEDIANTE LA DESIGNACI?N DE APODERADOS.

C. SUSCRIBIR LOS FORMATOS DE AUTORIZACI?N DE CREACI?N DE CLIENTES Y PROVEEDORES DE LA EMPRESA.

D. EN RELACI?N CON LOS VEH?CULOS DE TODO TIPO QUE FIGUREN A NOMBRE DE TECNOQU?MICAS, TIENE LA FACULTAD DE SUSCRIBIR LOS FORMULARIOS OFICIALES PARA TODO TIPO DE TRAMITE, ENTRE ELLOS EL TRASPASO, QUE SE REQUIERA REALIZAR, ANTE LAS SECRETARIAS DE TRANSITO Y ANTE LAS AUTORIDADES DE TRANSITO Y TRANSPORTE DE CUALQUIER ORDEN, AS? COMO FIRMAR TODO TIPO DE CONTRATOS RELACIONADOS CON LOS VEH?CULOS.

PAR?GRAFO. EN LA ATENCI?N DE TODOS LOS ASUNTOS MENCIONADOS TENDR? LA FACULTAD DE DESIGNAR APODERADOS PARA INICIAR, RESPONDER REQUERIMIENTOS O DEMANDAS, O HACERSE PARTE EN PROCESOS DE CAR?CTER JUDICIAL O ADMINISTRATIVO DE CUALQUIER ORDEN.

ESTOS PODERES ESTAR?N VIGENTES HASTA TANTO SEAN REVOCADOS O MODIFICADOS
EXPRESAMENTE POR DOCUMENTO PRIVADO.

CERTIFICA:

QUE POR DOCUMENTO PRIVADO DEL 10 DE JULIO DE 2008 DE CALI , INSCRITA EN LA CAMARA DE COMERCIO EL 29 DE JULIO DE 2008 BAJO EL NRO. 141 DEL LIBRO V , SE

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

Hora Certificado 11:23:52

Operacion : 02CP21027014

PAGINA No. 21

CONCEDE PODER ESPECIAL, AMPLIO Y SUFICIENTE A LOS SIGUIENTES FUNCIONARIOS DE LA EMPRESA:

- GERMAN ALBERTO SUAREZ HINCAPIE, C.C. 16.722.521 DE CALI, SUBGERENTE FINANCIERO Y ADMINISTRATIVO DE LA REGIONAL CENTRO PACIFICO DE LA SOCIEDAD, CON SEDE EN CALI.

- MARIA VICTORIA VARGAS PORRAS, C.C. 39.638.185 DE BOGOTA, SUBGERENTE FINANCIERO Y ADMINISTRATIVO DE LA REGIONAL CUNDINAMARCA DE LA SOCIEDAD, CON SEDE EN BOGOTA D.C.

- ESPERANZA GRANADOS JAIMES, C.C. 63.392.189 DE MALAGA (SANTANDER), SUBGERENTE ADMINISTRATIVO DE LA REGIONAL CUNDINAMARCA DE LA SOCIEDAD, CON SEDE EN BOGOTA D.C.

- DIEGO FERNANDO MUÑOZ QUINTERO, C.C. 94.282.452 DE CALI, SUBGERENTE FINANCIERO Y ADMINISTRATIVO DE LA REGIONAL ANTIOQUIA DE LA SOCIEDAD, CON SEDE EN MEDELLIN.

- CARLOS ORLANDO MUTIS PICON, C.C. 91.200.418 DE BUCARAMANGA, SUBGERENTE FINANCIERO Y ADMINISTRATIVO DE LA REGIONAL ORIENTE DE LA SOCIEDAD, CON SEDE EN BUCARAMANGA.

- DANIEL AMEZQUITA LIZARAZO, C.C. 8.681.962 DE BARRANQUILLA, SUBGERENTE FINANCIERO Y ADMINISTRATIVO DE LA REGIONAL ATLANTICO DE LA SOCIEDAD, CON SEDE EN BARRANQUILLA.

LOS MENCIONADOS FUNCIONARIOS EJERCERAN, EN SUS RESPECTIVAS REGIONALES, LAS SIGUIENTES FACULTADES:

1. PARA QUE EN NOMBRE DE TECNOQUIMICAS S.A., Y EN ASUNTOS QUE TENGA QUE VER CON SUS RESPECTIVOS DISTRITOS DE VENTAS SE NOTIFIQUEN Y PROMUEVAN ACCIONES EN NOMBRE DE ESTA ANTE ENTIDADES PUBLICAS, FUNCIONARIOS O EMPLEADOS NACIONALES, DEPARTAMENTALES, DISTRITALES Y MUNICIPALES DEL ORDEN JUDICIAL, ADMINISTRATIVO POLICIVO, PENAL O DE FISCALIA, YA SEA EN PROCESOS, ACTUACIONES, SIMPLES ACTOS O DILIGENCIAS Y GESTIONES, CON FACULTADES DE DESISTIMIENTO, ALLANAMIENTO Y CONCILIACION, EN LOS QUE EL ESTABLECIMIENTO ESTE VINCULADO COMO DEMANDANTE, DEMANDADO O TERCERO INTERVINIENTE.

PARAGRAFO: LA FACULTAD DE CONCILIACION, DESISTIMIENTO Y ALLANAMIENTO SE LIMITA HASTA LA SUMA EQUIVALENTE A CINCUENTA (50) SALARIOS MINIMOS LEGALES MENSUALES.

2. PARA QUE OTORGUEN PODERES Y CONSTITUYAN MANDATARIOS PARA INICIAR LAS ACCIONES CIVILES, COMERCIALES Y PENALES TENDIENTES A LA RECUPERACION DE LA CARTERA, SIN LIMITACION DE CUANTIA, CON EXPRESAS FACULTADES PARA ASISTIR EN NOMBRE DE LA SOCIEDAD A LAS AUDIENCIAS DE CONCILIACION E INTERROGATORIOS DE PARTE, CON AUTORIZACION PARA TRANSIGIR, DESISTIR, CONCILIAR O COMPROMETER A LA

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

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PAGINA No. 22

SOCIEDAD EN TODOS LOS PROCESOS, GESTIONES JUDICIALES, ADMINISTRATIVOS O RECLAMACIONES EXTRA PROCESO EN QUE INTERVENGA EN ASUNTOS RELACIONADOS CON EL ESTABLECIMIENTO DE COMERCIO, CON LAS LIMITACIONES PREVISTAS EN EL PARAGRAFO DEL NUMERAL ANTERIOR.

3.PARA QUE OTORQUE PODERES Y CONSTITUYAN MANDATARIOS PARA HACERSE PARTE EN LOS PROCESOS CONCORDATARIOS, DE LIQUIDACION OBLIGATORIA, O REESTRUCTURACION ECONOMICA QUE SE TRAMITEN ANTE LA SUPERINTENDENCIA DE SOCIEDADES O ANTE OTRAS SUPERINTENDENCIAS O ENTIDADES CUANDO SE TRATE DE OTRA CLASE DE DEUDORES, TENDIENTES A LA RECUPERACION DE LA CARTERA, SIN LIMITACION DE CUANTIA, CON EXPRESAS FACULTADES PARA ASISTIR EN NOMBRE DE LA SOCIEDAD A LOS INTERROGATORIOS DE PARTE, A LAS DIVERSAS AUDIENCIAS, ENTRE ELLAS LAS DE CONCILIACION, CON AUTORIZACION PARA TRANSIGIR, DESISTIR, CONCILIAR O COMPROMETER A LA SOCIEDAD EN TODOS LOS PROCESOS, GESTIONES, JUDICIALES, ADMINISTRATIVAS O RECLAMACIONES EXTRA PROCESO EN QUE INTERVENGA EN ASUNTOS DEL ESTABLECIMIENTO CON LAS LIMITACIONES PREVISTAS EN EL PARAGRAFO DEL NUMERAL PRIMERO.

4.PARA SUSCRIBIR LOS CONTRATOS DE TRABAJO Y DARLOS POR TERMINADO DEL PERSONAL VINCULADO O QUE SE VINCULE AL ESTABLECIMIENTO DE COMERCIO Y EXPEDIR CERTIFICACIONES LABORALES.

5.PARA CONSTITUIR APODERADO O APODERADOS EN DESARROLLO DE LA REPRESENTACION LABORAL, SI ASI LO CONSIDERA NECESARIO, TENIENDO SUMA DILIGENCIA PARA QUE TECNOQUIMICAS S.A., EN NINGUN CASO, QUEDE SIN LA DEBIDA REPRESENTACION EN LA SALVAGUARDIA DE SUS DERECHOS Y OBLIGACIONES LABORALES Y A ASISTIR EN NOMBRE DE LA SOCIEDAD A LAS DILIGENCIAS DE INTERROGATORIOS DE PARTE.

6.SUSCRIBIR LOS CONTRATOS DE PRENDA SOBRE VEHICULOS DE PROPIEDAD DE TERCEROS PARA RESPALDAR LOS PRESTAMOS QUE LA EMPRESA OTORQUE Y TODO LOS DOCUMENTOS QUE SEAN REQUERIDOS PARA SU FORMALIZACION ANTE LAS SECRETARIAS DE TRANSITO Y/O MOVILIDAD DE LOS RESPECTIVOS MUNICIPIOS. ESTE PODER TAMBIEN COMPRENDE LA CANCELACION DE LAS PRENDAS Y LA FIRMA DE TODOS LOS DOCUMENTOS QUE SEAN REQUERIDOS PARA TAL FIN.

7.PARA QUE EN DESARROLLO DE LAS ACTIVIDADES DEL ESTABLECIMIENTO DE COMERCIO ADQUIERA Y ENAJENE TODA CLASE DE BIENES MUEBLES CUYA FINALIDAD SEA NECESARIA PARA EL MEJOR DESEMPEÑO DE LAS ACTIVIDADES DEL ESTABLECIMIENTO HASTA POR LA SUMA QUE INDIQUE LOS MANUALES Y PROCEDIMIENTOS INTERNOS DE LA SOCIEDAD.

ESTOS PODERES ESTARAN VIGENTES HASTA TANTO SEAN REVOCADOS O MODIFICADOS
EXPRESAMENTE POR DOCUMENTO PRIVADO.

CERTIFICA:

CAPITAL AUTORIZADO: \$27,200,000,000
NUMERO DE ACCIONES: 54,400,000

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

Hora Certificado 11:23:52

Operacion : 02CP21027014

PAGINA No. 23

VALOR NOMINAL: \$500

CAPITAL SUSCRITO: \$27,123,804,000

NUMERO DE ACCIONES: 54,247,608

VALOR NOMINAL: \$500

CAPITAL PAGADO: \$27,123,804,000

NUMERO DE ACCIONES: 54,247,608

VALOR NOMINAL: \$500

CERTIFICA:

QUE POR DOCUMENTO PRIVADO DEL 17 DE NOVIEMBRE DE 2005, INSCRITO EN LA CAMARA DE COMERCIO EL 23 DE NOVIEMBRE DE 2005 BAJO EL NRO. 13.158 DEL LIBRO IX, EN LA CUAL CONSTA LA SITUACION DE CONTROL EJERCIDA POR TECNOQUIMICAS S.A.

CONTROLANTE: TECNOQUIMICAS S.A.

DOMICILIO: CALI

NACIONALIDAD: COLOMBIANA

CONTROLADA: INDUGRAFICAS S.A.

DOMICILIO: CALI

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE INDUGRAFICAS S.A. CORRESPONDEN AL DESARROLLO DE NEGOCIOS RELACIONADOS CON LAS ARTES GRAFICAS, LA DISTRIBUCION DE LAS MISMAS YA SEA DE SUS PRODUCTOS PROPIOS O POR CONTRATO, TANTO EN EL MERCADO NACIONAL COMO EN EL INTERNACIONAL.

UNIDAD DE PROPOSITO Y ADMINISTRACION. ENTRE TECNOQUIMICAS E INDUGRAFICAS S.A. EXISTE UNIDAD DE PROPOSITO Y DIRECCION YA QUE LOS PLANES Y OBJETIVOS DE ESTA ULTIMA ESTAN DETERMINADAS POR LA PRIMERA.

DE IGUAL MANERA SE CONCRETA EL CONTROL ADMINISTRATIVO SOBRE LA FILIAL A TRAVES DE LA GERENCIA Y LA JUNTA DIRECTIVA CUYOS MIEMBROS PRINCIPALES HACEN PARTE IGUALMENTE DE LA JUNTA Y ADMINISTRACION DE LA MATRIZ.

CERTIFICA:

QUE POR DOCUMENTO PRIVADO DEL 17 DE NOVIEMBRE DE 2005, INSCRITO EN LA CAMARA DE COMERCIO EL 23 DE NOVIEMBRE DE 2005 BAJO EL NRO. 13.159 DEL LIBRO IX, EN LA CUAL CONSTA LA SITUACION DE CONTROL EJERCIDA POR TECNOQUIMICAS S.A.

CONTROLANTE: TECNOQUIMICAS S.A.

DOMICILIO: CALI

NACIONALIDAD: COLOMBIANA

CONTROLADA: TECNOFAR TQ S.A.

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

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Operacion : 02CP21027014

PAGINA No. 24

DOMICILIO: VILLA, RICA DEPARTAMENTO DEL CAUCA

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE TECNOFAR TQ S.A. CORRESPONDEN A LA PRODUCCION Y COMERCIALIZACION DE PRODUCTOS BIOLOGICOS, QUIMICOS, MEDICAMENTOS Y PRODUCTOS FARMACEUTICOS, PRODUCTOS VETERINARIOS Y AGRICOLAS, ALIMENTOS, COSMETICOS Y DE TOCADOR, PRODUCTOS DE ASEO PARA EL HOGAR Y LA FABRICACION Y DISTRIBUCION DE ENVASES PLASTICOS PARA TODO TIPO DE USO.

UNIDAD DE PROPOSITO Y ADMINISTRACION. ENTRE TECNOQUIMICAS Y TECNOFAR, EXISTE UNIDAD DE PROPOSITO Y DIRECCION YA QUE LOS PLANES Y OBJETIVOS DE ESTA ULTIMA ESTAN DETERMINADAS POR LA PRIMERA.

DE IGUAL MANERA SE CONCRETA EL CONTROL ADMINISTRATIVO SOBRE LA FILIAL A TRAVES DE LA GERENCIA Y LA JUNTA DIRECTIVA CUYOS MIEMBROS PRINCIPALES HACEN PARTE IGUALMENTE DE LA JUNTA Y ADMINISTRACION DE LA MATRIZ.

CERTIFICA

DOCUMENTO: DOCUMENTO PRIVADO DEL 17 DE SEPTIEMBRE DE 2008

INSCRIPCION: 18 DE SEPTIEMBRE DE 2008 No. 10710 DEL LIBRO IX

CONSTA LA SITUACION DE CONTROL:

SOCIEDAD CONTROLANTE

DENOMINACION: TECNOQUIMICAS S.A.

DOMICILIO: SANTIAGO DE CALI, DEPARTAMENTO DEL VALLE DEL CAUCA

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE TECNOQUIMICAS CORRESPONDEN A LA FABRICACION, EL ENVASADO, LA IMPORTACION, LA EXPORTACION, LA VENTA Y DISTRIBUCION DE PRODUCTOS BIOLOGICOS Y QUIMICOS, MEDICAMENTOS O PRODUCTOS FARMACEUTICOS, PERFUMERIA O EFECTOS DE TOCADOR, PRODUCTOS VETERINARIOS Y PRODUCTO DE CONSUMO POPULAR DE CUALQUIER NATURALEZA.

FILIAL

DENOMINACION: COLOMBIANA DE ADHESIVOS COLDESIVOS S.A.

DOMICILIO: CALI

NACIONAL: COLOMBIANA

ACTIVIDAD: LA FABRICACION, IMPORTACION Y EXPORTACION DE PRODUCTOS ADHESIVOS, ABRASIVOS Y AISLANTES Y DE CONSUMO POPULAR.

SUBORDINACION. TECNOQUIMICAS S.A., TIENE SUSCRITAS Y PAGADAS ACCIONES EN COLOMBIANA DE ADHESIVOS COLDESIVOS S.A. EN PORCENTAJE EQUIVALENTE AL 94.99% DEL CAPITAL SUSCRITO Y PAGADO DE DICHA SOCIEDAD, LO QUE CONFIGURA SITUACION DE SUBORDINACION EN QUE LA PRIMERA ES LA MATRIZ Y LA SEGUNDA LA FILIAL-

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

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PAGINA No. 25

CERTIFICA

DOCUMENTO: DOCUMENTO PRIVADO DEL 14 DE OCTUBRE DE 2008
INSCRIPCION: 17 DE OCTUBRE DE 2008 No.11849 DEL LIBRO IX

DOCUMENTO: DOCUMENTO PRIVADO DEL 14 DE OCTUBRE DE 2008
INSCRIPCION: 17 DE OCTUBRE DE 2008 No.11852 DEL LIBRO IX

CONSTA LA SITUACION DE CONTROL:

SOCIEDAD CONTROLANTE

DENOMINACION: TECNOQUIMICAS S.A.

DOMICILIO: SANTIAGO DE CALI, DEPARTAMENTO DEL VALLE DEL CAUCA

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE TECNOQUIMICAS CORRESPONDEN A LA FABRICACION, EL ENVASADO, LA IMPORTACION, LA EXPORTACION, LA VENTA Y DISTRIBUCION DE PRODUCTOS BIOLÓGICOS Y QUÍMICOS, MEDICAMENTOS O PRODUCTOS FARMACÉUTICOS, PERFUMERÍA O EFECTOS DE TOCADOR, PRODUCTOS VETERINARIOS Y PRODUCTO DE CONSUMO POPULAR DE CUALQUIER NATURALEZA.

SOCIEDAD CONTROLADA

DENOMINACION: UROTEC S.A.

DOMICILIO: CALI

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LA PROMOCION Y REALIZACION DE ACTIVIDADES DE INVESTIGACIONES MÉDICAS FARMACÉUTICAS EN EL ÁREA DE LA UROLOGÍA Y OTRAS ESPECIALIDADES, BIEN SEA DIRECTAMENTE O A TRAVÉS DE OTRAS INSTITUCIONES CIENTÍFICAS RECONOCIDAS. LA PROMOCION DE LA EDUCACION MÉDICA Y DE LA PREVENCIÓN, ASÍ COMO LA FABRICACION, IMPORTACION Y EXPORTACION DE LOS PRODUCTOS FARMACÉUTICOS AFINES. SUBORDINACION. TECNOQUIMICAS S.A., TIENE SUSCRITAS Y PAGADAS ACCIONES EN UROTEC S.A. EN PORCENTAJE SUPERIOR AL NOVENTA POR CIENTO (90%) DEL CAPITAL SUSCRITO Y PAGADO DE DICHA SOCIEDAD, LO QUE CONFIGURA SITUACION DE SUBORDINACION EN QUE LA PRIMERA ES LA MATRIZ Y LA SEGUNDA LA FILIAL.

CERTIFICA

DOCUMENTO: DOCUMENTO PRIVADO DEL 14 DE OCTUBRE DE 2008
INSCRIPCION: 17 DE OCTUBRE DE 2008 No.11850 DEL LIBRO IX

CONSTA LA SITUACION DE CONTROL:

SOCIEDAD CONTROLANTE

DENOMINACION: TECNOQUIMICAS S.A.

DOMICILIO: SANTIAGO DE CALI, DEPARTAMENTO DEL VALLE DEL CAUCA

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE TECNOQUIMICAS CORRESPONDEN A LA FABRICACION, EL ENVASADO, LA IMPORTACION, LA EXPORTACION, LA VENTA Y DISTRIBUCION DE PRODUCTOS BIOLÓGICOS Y QUÍMICOS, MEDICAMENTOS O PRODUCTOS FARMACÉUTICOS, PERFUMERÍA O

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

Hora Certificado 11:23:52

Operacion : 02CP21027014

PAGINA No. 26

EFECTOS DE TOCADOR, PRODUCTOS VETERINARIOS Y PRODUCTO DE CONSUMO POPULAR DE CUALQUIER NATURALEZA.

SOCIEDAD CONTROLADA

DENOMINACION: INVESTIGACIONES FARMOQUIMICAS COLOMBIANAS S.A. IFC S.A.

DOMICILIO: BOGOTÁ D.C.

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LA INVESTIGACION CIENTÍFICA, EL PROCESAMIENTO, LA PRODUCCION Y EL MERCADO DE MATERIAS PRIMAS, ARTÍCULOS Y ELEMENTOS PROPIOS DE LA QUÍMICA FARMACÉUTICA, FARMACOLOGÍA, ODONTOLOGÍA, BIOLOGÍA Y MEDIOS DE DIAGNÓSTICO TANTO EN LA MEDICINA HUMANA COMO EN LA VETERINARIA.

SUBORDINACION. TECNOQUIMICAS S.A., TIENE SUSCRITAS Y PAGADAS ACCIONES EN INVESTIGACIONES FARMOQUIMICAS COLOMBIANAS S.A. EN PORCENTAJE SUPERIOR AL NOVENTA POR CIENTO (90%) DEL CAPITAL SUSCRITO Y PAGADO DE DICHA SOCIEDAD, LO QUE CONFIGURA SITUACION DE SUBORDINACION EN QUE LA PRIMERA ES LA MATRIZ Y LA SEGUNDA LA FILIAL.

CERTIFICA

DOCUMENTO: DOCUMENTO PRIVADO DEL 03 DE OCTUBRE DE 2008

INSCRIPCION: 17 DE OCTUBRE DE 2008 No.11851 DEL LIBRO IX

CONSTA LA SITUACION DE CONTROL:

SOCIEDAD CONTROLANTE

DENOMINACION: TECNOQUIMICAS S.A.

DOMICILIO: SANTIAGO DE CALI, DEPARTAMENTO DEL VALLE DEL CAUCA

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE TECNOQUIMICAS CORRESPONDEN A LA FABRICACION, EL ENVASADO, LA IMPORTACION, LA EXPORTACION, LA VENTA Y DISTRIBUCION DE PRODUCTOS BIOLÓGICOS Y QUÍMICOS, MEDICAMENTOS O PRODUCTOS FARMACÉUTICOS, PERFUMERÍA O EFECTOS DE TOCADOR, PRODUCTOS VETERINARIOS Y PRODUCTO DE CONSUMO POPULAR DE CUALQUIER NATURALEZA.

SOCIEDAD CONTROLADA

DENOMINACION: TECNOQUIMICAS DE ECUADOR S.A.

DOMICILIO: DISTRITO METROPOLITANO DE QUITO, REPÚBLICA DEL ECUADOR

NACIONALIDAD: ECUATORIANA

ACTIVIDAD: VENTA AL POR MAYOR DE PRODUCTOS FARMACÉUTICOS, VETERINARIOS Y AGRÍCOLAS; DE SUSTANCIAS ADHESIVAS, COSMÉTICAS Y DE HIGIENE Y DE PRODUCTOS QUÍMICOS ORGÁNICOS E INORGÁNICOS.

SUBORDINACION. TECNOQUIMICAS S.A., TIENE SUSCRITAS Y PAGADAS ACCIONES EN TECNOQUIMICAS DEL ECUADOR S.A. EN PORCENTAJE EQUIVALENTE AL 94.55% DEL CAPITAL SUSCRITO Y PAGADO DE DICHA SOCIEDAD, LO QUE CONFIGURA SITUACION DE SUBORDINACION EN QUE LA PRIMERA ES LA MATRIZ Y LA SEGUNDA LA FILIAL.

CERTIFICA:

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

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Operacion : 02CP21027014

PAGINA No. 27

QUE EL 27 DE MARZO DE 2001 BAJO EL NRO.1979 DEL LIBRO IX, SE INSCRIBIO EN LA CAMARA DE COMERCIO UN DOCUMENTO PRIVADO DE FECHA MARZO 21 DE 2001, EN LA CUAL CONSTA LA SITUACION DE CONTROL EJERCIDA POR LA SOCIEDAD TECNOQUIMICAS S.A.

MATRIZ: TECNOQUIMICAS S.A.

DOMICILIO: SANTIAGO DE CALI.

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE TECNOQUIMICAS CORRESPONDEN A LA PRODUCCION Y COMERCIALIZACION DE PRODUCTOS BIOLOGICOS, QUIMICOS, MEDICAMENTOS Y PRODUCTOS FARMACEUTICOS, PANALES, PRODUCTOS VETERINARIO Y AGRICOLAS, ALIMENTOS, COSMETICOS Y DE TOCADOR Y PRODUCTOS DE ASEO PARA EL HOGAR.

SUBORDINADA: ADHESIVOS INTERNACIONALES S.A.- ADHINTER S.A. DOMICILIO: CALI VALLE DEL CAUCA

NACIONALIDAD: COLOMBIANA

ACTIVIDAD: LAS ACTIVIDADES DE ADHINTER S.A. SE DESARROLLAN EXCLUSIVAMENTE EN LA ZONA FRANCA DEL PACIFICO CORRESPONDEN A LA PRODUCCION Y COMERCIALIZACION EN EL MERCADO NACIONAL E INTERNACIONAL DE ADHESIVOS MEDICINALES TALES COMO CURAS, VENDITAS, ESPARADRAPOS, PARCHES, VENDAS; ADHESIVOS PARA USO EN OFICINA TALES COMO CINTAS, PEGANTES, PAPELES ADHESIVOS Y CINTAS ADHESIVAS PARA USO INDUSTRIAL.

PRESUPUESTO DE CONTROL: TECNOQUIMICAS S.A., TIENE SUSCRITAS EN LA SOCIEDAD ADHESIVOS INTERNACIONALES S.A. ADHINTER S.A., LA CANTIDAD DE DOS MILLONES CUATROCIENTOS TREINTA MIL (2.430.000) ACCIONES ORDINARIAS DE VALOR NOMINAL DE CIEN PESOS (\$100.00) SOBRE UN TOTAL DE TRES MILLONES (3.000.000) DE ACCIONES ORDINARIAS SUSCRITAS QUE REPRESENTA UNA PARTICIPACION DIRECTA DEL 81% SOBRE EL TOTAL DEL CAPITAL SUSCRITO Y PAGADO DE LA SOCIEDAD.

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO EL NRO.7050-2 ESTABLECIMIENTO DE COMERCIO: TECNOQUIMICAS

UBICADO EN: ---C 23 7 39 DE CALI

RENOVO : POR EL A?O 2008

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO EL NRO.311234-2 ESTABLECIMIENTO DE COMERCIO: TECNOQUIMICAS

UBICADO EN: -K 7 22 122 DE CALI

FECHA MATRICULA : 22 DE ABRIL DE 1992

RENOVO : POR EL A?O 2008

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027 Hora Certificado 11:23:52

Operacion : 02CP21027014 PAGINA No. 28

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO
EL NRO.311235-2 ESTABLECIMIENTO DE COMERCIO: TECNOQUIMICAS
UBICADO EN: -C 23 4 66 DE CALI
FECHA MATRICULA : 22 DE ABRIL DE 1992
RENOVO : POR EL A?O 2008

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO
EL NRO.606730-2 ESTABLECIMIENTO DE COMERCIO: TECNOQUIMICAS S A JAMUNDI
UBICADO EN: --CARRETERA JAMUNDI KM. 23 DE JAMUNDI
FECHA MATRICULA : 14 DE ABRIL DE 2003
RENOVO : POR EL A?O 2008

CERTIFICA:

QUE A NOMBRE DE LA SOCIEDAD FIGURA MATRICULADO EN LA CAMARA DE COMERCIO BAJO
EL NRO.606736-2 ESTABLECIMIENTO DE COMERCIO: TECNOQUIMICAS S A YUMBO
UBICADO EN: --CL. 15 NRO. 30 98 AUTOPISTA CALI-YUMBO KILOMETRO 4 DE YUMBO
FECHA MATRICULA : 14 DE ABRIL DE 2003
RENOVO : POR EL A?O 2008

CERTIFICA:

QUE LA SOCIEDAD EFECTUO LA RENOVACION DE SU MATRICULA MERCANTIL EL 29 DE
MARZO DE 2008 .

CERTIFICA:

QUE NO FIGURAN OTRAS INSCRIPCIONES QUE MODIFIQUEN TOTAL O PARCIALMENTE EL
PRESENTE CERTIFICADO.
LOS ACTOS Y DOCUMENTOS REGISTRADOS QUEDAN EN FIRME CINCO (5) DIAS HABILES
DESPUES DE LA FECHA DE SU INSCRIPCION, SIEMPRE Y CUANDO DENTRO DE DICHO
TERMINO NO SEAN OBJETO DE RECURSOS EN LA VIA GUBERNATIVA.

DE CONFORMIDAD CON EL DECRETO 2150 DE 1.995 Y LA AUTORIZACION IMPARTIDA POR
LA SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO LA FIRMA MECANICA QUE APARECE A

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CERTIFICADO NACIONAL

CAMARA DE COMERCIO DE CALI

Fecha : 20081027

Hora Certificado 11:23:52

Operacion : 02CP21027014

PAGINA No. 29

CONTINUACION TIENE PLENA VALIDEZ PARA TODOS LOS EFECTOS LEGALES.
DADO EN CALI A LOS 27 DIAS DEL MES DE OCTUBRE DEL AÑO 2008 HORA: 11:24:37


DIEGO FERNANDO OSPINA GARCIA

T. Q.

218

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 80

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-055028- -00006-0000

RECIBO OFICIAL DE CAJA : 06 - 101,249

FECHA : DICIEMBRE 29 DE 2008

Fecha: 2008-12-30 17:23:38 Dep. 2020 NULCREACIONE
 Tra 11 PATENTLIYII Lve. 378 FASENACIONALI
 Act. 400 OPOSIOBSERVIER Folios 81

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	NO. PAGO	FECHA PGO	Vr. PAGO
REYES Y REYES ABOGADOS	CONSIGNACION	BANCO DE BOGOTA	062754387	20259875	29/12/2008	266,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-04	PRESENTACION DE OBSERVACIONES	
		12 MARCAS Y LEMAS COMERCIALES	266,000.00
		TOTAL :	\$ 266,000.00

SUN: DOSCIENTOS SESENTA Y SEIS MIL PESOS

RESPONSABLE :

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

235

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No.07-055028

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION**
FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **596** DE
FECHA **30 DE SEPTIEMBRE DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR
LA LEY EXPIRA EL **30 DE DICIEMBRE DEL 2008**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI **X**

NO