PETITORIO

Industria y Comercio
SUPERINTENDENCIA

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licación

FORMULARIO ÚNICO DE SOLICITUD DE PATENTE
PCT
ENTRADA EN FASE NACIONAL

(1) SOLICITUD DE :

[X]	Patente de Invención	[ ]	Patente de Modelo de Utilidad
[X]	Capítulo I.	[ ]	Capítulo II.

(2) SOLICITANTE (71)

Nombre: WYETH

Dirección: Five Giralda Farms, Madison, New Jersey 07940, Estados Unidos de América

Nacionalidad o Domicilio: Nueva Jersey, Estados Unidos de América

Lugar de Constitución: Delaware, Estados Unidos de América

Teléfono: Fax:

E-Mail

IDENTIFICACION

C.C. [ ] NIT [ ]

C.E. [ ] Otro [ ]

Cual

Número

(3) REPRESENTANTE O APODERADO

Nombre: ALVARO CORREA ORDOÑEZ

Dirección: Avenida 82 No.10-62 Piso 6

Teléfono: 634 1500 Fax: 376 2211

E-Mail: office.bogota@bakernet.com

IDENTIFICACION

C.C. [X] NIT [ ]

C.E. [ ] Otro [ ]

Cual

Número 79.143.366 de Usaquén TP 20.281

(4) INVENTOR (ES) (72)

Nombre: ALBRIGHT, Robert B.

Dirección: 213 Green Valley Way, Chalfont, Pennsylvania 18914, Estados Unidos de América

Nacionalidad o Domicilio: Estadounidense

(5) PCT (85)

Solicitud Internacional No. PCT/US2006/019513 Fecha 19-MAY-06

Publicación Internacional No. WO/2006/127487 Fecha 30-NOV-06

(6) Título (54) COMPOSICIONES CONCENTRADAS DE ALTA CARGA ÚTILES PARA EL CONTROL DE ECTO Y ENDO PARÁSITOS

(7) Clasificación Internacional (51) A01P 5/00, A01N 43/90, A01N 47/34, A01P 7/02, A01P 7/04 //A61P33/14

(8) Prioridad	(33) País de Origen	(32) Fecha	(31) Número de Solicitud
[ ] [ ]	US	24-MAY-05	60/683,950

2 2

(10) **ANEXOS**

- [X] Comprobante de pago de la tasa de presentación de la solicitud
- [ ] Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica
- [ ] Poderes, si fuere el caso
- [X] Documento de cesión del inventor al solicitante o a su causante
- [ ] Declaraciones
- [X] Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos)
- [X] Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos)
- [ ] Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen preliminar (IPEA)
- [ ] Traducción del examen preliminar internacional efectuado por la IPEA
- [ ] De ser el caso, copia del contrato de acceso
- [ ] De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas
- [ ] De ser el caso, certificado de depósito del material biológico
- [ ] Arte final 12 x 12
- [ ] De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud
- [ ] De ser el caso, modificaciones efectuadas a la solicitud internacional.
- [X] Otros: Extractos, Reporte de Búsqueda Internacional y Opinión escrita y notificación de presentación de documento de prioridad.

(11) **FIGURA CARATERISTICA**

(12) Solicito la concesión de la patente.

NOMBRE: ALVARO CORREA ORDOÑEZ

FIRMA:

C.C. 79.143.366 de Usaquén T.P. 26.281

TRADUCCIÓN OFICIAL N° 2011073 al español de un documento escrito en inglés, efectuada por Jaime Armando Garavito Burgos, c.c. N° 19.130.702 de Bogotá, Traductor e Intérprete Oficial inglés-español-inglés según Resolución N° 034 de enero 11 de 1983 expedida por el Ministerio de Justicia de la República de Colombia

DECLARACIÓN JURAMENTADA SOBRE CESIÓN A WYETH
COMPOSICIONES CONCENTRADAS VERSÁTILES DE ALTA CARGA PARA EL CONTROL DE ECTOPARÁSITOS

APOSTILLA

1. PAÍS: ESTADOS UNIDOS DE AMÉRICA
2. ESTE DOCUMENTO PÚBLICO HA SIDO FIRMADO POR:

   BARBARA A. KIELY
3. QUIEN ACTÚA EN CALIDAD DE:

   NOTARIO PÚBLICO DE NUEVA JERSEY
4. LLEVA EL SELLO DE:

   BARBARA A. KIELY, NOTARIO

JAIME A. GARAVITO B.
TRADUCTOR E INTERPRETE OFICIAL
Res 034 de Enero 11 de 1983
MINISTERIO DE JUSTICIA

CERTIFICADO

5. EN TRENTON, NUEVA JERSEY
6. EL DÍA 26 DE ENERO DE 2007
7. POR: Bradley Abelow, TESORERO DE NUEVA JERSEY
8. N° A281600
9. SELLO (APARECE ADHERIDO SELLO DORADO)
10. FIRMA (Firma ilegible)

AM102089 L1

DECLARACIÓN JURAMENTADA

Yo, Michelle L. McGowan, Asociado de Legalizaciones de Wyeth, por medio del presente certifico que la copia anexa ha sido comparada con la

TRADUCCIÓN OFICIAL N° 2011073 al español de un documento escrito en inglés, efectuada por Jaime Armando Garavito Burgos, c.c. N° 19.130.702 de Bogotá, Traductor e Intérprete Oficial inglés-español-inglés según Resolución N° 034 de enero 11 de 1983 expedida por el Ministerio de Justicia de la República de Colombia

misma en un país extranjero, para la invención titulada: "COMPOSICIONES CONCENTRADAS VERSÁTILES DE ALTA CARGA PARA EL CONTROL DE ECTOPARÁSITOS") de fecha junio 20, 2005 de Robert B. Albright a Wyeth y que la mencionada copia es una copia auténtica del original.

Fechada hoy 23 de enero de 2007 en Madison, Nueva Jersey, Estados Unidos de América.

Wyeth
(Firmado) Michelle L. McGowan
Asociado de Legalizaciones

PARA SER USADA EN COLOMBIA

JAIME A. GARAVITO B
TRADUCTOR E INTERPRETE OFICIAL
Res. 034 de Enero 11 de 1983
MINISTERIO DE JUSTICIA

RECONOCIMIENTO

Estado de Nueva Jersey)
)
Condado de Morris)

Hoy 23 de enero de 2007, compareció personalmente ante mí Michelle L. McGowan, Asociado de Legalizaciones de Wyeth, a quien conozco como la persona descrita en el anterior instrumento y quien suscribió el mismo y reconoció haberlo suscrito.

(Firmado) Barbara A. Kiely, Notario Público

[Sello en tinta que dice: "Barbara A. Kiely ID. 33893, Notario Público de Nueva Jersey. Mi comisión vence el 20 de junio de 2009"]

[Sello realzado que dice: "Barbara A. Kiely - Notario Público - Nueva Jersey"]

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Cesión de Invención

En consideración del pago por la CESIONARIA a la CEDENTE de una contraprestación válida y suficiente cuyo recibo se acusa por medio del presente, los CEDENTES:

(1) Nombre Completo del Inventor: Robert B. Albright
Residencia: 213 Green Valley Way, Chalfont, Pennsylvania, 18914, USA
Ciudadanía: Estados Unidos de América

por medio del presente venden, ceden y transfieren a la CESIONARIA:

Wyeth
Five Giralda Farms
Madison, New Jersey 07940

JAIME A. GARAVITO B
TRADUCTOR OFICIAL
Res. 034 de Enero 11 de 1983
MINISTERIO DE JUSTICIA

y los sucesores, cesionarios y representantes legales de la CESIONARIA, la totalidad del derecho, título e intereses para los Estados Unidos y sus posesiones territoriales y en todos los países extranjeros, incluyendo todos los derechos a reivindicar prioridad con respecto a la invención titulada: **COMPOSICIONES CONCENTRADAS VERSÁTILES DE ALTA CARGA PARA EL CONTROL DE ECTOPARÁSITOS**

Y la cual se encuentra en

(a) [X] Solicitud de los Estados Unidos No. **60/683.950** presentada el **24 de mayo de 2005**

(b) [ ] Yo/nosotros los CEDENTES que abajo firmamos, por medio del presente autorizamos y solicitamos se inserte arriba el número de la solicitud y la fecha de presentación cuando se conozcan,

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(c) [X] y cualquier equivalente legal de la misma en un país extranjero,

Incluyendo el derecho a invocar prioridad, incluyendo todas y cada una de las mejoras divulgadas en la misma y en todas las patentes que se obtengan para la mencionada invención a través de la anterior solicitud y cualquier solicitud provisional, no provisional, continuación, divisional, renovación o sustitución de la misma presentada posteriormente y en cuanto a la patente, cualquier re-expedición o nuevo examen de la misma.

Los CEDENTES por medio del presente acuerdan que no se ha hecho ni se hará o suscribirá ninguna cesión, venta, acuerdo o gravamen que pueda estar en conflicto con esta cesión.

Los CEDENTES autorizan a la CESIONARIA para que haga solicitudes y para que reciban patentes para la mencionada invención en cualquiera de los mencionados países en su propio nombre, o en el nombre de los CEDENTES o a su elección.

Los CEDENTES acuerdan suscribir u obtener cualquier seguridad adicional necesaria del título a dicha invención y cualquier patente que pueda ser expedida para la misma y a entregar en cualquier momento y a solicitud y expensas de la CESIONARIA cualquier testimonio en cualquier derecho preexistente que impida el patentamiento de la invención, litigio o procedimiento relacionado y a suscribir todos los documentos que puedan ser necesarios o convenientes para perfeccionar el título a dicho invento o cualquier patente que pueda ser otorgada para el mismo a la CESIONARIA, sus sucesores

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momento, a solicitud y expensas de la CESIONARIA, cualquier continuación, continuación parcial, divisional, renovación o sustitución de la misma y en cuanto a patentes a re-expedir o re-examinar las mismas, o cualesquier otras solicitudes adicionales de patentes para dicho invento o cualquier parte del mismo, todas las cuales y cualquier patente que se expida se ceden por medio del presente a la CESIONARIA y prestará todos los juramentos legales o declaraciones y hará todos los actos legales requeridos para adquirirlos, sin compensación adicional, pero a expensas de la CESIONARIA, sus sucesores, cesionarios u otros representantes legales.

Los CEDENTES autorizan y solicitan al Comisionado de Patentes expedir todas y cada una de las patentes de los Estados Unidos para la mencionada invención, que resulte de cualquiera de las solicitudes a su CESIONARIA.

(Firmado) Junio 20, 2005
Robert B. Albright Fecha

RECONOCIMIENTO

Estado de Nueva Jersey)
) Declaración juramentada
Condado de Mercer)

El día 20 de junio de 2005, Robert B. Albright, compareció personalmente ante mí, a quien conozco como la persona descrita en el anterior instrumento y quien suscribió el mismo y reconoció haberlo suscrito en forma libre y espontánea para los fines consignados en él.

[Firmado] Janice Capasso, Notario Público

TRADUCCIÓN OFICIAL N° 2011073 al español de un documento escrito en inglés, efectuada por Jaime Armando Garavito Burgos, c.c. N° 19.130.702 de Bogotá, Traductor e Intérprete Oficial inglés-español-inglés según Resolución N° 034 de enero 11 de 1983 expedida por el Ministerio de Justicia de la República de Colombia

[Sello que dice: "Janice Capasso, Notario Público de Nueva Jersey. Comisión vence el 29 de mayo de 2008"]

(Firma ilegible) Junio 29, 2005
Shobhan Sabnis Fecha

RECONOCIMIENTO

Estado de)
) Declaración juramentada
Condado de)

El día 29 de junio de 2005, Shobhan Sabnis, compareció personalmente ante mí, a quien conozco como la persona descrita en el anterior instrumento y quien suscribió el mismo y reconoció haberlo suscrito en forma libre y espontánea para los fines consignados en él.

[Firmado] Janice Capasso, Notario Público

[Sello que dice: "Janice Capasso, Notario Público de Nueva Jersey. Comisión vence el 29 de mayo de 2008"]

La anterior es traducción fiel y completa de la cual se deja copia en esta oficina para su confrontación.

Jaime Armando Garavito Burgos
c.c. N° 19.130.702 de Bogotá
Traductor e Intérprete Oficial según Resolución N° 034 de enero 11 de 1983 expedida por el Ministerio de Justicia

10

APOSTILLE

(CONVENTION DE LA HAYE DU 5 OCTOBRE 1961)

1. COUNTRY: UNITED STATES OF AMERICA

2. THIS PUBLIC DOCUMENT HAS BEEN SIGNED BY:
BARBARA A KIELY

3. ACTING IN THE CAPACITY OF:
NOTARY PUBLIC OF NEW JERSEY

4. BEARS THE SEAL/STAMP OF:
BARBARA A KIELY, NOTARY

CERTIFIED

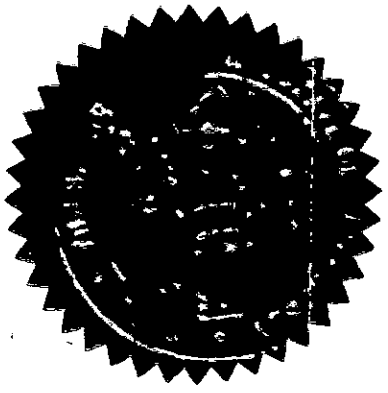
5. AT TRENTON, NEW JERSEY

6. THE 26TH DAY OF JANUARY 2007

7. BY: Bradley Abelow, NEW JERSEY TREASURER

8. NO. A281600

9. SEAL/STAMP:



10. SIGNATURE

Bradley Abelow

11

AM102089 L1

AFFIDAVIT

I, Michelle L. McGowan, Legalization Associate, Wyeth, do hereby certify that the attached copy has been compared with the original Assignment (for U.S.S.N. 60/683,950, and any legal equivalent thereof in a foreign country, for the invention entitled: "VERSATILE HIGH LOAD CONCENTRATE COMPOSITIONS FOR CONTROL OF ECTO-PARASITES") dated June 20, 2005 from Robert B. Albright to Wyeth and that the said copy is a true copy of the original.

Dated this 23rd day of January, 2007, at Madison, New Jersey, United States of America.

Wyeth

Michelle L. McGowan
Legalization Associate

TO BE USED IN COLOMBIA

ACKNOWLEDGMENT

State of New Jersey)
)
County of Morris)

On this 23rd day of January, 2007, before me personally appeared Michelle L. McGowan, Legalization Associate of Wyeth, to me known and known to me to be the individual described in and who executed the foregoing instrument, and she acknowledged to me that she executed the same.

Notary Public

Barbara A. Kiely ID. 33893
Notary Public of New Jersey
My Commission Expires June 20, 2009

Docket No: AM102089 L1
Patent

Assignment of Invention

In consideration of the payment by ASSIGNEE to ASSIGNOR of good and valuable consideration, the receipt of which is hereby acknowledged,

ASSIGNOR:

(1) Full Name of Inventor: **Robert B. ALBRIGHT**
Residence: **213 Green Valley Way - Chalfont, Pennsylvania 18914 - USA**
Citizenship: **United States of America**

---

(2) Full Name of Inventor:
Residence:
Citizenship:

---

(3) Full Name of Inventor:
Residence:
Citizenship:

---

(4) Full Name of Inventor:
Residence:
Citizenship:

---

(5) Full Name of Inventor:
Residence:
Citizenship:

---

(6) Full Name of Inventor:
Residence:
Citizenship:

---

hereby sells, assigns and transfers to ASSIGNEE:

Wyeth
Five Giralda Farms
Madison, New Jersey 07940

and the successors, assigns and legal representatives of the ASSIGNEE the entire right, title and interest for the United States and its territorial possessions and in all foreign countries, including all rights to claim priority, in and to the invention entitled:

VERSATILE HIGH LOAD CONCENTRATE COMPOSITIONS FOR CONTROL OF ECTO-PARASITES

and which is found in

(a) ☒ U.S. Application No. **60/683,950** filed on **May 24, 2005**
(b) ☐ U.S. Patent No. issued on:

☒ I/we the ASSIGNOR signing below, hereby authorize and request insertion above of the application number and filing date, when they become known,

[Check (c) if foreign application(s) is also being assigned]

(c) ☒ and any legal equivalent thereof in a foreign country,

including the right to claim priority, including any and all improvements disclosed therein, and in and to all Letters Patent to be obtained for said invention by the above application or any subsequently filed provisional, nonprovisional, continuation, divisional, renewal, extension, or substitute thereof, and as to Letters Patent any reissue or re-examination thereof.

ASSIGNOR hereby covenants that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this assignment.

ASSIGNOR authorizes ASSIGNEE to make applications for and to receive Letters Patent for said invention in any of said countries in its own name, or in ASSIGNOR'S name, at its election.

ASSIGNOR covenants and agrees to execute or procure any further necessary assurance of the title to said invention and any Letters Patent which may issue therefore and to, at any time, upon the request and at the expense of ASSIGNEE deliver any testimony in any interference, litigation or proceeding related thereto and execute all papers that may be necessary or desirable to perfect the title to said invention or any Letters Patent which may be granted therefore in ASSIGNEE, its successors, assigns or other legal representatives, and that to, at any time, upon the request and at the expense of ASSIGNEE execute any continuations, continuations-in-part, divisional, renewal or substitute thereof, and as to Letters Patent and reissue or re-examination thereof, or any other additional applications for Letters Patent for said invention or any part or parts thereof, all of which applications and any Letters Patent issuing thereon are hereby assigned to ASSIGNEE, and will make all rightful oaths or declarations, and do all lawful acts requisite for procuring the same therein, without further compensation, but at the expense of ASSIGNEE, its successors, assigns or other legal representatives.

ASSIGNOR authorizes and requests the Commissioner of Patents to issue any and all Letters Patent of the United States for said invention, resulting from any of the aforesaid applications to its ASSIGNEE.

~~14~~
14

Robert B. Albright — June 20, 2005

Robert B. ALBRIGHT — Date

ACKNOWLEDGMENT

JANICE CAPASSO
NOTARY PUBLIC OF NEW JERSEY
Commission Expires 5/29/2008

State of New Jersey }
ss:
County of Mercer }

On the 20th day of June **2005, Robert B. ALBRIGHT** personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Janice Capasso
Notary Public

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 November 2006 (30.11.2006)

PCT

(10) International Publication Number
WO 2006/127487 A1

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A01P 7/04 (2006.01)

(21) International Application Number:
PCT/US2006/019513

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(30) Priority Data:
60/683,950 24 May 2005 (24.05.2005) US

(71) Applicant *(for all designated States except US)*: **WYETH** [US/US]; Five Giralda Farms, Madison, New Jersey 07940 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **ALBRIGHT, Robert B.** [US/US]; 213 Green Valley Way, Chalfont, Pennsylvania 18914 (US).

(74) Agents: **RENDA, Barbara, L.** et al.; Wyeth, Patent Law Department, Five Giralda Farms, Madison, New Jersey 07940 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2006/127487 A1

(54) Title: USEFUL HIGH LOAD CONCENTRATE COMPOSITIONS FOR CONTROL OF ECTO-AND ENDO-PARASITES

USEFUL HIGH LOAD CONCENTRATE COMPOSITIONS FOR CONTROL OF ECTO-AND ENDO-PARASITES

BACKGROUND OF THE INVENTION

Arthropod ectoparasites commonly infecting warm-blooded animals include ticks, mites, lice, fleas, blowfly, the ectoparasite *Lucilia sp.* of sheep, biting insects including keds (*Melophagus ovinus*) and migrating dipterous larvae such as *Hypoderma sp.and Dermataobia* in cattle, *Gastrophilus* in horses and *Cuterebra sp.* in rodents.

Helminthiasis is a widespread disease found in many animals and is responsible for significant economic losses throughout the world. Among the helminths most frequently encountered are the group of worms referred to as nematodes. The nematodes are found in the gastrointestinal tract, heart, lungs, blood vessels and other body tissues of animals and are a primary cause of anemia, weight loss and malnutrition in the infected animals. They do serious damage to the walls and tissue of the organs in which they reside and, if left untreated, may result in death to the infected animals.

The nematodes most commonly found to be the infecting agents of ruminants include Haemonchus and Ostertagia generally found in the abomasum; Cooperia, Trichostrongylus and Nematodirus generally found in the intestinal tract, and Dictyocaulus found in the lungs. In non-ruminant animals, important nematodes include Toxocara and Ancylostoma in the intestine and Dirofilaria in the heart of dogs and cats; Ascaridae in the intestine of swine; and large and small strongyles in equines.

Arthropod ectoparasites commonly infecting warm-blooded animals include ticks, mites, lice, fleas, blowfly, the ectoparasite Lucilia sp. of sheep, biting insects and migrating dipterous larvae such as Hypoderma sp. in cattle, Gastrophilus in horses and Cuterebra sp. in rodents.

Anti-parasitic macrolide compounds such as LL-F28249α-λ compounds, 23-oxo or 23-imino derivatives of LL-F28249α-λ compounds, including, but not limited to, moxidectin, milbemycin compounds, including but not limited to milbemycin oxime, avermectin compounds, including, but not limited to abamectin, ivermectin, and mixtures thereof, are useful for the prevention and control of helminthiasis and

infection by acarids and arthropod endo- and ectoparasites in warm-blooded animals.

Metaflumizone is useful for the prevention and control of infestation by ectoparasites in warm-blooded animals. Topical administration of this active is a preferred method for administering this compound.

To provide useful protection against both endoparasitic infections and ectoparasitic infection or infestation in warm-blooded animals it is desirable to use formulations having a relatively high loading of active agent, but such formulations must be stable, both with respect to the physical formulation, and also, with respect to the chemical stability of the actives. Metaflumizone is one of several useful insecticidal agents which have found particular application for the control of fleas and ticks on animals, particularly companion animals such as dogs, cats and horses. It is particularly advantageous in that it can provide 4-6 weeks of protection from fleas and ticks in companion animals, but it would be potentially useful for many other species if suitable formulations could be developed. Nonetheless, formulation of metaflumizone is made difficult by its insolubility in many solvents, and its instability in the presence of primary alcohols.

It is the object of the present invention to provide a method for preventing, controlling or treating helminth, acarid or arthropod endo- or ectoparasitic infection or infestation in warm-blooded animals which method comprises topically administering to the warm-blooded animals an anthelmintically, acaricidally or arthropod endo- or ectoparasiticidally effective amount of a nonaqueous composition which comprises about 0.1 to 10% w/v of a substantially water-insoluble anti-parasitic macrolide compound, about 5% to about 40% of metaflumizone; about 0% to about 15% of a bridging or penetrating agent; about 2 to 8% of a surfactant, and about 50 to 80% w/v of a pharmaceutically acceptable water-miscible or water immiscible solvent or solvent system as the carrier.

It is also an object of the present invention to provide a versatile composition for topical administration which comprises a relatively high loading of metaflumizone in combination with an anti-parasitic macrolide compound, and which will provide protection from ecto- and endo-parasitic infestation. Most advantageously, the formulation can function as a concentrate, which with simple modifications, can be extended to use for a wide variety of other animals. Thus, the concentrated formulation can be utilized as a small volume spot-on formulation, for instance, for protection of companion animals, while further dilutions can be utilized as

conventional pour-on products for farm animals, with still further dilutions utilizable for sprays and application to the feed.

It is also an object of the present invention to provide a method for preventing or treating acarid or arthropod ectoparasitic infestation in warm-blooded animals, using the compositions of the invention.

It is another object of this invention to reduce or control the proliferation of such insects in warm-blooded animals for prolonged periods of time by a topically applied active, with the formulation being mild and gentle enough to avoid adverse skin reactions upon administration, yet with the ability to be retained in the animal's skin and/or coat over the time needed for protection.

These and other objects of the present invention will become more apparent from the description thereof set forth below and the appended claims.

SUMMARY OF THE INVENTION

The present invention provides high-load concentrate compositions for topical administration which comprise on a weight to volume basis:

about 0.1 to about 10% of substantially water-insoluble anti-parasitic macrolide compound, especially, moxidectin:
about 5% to about 40% of metaflumizone;
about 0% to about 15% of a bridging or penetrating agent;
about 2 to about 8% of a surfactant and
about 50% to about 80% of a carrier solvent.

The present invention further provides a method for preventing or treating ectoparasitic and endoparasitic infection or infestation in a warm-blooded animal which method comprises topically administering to the animal an acaricidally or arthropod ectoparasiticidally effective amount of the composition of this invention.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, the high load concentrate compositions comprise a substantially water-insoluble anti-parasitic macrolide compound, especially, moxidectin, metaflumizone; an optional bridging agent or penetration enhancer, a surfactant, and a carrier solvent. The invention also

provides a method for preventing or treating acarid or arthropod ectoparasitic infection or infestation in warm-blooded animals by topical application of the aforesaid formulations.

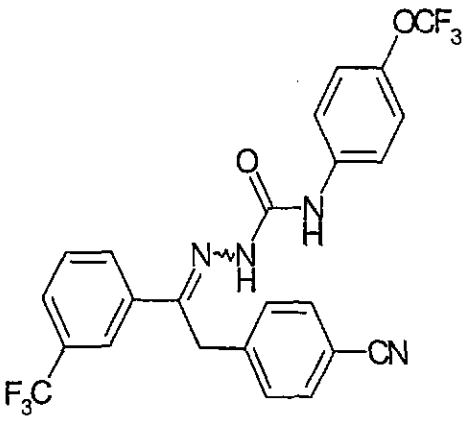
Preferred high load concentrate compositions of this invention comprise on a weight to volume basis:

About 0.1 to about 10% of a substantially water-insoluble anti-parasitic macrolide compound, especially, moxidectin
about 5% to about 40% of metaflumizone;
about 0% to about 15% of a bridging or penetrating agent;
about 2 to about 8% of a surfactant and
about 50% to about 80% of a carrier solvent.

While not wishing to be bound by any particular theory, it is believed that the compositions of the present invention have the requisite stability by virtue of physical and or chemical interactions between the surfactant and the metaflumizone. The exact nature of the interactions is unknown, but apparently the surfactant stabilizes the metaflumizone in solution so as to ensure that the resultant formulation retains the desired physical characteristics over time, without loss of potency of the active. Further, the formulation is sufficiently viscous to be retained upon the animal's skin, hair, and be released over the desired period of time.

Uniquely, it has been found these high load concentrate compositions can be further utilized to prepare more dilute compositions for application in various other manners, *i.e.*, for use as a pour-on for large animals, as a spray for large animals or for outdoor use, and as a water-dilutable formulation for addition to the feed and/or water supply of animals under treatment. This has the dual advantage of providing a concentrated formulation that can be shipped to the end-user for dilution and use, or to an intermediate formulator to prepare the compositions. The high loading of metaflumizone in the formulation thus provides a small volume of formulation to use as a "spot-on" formulation, for instance, for companion animals, especially felines. The concentrate can then be diluted by an appropriate organic solvent for use as a pour-on or in a spray, or with water, to provide the feed/water additive.

Metaflumizone is described in U.S. Patent No. 5,543,573, and U. S. Published Application 2004-0122075A1, both incorporated herein by reference



Chemically, metaflumizone is known as (E Z)-2-[2-(4-cyanophenyl)-1-[3-(trifluoromethyl)phenyl]ethylidene]-*N*-[4-(trifluoromethoxy)phenyl] hydrazinecarboxamide.

The substantially water-insoluble anti-parasitic macrolide compounds useful for the compositions of the present invention are well-know in the art, and are described in detail in, for instance, "Macrocyclic Lactones in Antiparasitic Therapy," edited by J. Vercruysse and R. S. Rew, CABI Publishing, London, 2002. Such macrolide compounds are subclassed into avermectins and milbemycins, with avermectins being glycosylated milbemycins. Highly preferred, due to its persistency of activity, and its environmental friendliness, is the milbemycin moxidectin, sold in various forms for administration under the Cydectin® tradename.

Bridging agents or penetrating agents or enhancers suitable for use in the compositions of this invention include, but are not limited to, alkyl methyl sulfoxides (such as dimethyl sulfoxide, decylmethyl sulfoxide and tetradecylmethyl sulfoxide); pyrrolidones (such as 2-pyrrolidone, N-methyl-2-pyrrolidone and N-(2-hydroxyethyl) pyrrolidone); laurocapram; and miscellaneous solvents such as acetone, dimethyl acetamide, dimethyl formamide, tetrahydrofurfuryl alcohol, cineole, N,N-diethyl-3-methylbenzamide (DEET), isopropyl myristate (IPM) and dimethyl isosorbide. Other bridging agents include amphiphiles such as L-amino acids, and fatty acids. Additional bridging agents are disclosed in *Remington: The Science and Practice of Pharmacy,* 19th Edition (1995) on page 1583. Typically, the penetrating agent is used at a level of about 10% w/v of the formulation where the end use is for a topical application, but this may vary, especially when the end use of the composition is for oral administration.

The surfactant utilized in the present invention may be a single surfactant, or a mixture of two or more surfactants, again, in part dependent upon whether the end use of the composition is topical or oral. The surfactant should be non-irritating, and non-toxic. Preferred are non-ionic, low foaming surfactants, such as the alcohol alkoxylate surfactants, with those such as nonylphenol ethoxylate (sold under the tradename Surfonic N-95), and alcohol alkoxylates (sold under the tradename Synperonic® NCA by Uniqema), and the polyethoxylated caster oil surfactants (also known as macrogolglycerol ricinoleate, and sold under the Cremaphore® EL tradename by BASF) being especially suitable. Also useful are ionic surfactants such as sodium lauryl sulfate and dioctyl sodium sulfosuccinate.

Typically, the surfactant is utilized at a level of about 2 to about 8% w/v of the composition, but this may vary somewhat depending upon the end use of the composition. In the case where the end use of the concentrate is as a spray formulation, or as a water-dispersible feed /water additive, it may be desirable to add a further surfactant to ensure that the diluted formulation will be a unitary phase. This ensures that the spray will not block the spray nozzle, and that the active will be dispersed equally throughout the diluted product. In such cases, the additional surfactant may be added to the concentrate formulation, or added to the end use formulation with the diluting solvent. Particularly useful surfactants for use with an organic solvent diluent are non-ionic surfactants such as polyethoxylated castor oil, sold under the tradename Cremophor® EL by BASF Corporation.

The carrier solvent for the compositions of the present invention may be a single solvent, or a mixture of solvents. Due to the instability of metaflumizone in the presence of primary alcohols, preferred solvents are non-hydroxyl-group-containing solvents, especially those such as γ-hexalactone (gamma-hexalactone). Optionally, other such solvents such as N,N-diethyl-m-toluamide, eucalyptol, dimethyl isosorbide, diisopropyl adipate and/or methoxypropyl acetate (1-methoxy-2-propyl acetate) can be utilized in combination with the γ-hexalactone to comprise the carrier solvent.

To manufacture the high load concentrate composition of the present invention, the metaflumizone is dissolved in the carrier solvent or solvents, and the surfactant and bridging agent, if desired added to the mixture. This composition can then be utilized as a high load spot-on, or further diluted for additional uses.

An especially preferred composition for topical administration to warm-blooded animals comprises, on a weight to volume basis, about 20% to about 30%

metaflumizone; 0.5% moxidectin, about 10% of a bridging or penetrating agent, especially dimethyl sulfoxide, about 2 to-about 8%, and especially about 5%, of a non-ionic, low foam surfactant, and about 50-60% carrier solvent, especially γ-hexalactone.

The high load concentrate compositions of this invention may further comprise other agents known in the art, such as preservatives (*e.g.*, methylparaben and propylparaben), colorants, antioxidants, and the like. Generally, these agents would be present in the compositions in an amount up to about 2% on a weight to volume basis.

When topically administered, the compositions of this invention are highly effective for preventing or treating ectoparasitic infection and infestation for prolonged periods of time in warm-blooded animals such as cows, sheep, horses, camels, deer, swine, goats, dogs, cats, birds, and the like. Additionally, the composition is highly effective against endoparasitic infections.

In order to facilitate a further understanding of the invention, the following examples are presented primarily for the purpose of illustrating specific embodiments thereof. The invention is not to be deemed limited thereby, except as defined in the claims.

EXAMPLE 1

Preparation of metaflumizone/moxidectin High Load Concentrate, suitable for use as a Spot-on

A 100 gram weight of dimethyl sulfoxide (DMSO) is added to 400 grams γ-hexalactone. To this solvent system is added 200 grams metaflumizone. Dissolve metaflumizone in the solvent system. Weigh 10 grams of moxidectin and add it to the current solution containing metaflumizone. Allow the moxidectin to dissolve. To the resulting solution, add 60 grams alcohol alkoxylate surfactant (sold under the tradename Synperonic® NCA) and allow the surfactant to dissolve. Lastly, bring the solution to 1000 ml with γ-hexalactone

EXAMPLE 2

Preparation of metaflumizone/moxidectin Pour-On from High Load Concentrate of Example 1

To 25 ml of the high load concentrate prepared in Example 1 is added q.s. to 100 ml γ-hexalactone. This provides a pour-on formulation having sufficient metaflumizone and moxidectin and volume to treat 5 head of cattle weighed 200 Kg each at 5 mg/kg dose rate metaflumizone and 0.25 mg/kg dose rate moxidectin.

EXAMPLE 3

Preparation of High Load Concentrate for use as a Concentrate to prepare metaflumizone Spray or Feed/Water Supplement

12.59 grams of metaflumizone is added to methoxypropyl acetate using mild heating (approximately 40°C). To this solution is added 109.92 grams polyethoxylated castor oil (sold under the tradename Cremophor® EL), with stirring, followed by 1.0 grams moxidectin and then brought to volume with methoxypropyl acetate. The resultant solution is stored until ready for use, whereupon it can be diluted with water for use as a spray (17 ml of concentrate diluted to 3500 ml with water), or with water for use as a feed/water additive (in approximately the same ratio) or additionally, applied directly as a backline pour-on.

EXAMPLE 4

Preparation of various formulations of a metaflumizone/moxidectin High Load Concentrate, suitable for use as a Spot-on treatment

Formulation:	1	2	3	4	5	6	7	8	9
Moxidectin	0.1	0.5	2.5	0.1	0.5	2.5	0.1	0.5	2.5
Metaflumizone	30	30	30	20	20	20	5	5	5
Nonylphenol ethoxylate	5					5	5		
alcohol ethoxylate, e.g.		5			5			5	

Synperonic® NCA									
Dioctyl sodium sulfosuccinate			5	5					5
Cineole	10								
DEET		10							
IPM			10						
Methoxypropyl acetate					10	10	10	10	10
DMSO	10	10	10	10					
γ-hexalactone	qs	qs	qs	qs	qs	qs	qs	qs	qs

The preceding formulations are prepared using essentially the same procedures as are listed in Example 1.

EXAMPLE 5

Preparation of various formulations of a metaflumizone/macrolide High Load Concentrate, suitable for use as a Spot-on

Formulation:	10	10B	10C
Ivermectin			5
Abarmectin		5	
Moxidectin	5		
Metaflumizone	30	30	20
alcohol ethoxylate, e.g. Synperonic NCA	5	5	5
Methoxypropyl acetate	10	10	10
γ-hexalactone	qs	qs	qs

The preceding formulations are prepared using essentially the same procedures as are listed in Example 1.

Example 6

Preparation of various formulations of a *metaflumizone/moxidectin* High Load Concentrate, suitable for use as a Spot-on

Formulation:	11	12	14	15	16	17	18	19	20
Moxidectin	0.1	0.5	0.1	1	10	0.25	5	0.1	0.1
Metaflumizone	30	30	20	20	20	5	5	5	5
Cineole									
DEET									
Isopropyl myristate	5				1				
polyethoxylated castor oil		5		1		5	5	5	5
Sodium lauryl sulfate			1						
Methoxypropyl acetate			5	5	5				
DMSO	30	30							
Dimethyl isosorbide						30	30	30	30
γ-hexalactone	qs	qs	qs	qs	qs	qs	qs	qs	qs

The preceding formulations are prepared using essentially the same procedures as are listed in Example 1.

WHAT IS CLAIMED IS:

1. A composition for topical administration which comprises on a weight to volume basis from about 0.1 to about 10% of a substantially water-insoluble anti-parasitic macrolide compound, about 5% to about 40% of metaflumizone; about 0% to about 15% of a penetrating agent; about 2 to about 8% of a surfactant; and about 50% to about 80% of a carrier solvent.

2. The composition according to Claim 1 which comprises from about 20% to about 30% of the metaflumizone.

3. The composition in Claim 1 or Claim 2 wherein the macrolide compound is moxidectin, abamectin or ivermectin.

4. The composition according to any one of Claims 1 to 3 wherein the surfactant is a non-ionic low foam surfactant.

5. The composition according to any one of Claims 1 to 4 wherein the macrolide compound is moxidectin.

6. The composition according to any one of Claims 1 to 5 wherein the penetrating agent is dimethyl sulfoxide.

7. The composition according to any one of Claims 1 to 6 wherein the carrier solvent comprises gamma-hexalactone.

8. The composition according to any one of Claims 1 to 7 wherein the carrier solvent comprises dimethyl isosorbide.

9. The composition according to any one of Claims 1 to 8 which additionally contains up to about 2% of one or more preservatives, colorants, antioxidants, or stabilizers.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/019513

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	WO 2006/042099 A (WYETH; SABNIS, SHOBHAN, SHASHI; ZUPAN, JACOB, A; ALBRIGHT, ROBERT, BRU) 20 April 2006 (2006-04-20) claims 1,4,5 page 5, lines 1,2 examples 1-3	1-16
Y	WO 2004/089239 A (MERIAL LTD; SOLL, MARK, D; KUMAR, KRISHAN; WARANIS, ROBERT, P; SHUB, N) 21 October 2004 (2004-10-21) page 1, paragraph 2 page 3, paragraph 2 page 6, last paragraph - page 7, paragraph 2 page 9, paragraph 1 page 9, last paragraph - page 10, paragraph 1 page 19, paragraph 4 claims 1-26	1-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/019513

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 10-16 are directed to a method of treatment of the animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2006/019513

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 1413201 A	28-04-2004	AU 2003255177 A1	06-05-2004
		BR 0304618 A	31-08-2004
		CA 2444692 A1	21-04-2004
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		CA 2521268 A1	21-10-2004
		EP 1610613 A2	04-01-2006
		MX PA05010659 A	12-12-2005

COMPOSICIONES CONCENTRADAS DE ALTA CARGA ÚTILES PARA EL CONTROL DE ECTO Y ENDO PARÁSITOS.

ANTECEDENTES DE LA INVENCIÓN

Los ectoparásitos artrópodos que infectan comúnmente animales de sangre caliente incluyen garrapatas, ácaros, piojos, pulgas, moscardones, el ectoparásito *Lucilia sp*, de la oveja, insectos picadores que incluyen piojos de ovejas, (*Melophanos ovinus*) y larvas de dípteros migratorios tales como *Hipoderma sp, y Dermataobia* en ganado, *Gastrophilus* en caballos y *Cuterebra sp*. en roedores.

La Helmintiasis es una enfermedad ampliamente difundida encontrada en muchos animales y es responsable por pérdidas económicas significativas en todo el mundo. Entre los helmintos más frecuentemente encontrados están los grupos de gusanos denominados como nemátodos. Los nemátodos se encuentran en el tracto gastrointestinal, corazón, pulmones, vasos sanguíneos y otros tejidos corporales de animales y son la causa principal de anemia, pérdida de peso y malnutrición en animales infectados. Ellos dañan seriamente las paredes y el tejido de los órganos en los cuales ellos residen y, si se dejan sin tratar, pueden dar como resultado la muerte de los animales infectados.

Trichostrongilus y Nematodirus encontrados generalmente en el tracto gastrointestinal, y Dictiocaulus encontrado en pulmones. En animales no rumiantes, los nemátodos importantes incluyen Toxocara y Ancilostoma en el intestino y Dirofilaria en el corazón de perros y gatos; Ascaridae, en el intestino de cerdos; y estróngilos grandes y pequeños en equinos.

Los ectoparásitos artrópodos que infectan comúnmente animales de sangre caliente incluyen garrapatas, ácaros, piojos, pulgas, moscardones, ectoparásitos Lucilia sp. de la oveja, insectos picadores y larvas de dípteros migratorios tales como Hipoferma sp. en ganado, Gastrofilus en caballos y Cuterebra sp. en roedores.

Los compuestos macrólidos antiparasíticos tales como los compuestos LL-F28249 α-λ, los derivados 23-oxo o 23-imino de los compuestos LL-F28249α-λ, incluyen, pero no están limitados a, moxidectina, los compuestos milbemicina, que incluyen pero no están limitados a milbemicin oxima, los compuestos de avermectin, que incluyen, pero no están limitados a abamectina, ivermectina, y mezclas de estos, son útiles para la prevención y control de helmintiasis e infección por acáridos y artrópodos endo y ectoparásitos en animales de sangre caliente.

La metaflumizona es útil para la prevención y control de

~~34~~ 34

Para suministrar protección útil contra infecciones endoparasíticas e infecciones ectoparasíticas o infestación en animales de sangre caliente es deseable utilizar formulaciones que tengan una carga relativamente alta del agente activo, pero tales formulaciones deben ser estables, con respecto a la formulación física, y también, con respecto a la estabilidad química de los activos. La metaflumizona es uno de varios agentes insecticidas útiles que han encontrado aplicación particular para el control de pulgas y garrapatas en animales, particularmente animales de compañía tales como perros, gatos y caballos. Es particularmente ventajoso por que este puede suministrar 4-6 semanas de protección contra pulgas y garrapatas en animales de compañía, pero sería potencialmente útil para muchas otras especies si se pudieran desarrollar formulaciones adecuadas. Sin embargo, la formulación de metaflumizona se hace difícil por su insolubilidad en muchos disolventes, y su inestabilidad en la presencia de alcoholes primarios.

Es el objeto de de la presente invención suministrar un método para evitar, controlar o tratar helmintos, acáridos artrópodos o infección endo o ectoparasítica artrópodos o infestación en animales de sangre caliente cuyo método comprende administrar tópicamente a los animales de sangre caliente una cantidad antihelmínticamente, acaricidamente o

disoluble en agua, aproximadamente 5% a aproximadamente 40% de metaflumizona; a aproximadamente 0% a aproximadamente 15% de un agente puente o penetrante; aproximadamente 2 a 8% de un tensoactivo, y aproximadamente 50 a 80% p/v de un disolvente o sistema disolvente miscible en agua o no miscible en agua farmacéuticamente aceptable como un portador.

También es un objeto de la presente invención suministrar una composición versátil para la administración tópica que comprende una carga relativamente alta de metaflumizona en combinación con un compuesto macrólido antiparasítico, y que suministrará protección de infestación ecto y endoparasítica. Más ventajosamente, la formulación puede funcionar como un concentrado, con el cual simples modificaciones, pueden extender el uso a una amplia variedad de otros animales. Así, la formulación concentrada se puede utilizar como una formulación "spot on" de volumen pequeño, por ejemplo, para la protección de animales de compañía, aunque disoluciones adicionales se pueden utilizar como productos "pour on" convencionales para animales de granja, con aún disoluciones utilizables para pulverizados y aplicaciones al alimento.

También es un objeto de la presente invención suministrar un método para evitar o tratar infestación ectoparasítica de ácaros o artrópodos en animales de sangre caliente

Es otro objeto de esta invención reducir o controlar la proliferación de tales insectos en animales de sangre caliente durante periodos prolongados de tiempo mediante un activo tópicamente aplicado, siendo la formulación suficientemente suave y moderada para evitar las reacciones adversas de la piel luego de la administración, aunque con la capacidad de ser retenida en la piel y/o pelo de animales durante el tiempo necesario para la protección.

Estos y otros objetos de la presente invención serán más evidentes de la descripción de esta establecida adelante y en las reivindicaciones adjuntas.

RESUMEN DE LA INVENCIÓN

La presente invención suministra composiciones concentradas de alta carga para la administración tópica que comprende una base de peso o volumen:

Aproximadamente 0.1 a aproximadamente 10% de un compuesto macrólido antiparasítico sustancialmente insoluble en agua, especialmente, moxidectina:

Aproximadamente 5% a aproximadamente 40% de metaflumizona;

Aproximadamente 0% a aproximadamente 15% de un agente puente o penetrante;

Aproximadamente 2 a aproximadamente 8% de un tensoactivo

La presente invención suministra además un método para evitar o tratar la infección e infestación ectoparasítica y endoparasítica en animales de sangre caliente cuyo método comprende administrar tópicamente al animal una cantidad acaricida o ectoparasíticamente efectiva para artrópodos de la composición de esta invención.

DESCRIPCIÓN DETALLADA DE LA INVENCIÓN

De acuerdo con la presente invención, las composiciones concentradas de alta carga comprenden un compuesto macrólido antiparasítico sustancialmente insoluble en agua, especialmente, moxidectina, metaflumizona; un agente puente opcional o un mejorador de penetración, un tensoactivo, y un disolvente portador. La invención también suministra un método para tratar o evitar la infección o infestación ectoparasítica de ácaros o de artrópodos en animales de sangre caliente mediante la aplicación tópica de las formulaciones anteriormente mencionadas.

Las composiciones concentradas preferidas de alta carga de esta invención comprenden una base de peso volumen:

Aproximadamente 0.1 a aproximadamente 10% de un compuesto macrólido antiparasítico sustancialmente insoluble

Aproximadamente 0% a aproximadamente 15% de un agente puente o penetrante;

Aproximadamente 2% a aproximadamente 8% de un tensoactivo y

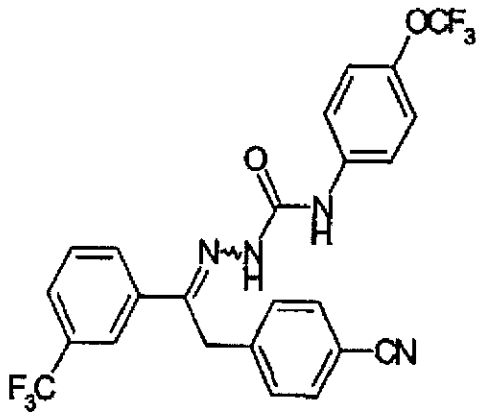
Aproximadamente 50% a aproximadamente 80% de un disolvente portador.

Aunque no se quiere estar ligado por ninguna teoría particular, que cree que las composiciones de la presente invención tienen la estabilidad requisito en virtud de las interacciones físicas y/o químicas entre el tensoactivo y la metaflumizona. La naturaleza exacta de las interacciones es desconocida, pero aparentemente el tensoactivo estabiliza la metaflumizona en solución con el fin de asegurar que la formulación resultante retenga las características físicas deseadas durante el tiempo, sin la pérdida de potencia del activo. Además, las formulaciones suficientemente viscosas para ser retenidas sobre la piel, pelo, del animal y ser liberada durante el periodo deseado de tiempo aparte.

Únicamente, se ha encontrado que estas composiciones concentradas de alta carga se pueden además utilizar para preparar composiciones no diluidas para aplicaciones de otras varias maneras, es decir, para el uso como un "pour on" para animales grandes, como un pulverizado para animales grandes o para uso exterior, y una formulación diluible en agua para la

final para la disolución y uso, o a un formulador intermedio para preparar las composiciones. La alta carga de la metaflumizona en la formulación suministra así un pequeño volumen de formulación para uso como una formulación "spot on", por ejemplo, para animales de compañía, especialmente felinos. El concentrado se puede diluir mediante un disolvente orgánico apropiado para uso como un "pour on" o con en un pulverizado, o con agua, para suministrar un aditivo para el alimento/agua.

La metaflumizona se describe en la Patente U.S. No. 5,543,573, y la Solicitud Publicada U.S. 2004-0122075A1, incorporadas ambas aquí como referencia.



Químicamente, la metaflumizona es conocida como (E Z)-2[2-(4-cianofenil)-1-[3-(trifluorometil)fenil]etilideno]-N-[4-(trifluorometoxi)fenil]hidrazinocarboxamida.

El compuesto macrólido antiparasítico sustancialmente disoluble en agua útil para las composiciones de la presente

Publishing, Londres, 2002. Tales compuestos de macrólido son subclases dentro de las avermectinas y milbemicinas, siendo las avermectinas milbemicinas glicosiladas. Altamente preferidas, debido a su persistencia de actividad, y su amigabilidad ambiental, es la milbemicina moxidectina, vendida en varias formas para administración bajo el nombre comercial Cidectin®.

Los agentes puente o agentes penetrantes o mejoradores adecuados para el uso en las composiciones de esta invención incluyen, pero no están limitados a, alquil metil sulfóxidos (tales como dimetil sulfóxido, decilmetil sulfóxido, y tetradecilmetil sulfóxido); pirrolidonas (tales como 2-pirrolidona, N-metil-2-pirrolidona y N-(2-hidroxietil)pirrolidona; laurocapram; y disolventes miscelaneos tales como acetona, dimetil acetamida, dimetil formamida, tetrahidrofurfuril alcohol, cineol, N,N-dietil-3-metilbenzamida (DEET), isopropil miristato, (IPM) y dimetil isosorburo. Otros agente puente incluyen amfifilas tales como L-amino ácidos, y ácidos grasos. Los agentes puente adicionales se describen en *Remington*: The Science and Practice of Pharmacy, 19 edición (1995) en la página 1583. Típicamente, el agente penetrante se utiliza a un nivel de aproximadamente 10% p/v de la formulación donde el uso final es para la aplicación tópica, pero este puede variar, especialmente cuando el uso final de la composición es para

El tensoactivo utilizado en la presente invención puede ser un tensoactivo simple, o una mezcla de dos o más tensoactivos, contra, en parte dependiendo de si el uso final de la composición es tópica u oral. El tensoactivo no debe ser irritante, y no tóxico. Se prefieren los tensoactivos no iónicos, bajos en espuma, tales como, los tensoactivos de alcohol alcoxilado, con aquellos tales como el nonil fenol etoxilado (vendido bajo el nombre comercial Surfonic N-95), y el alcohol alcoxilatos (vendidos bajo el nombre comercial Sinperonic® NCA de Uniquema), y los tensoactivos de aceite de ricino polietoxilados (también conocidos como macrogoglicerol ricinolato, y vendidos bajo el nombre comercial Cremafore® EL de BASF) siendo especialmente adecuado. También útiles son los tensoactivos iónicos tales como laurel sulfato de sodio y el dioctil sulfosuccinato de sodio.

Típicamente, el tensoactivo se utiliza a un nivel de aproximadamente 2 a aproximadamente 8% de p/v de la composición, pero este puede variar un poco dependiendo del uso final de la composición. En el caso donde el uso final del concentrado es una formulación no pulverizada, o como un aditivo de alimento/agua dispersable en agua, puede ser deseable agregar un tensoactivo adicional para asegurar que la formulación diluida será una fase unitaria. Este asegura que el pulverizado no bloqueará la boquilla del pulverizador, y que el activo se dispersará igualmente a través del

tensoactivos particularmente útiles para uso con un disolvente orgánico diluyentes son tensoactivos no iónicos tales como aceite de ricino polietoxilado, vendido bajo el nombre comercial Cremofor® por BASF Corporation.

El disolvente portador para las composiciones de la presente invención puede ser un disolvente simple, o una mezcla de disolventes. Debido a la inestabilidad de la metaflumizona en la presencia de alcoholes primarios, los disolventes preferidos son disolventes que no contienen grupos hidroxilo, especialmente aquellos tales como γ-hexalactona (gama-hexalactona). Opcionalmente, otros de tales disolventes tales como N,N-dietil-m-toluamid, eucaliptol, dimetil isosorburo, diisopropil adipato y/o metoxipropil acetato (1-metoxi -2-propil acetato) se pueden utilizar en combinación con la γ-hexalactona para comprender el disolvente portador.

Para elaborar la composición concentrada de alta carga de la presente invención, se disuelve metaflumizona en el disolvente de solventes portadores, y el tensoactivo y el agente puente, si se desea se agregan a la mezcla. Esta composición se puede entonces utilizar como una "spot on" de alta carga, o diluir adicionalmente para usos adicionales.

Una composición especialmente preferida para la administración tópica de animales de sangre caliente

especialmente dimetil sulfóxido, aproximadamente 2 a aproximadamente 8%, y especialmente aproximadamente 5%, de un tensoactivo no iónico, bajo en espuma, y aproximadamente 50-60% de un disolvente portador especialmente γ-hexalactona.

Las composiciones concentradas de alta carga de esta invención pueden comprender además otros agentes conocidos en la técnica, tales como preservativos (por ejemplo metil parabeno y propil parabeno), colorantes, antioxidantes, y similares. En general, estos agentes estarían presentes en las composiciones en una cantidad hasta de aproximadamente 2% sobre una base peso, volumen.

Cuando se administran tópicamente, las composiciones de esta invención son altamente efectivas para evitar o tratar infección e infestación ectoparasítica durante periodos prolongados de tiempo en animales de sangre caliente tales como vacas, ovejas, caballos, camellos, venados, cerdos, cabras, perros, gatos, pájaros, y similares. Adicionalmente, la composición es altamente efectiva contra infecciones endoparasíticas.

Con el fin de facilitar el entendimiento adicional de la invención, se presentan los siguientes ejemplos principalmente con el propósito de ilustrar las modalidades específicas de estos. La invención no se debe considerar

Ejemplo 1

Preparación de Concentrado de Alta Carga de metaflumizona/moxidectina, adecuado para uso como un "Spot-on".

Se agrega 100 gramos en peso de dimetil sulfóxido (DMSO) A 400 gramos de γ-hexalactona. A este sistema de solvente se agregan 200 gramos de metaflumizona. Se disuelve la metaflumizona en el sistema disolvente. Pesar 10 gramos de moxidectina y agregarlos a la disolución normal que contiene metaflumizona. Permitirle a la metaflumizona disolverse. A la disolución resultante, agregar 60 gramos de tensoactivo de alcohol alcoxilato (vendido bajo el nombre comercial Sinperonic® NCA) y permitirle al tensoactivo disolverse. Finalmente, llevar la disolución a 1000 ml con γ-hexalactona.

Ejemplo 2

Preparación de "Pour-On" de metaflumizona/moxidectina de Concentrado de Alta Carga del Ejemplo 1.

A 25 ml del concentrado de de alta carga preparado en el Ejemplo 1 se agregan q.s. a 100 ml de γ-hexalactona. Esto suministra una formulación "pour on" que tiene metaflumizona y moxidectina suficientes y volumen para tratar 5 cabezas de

Ejemplo 3

Preparación de Concentrado de Alta Carga para uso como Concentrado para preparar Pulverizado de metaflumizona o Suplemento de Alimento/Agua

12.59 gramos de metaflumizona se agregan a acetato de metoxipropilo utilizando calentamiento moderado (aproximadamente 40°C). A esta disolución se agregan 109.92 gramos de aceite de ricino polietoxilado (vendido bajo el nombre comercial Cremofor® EL) con agitación, seguido por 1.0 gramos de moxidectina y luego llevados a volumen con metoxipropil acetato. La disolución resultante se almacena hasta que está lista para uso, luego de lo cual se puede diluir con agua para uso como un pulverizado (17 ml de concentrado diluido a 3500 ml con agua), o con agua para uso como un aditivo de alimento/agua (en aproximadamente la misma proporción) o adicionalmente, aplicado directamente "Pour-On" como una línea sobre el lomo.

Ejemplo 4

Preparación de varias formulaciones de Concentrado de Alta Carga de metaflumizona/moxidectina, adecuado para uso como un tratamiento "Spot-on".

Formulación:	1	2	3	4	5	6	7	8	9
Moxidectina									
Metaflumizona	0.1	0.5	2.5	0.1	0.5	2.5	0.1	0.5	2.5
Nonilfenol Etoxilado	30	30	30	20	20	20	5	5	5
Alcohol etoxilado ejemplo	5					5	5		
Sinperonic® NCA		5			5			5	
sulfosuccinato Dioctil sodio			5	5					5
Cineol	10								
DEET		10							
IPM			10						
Metoxipropil Acetato					10	10	10	10	10
DMSO	10	10	10	10					
γ-hexalactona	qs	qs	qs	qs	qs	qs	qs	qs	Qs

Las formulaciones precedentes se preparan utilizando esencialmente los mismos procedimientos que se listan en el Ejemplo 1.

Ejemplo 5

Preparación de varias formulaciones de Concentrado de Alta Carga de metaflumizona/macrólido, adecuado como uso "Spot-on".

Formulación:	10	10B	10C
Ivermectina			5
Abermectina		5	
Moxidectina	5		
Metaflumizona	30	30	20
Alcohol etoxilado, por ejemplo	5	5	5

Las formulaciones precedentes se preparan utilizando esencialmente los mismos procedimientos que se listaron en el Ejemplo 1.

Ejemplo 6

Preparación de varias formulaciones de Concentrado de Alta Carga de metaflumizona/moxidectina, adecuado para uso como un "Spot-on"

Formulación:	11	12	14	15	16	17	18	19	20
Moxidectin	0.1	0.5	0.1	1	10	0.25	5	0.1	0.1
Metaflumizona	30	30	20	20	20	5	5	5	5
Cineol									
DEET									
Isopropil miristato	5				1				
Aceite de ricino polietoxilado		5		1		5	5	5	5
Lauril sulfato de sodio			1						
Metoxipropil acetato			5	5	5				
DMSO	30	30							
Dimetil Isosorburo						30	30	30	30
γ-hexalactona	qs	qs	qs	qs	qs	qs	qs	qs	qs

Las formulaciones precedentes se preparan utilizando esencialmente los mismos procedimientos que se listaron en el Ejemplo 1.

REIVINDICACIONES

1. Una composición para la administración tópica que comprende en una base peso a volumen de desde aproximadamente 0.1 a aproximadamente 10% de un compuesto macrólido antiparasítico sustancialmente insoluble en agua, aproximadamente 5% a aproximadamente 40% de metaflumizona; aproximadamente 0% a aproximadamente 15% de un agente penetrante; aproximadamente 2 a aproximadamente 8% de un tensoactivo; y aproximadamente 50% a aproximadamente 80% de un disolvente portador.

2. La composición de acuerdo con la reivindicación 1 que comprende desde aproximadamente 20% a aproximadamente 30% de la metaflumizona.

3. La composición en la reivindicación 1 o la reivindicación 2 en donde el compuesto macrólido de moxidectina, abemectina, o ivermectina.

4. La composición de acuerdo a una cualquiera de las reivindicaciones 1 a 3 en donde el tensoactivo es un tensoactivo bajo en espuma no iónico.

5. La composición de acuerdo a una cualquiera de las

6. La composición de cuerdo a una cualquiera de las reivindicaciones 1 a 5 en donde el agente penetrante es dimetil sulfóxido.

7. La composición de acuerdo a una cualquiera de las reivindicaciones 1 a 6 en donde el disolvente portador comprende gama-hexalatona.

8. La composición de acuerdo a una cualquiera de las reivindicaciones 1 a 7 en donde el disolvente portador comprende dimetil isosorburo.

9. La composición de acuerdo a una cualquiera de las reivindicaciones 1 a 8 que adicionalmente contienen hasta aproximadamente 2% de uno o más preservativos, colorantes, antioxidantes, o estabilizadores.

10. Un método para prevenir o tratar infección e infestación endoparasítica y ectoparasítica en animales de sangre caliente cuyo método comprende administrar tópicamente al animal una cantidad efectiva de una composición de acuerdo con una cualquiera de las reivindicaciones 1 a 9.

11. El método de acuerdo con la reivindicación 10 en donde el animal es seleccionado del grupo que

12. El método de acuerdo con la reivindicación 10 u 11 en donde la composición comprende aproximadamente 20% a 30% de la metaflumizona; aproximadamente 10% de un agente puente, aproximadamente 2% a aproximadamente 8% de un tensoactivo bajo en espuma no iónico y aproximadamente 50-60% de un disolvente portador.

13. El método de acuerdo a una cualquiera de las reivindicaciones 10 a 12 en donde la composición comprende una gama-hexalatona como el disolvente portador.

14. El método de acuerdo con la reivindicación 13 en donde la composición se diluye adicionalmente para uso como una composición "pour-on".

15. El método de acuerdo a una cualquiera de las reivindicaciones 10 a 12 en donde la composición comprende dimetil isosorburo como el disolvente portador.

16. El método de acuerdo con la reivindicación 15 en donde la composición se diluye además para uso como un pulverizado o como un aditivo del alimento/agua.

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COMPOSICIONES CONCENTRADAS DE ALTA CARGA ÚTILES PARA EL CONTROL DE ECTO Y ENDO PARÁSITOS

Resumen

Se preparan composiciones concentradas de alta carga que comprenden metaflumizona, un compuesto macrólido antiparasítico sustancialmente insoluble en agua, tal como moxidectina, un agente puente opcional, un tensoactivo y un disolvente portador adecuado. Estas composiciones pueden ser tópicamente administradas a animales, y son útiles para evitar o tratar infestaciones ectoparasíticas en animales de de sangre caliente durante periodos prolongados de tiempo. Adicionalmente, ellas pueden ser adicionalmente diluidas para suministrar otros tipos de formulaciones utilizables tanto para administración tópica como oral.

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PATENT COOPERATION TR. .TY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

To:
WYETH
Attn. Renda, Barbara L.
Patent Law Department
Five Giralda Farms
Madison, New Jersey 07940
ETATS-UNIS D'AMERIQUE

Applicant's or agent's file reference AM102089	Date of mailing *(day/month/year)* 26/09/2006
International application No. PCT/US2006/019513	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
Applicant WYETH	International filing date *(day/month/year)* 19/05/2006

DOCKETED
DUE DATE 11/26/06 ART. 19 DUE
BY: 10/2/06

1. [x] The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Fascimile No.: (41-22) 338.82.70

   For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims,description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

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PATENT COOPERATION TR[illegible] TY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference AM102089	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US2006/019513	International filing date *(day/month/year)* 19/05/2006	(Earliest) Priority Date *(day/month/year)* 24/05/2005
Applicant WYETH		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. ___

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/019513

A. CLASSIFICATION OF SUBJECT MATTER
INV. A01P5/00 A01P7/02 A01P7/04 A01N43/90
ADD. A01N47/34

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A01N

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 413 201 A (WYETH) 28 April 2004 (2004-04-28) paragraphs [0002] - [0006], [0022], [0023], [0027], [0028], [2935] examples 1-4 claims 15,21,22,28,32,35	1-16
Y	EP 1 334 661 A (NIHON NOHYAKU CO., LTD) 13 August 2003 (2003-08-13) paragraph [0009]; example 44 claims 1,2,6 paragraphs [0001], [0006], [0011], [0014], [0016], [0017]	1-16

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/019513

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	WO 2006/042099 A (WYETH; SABNIS, SHOBHAN, SHASHI; ZUPAN, JACOB, A; ALBRIGHT, ROBERT, BRU) 20 April 2006 (2006-04-20) claims 1,4,5 page 5, lines 1,2 examples 1-3	1-16
Y	WO 2004/089239 A (MERIAL LTD; SOLL, MARK, D; KUMAR, KRISHAN; WARANIS, ROBERT, P; SHUB, N) 21 October 2004 (2004-10-21) page 1, paragraph 2 page 3, paragraph 2 page 6, last paragraph - page 7, paragraph 2 page 9, paragraph 1 page 9, last paragraph - page 10, paragraph 1 page 19, paragraph 4 claims 1-26	1-16

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/019513

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 10-16 are directed to a method of treatment of the animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest [ ] The additional search fees were accompanied by

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2006/019513

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
EP 1413201	A	28-04-2004	AU	2003255177 A1	06-05-2004
			BR	0304618 A	31-08-2004
			CA	2444692 A1	21-04-2004
			HR	20030856 A2	28-02-2005
			JP	2004143172 A	20-05-2004
			MX	PA03009595 A	15-10-2004
			PL	362962 A1	04-05-2004
			ZA	200308147 A	20-04-2005
EP 1334661	A	13-08-2003	AU	9426901 A	29-04-2002
			BR	0114783 A	23-12-2003
			CA	2426275 A1	27-04-2003
			CN	1469708 A	21-01-2004
			WO	0232226 A1	25-04-2002
			JP	2002128614 A	09-05-2002
			MX	PA03003294 A	04-05-2004
			NZ	525191 A	29-10-2004
			US	2003199579 A1	23-10-2003
			ZA	200302735 A	08-04-2004
WO 2006042099	A	20-04-2006	NONE		
WO 2004089239	A	21-10-2004	AU	2004228041 A1	21-10-2004
			BR	PI0409185 A	11-04-2006
			CA	2521268 A1	21-10-2004
			EP	1610613 A2	04-01-2006
			MX	PA05010659 A	12-12-2005

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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2006/019513	19.05.2006	24.05.2005

International Patent Classification (IPC) or both national classification and IPC
INV. A01P5/00 A01P7/02 A01P7/04 A01N43/90
ADD. A01N47/34

Applicant
WYETH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2006/019513

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2006/019513

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 10-16

because:

☒ the said international application, or the said claims Nos. 10-16 relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☐ no international search report has been established for the whole application or for said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See Supplemental Box for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2006/019513

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/US2006/019513

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

see item V.3 below

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The documents to which this communication refers are numbered in their order of appearance in the international search report.

1. **Novelty (Article 33(2) PCT)**
   None of the cited documents disclose a composition suitable for topical administration which comprises the specific ingredient combination as given in present claim 1. The same applies to method claim 10.

2. **Inventive step (Article 33(3) PCT)**
   Document **D1** (see cited parts in the international search report), which is considered as the closest prior art document, describes compositions, e.g. spot-on or pour-on formulations, suitable for the control of ectoparasites in homeothermic animals. Said compositions comprise a compound of formula (I) to which metaflumizone belongs and a macrocyclic lactone, such as moxidectin, abamectin or ivermectin. The concentration used for the first compound is preferably around 20% w/v. The presence of N,N-diethyl-3-methylbenzamide (DEET) or isopropyl miristate (IPM), both of which being penetrating/bridging agents according to present claims 1 and 12, is also envisaged and given as a preferred embodiment in that document. This also applies to the carrier solvent and surfactant.

   The difference between the present application and said document lies in the specific combination of said ingredients in specific amounts.

The problem to be solved by the present invention is to provide an alternative concentrate composition based on metaflumizone and a macrolide compound.

The alternative proposed by the application is obvious because it merely consists in the choice of specific concentration values for the compounds which are proposed in the compositions of said prior art document.

In addition, it does not contain any further distinguishing feature which would lead to a surprising and/or non-obvious technical effect.

Therefore, no inventive step can be acknowledged for the present subject-matter claimed.

3. **Industrial applicability (Article 33(4) PCT)**

For the assessment of the present claims 10-16 on the question of whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The European Patent Office, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment (including prophilaxy), but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The subject-matter of claims 1-9 is considered to be susceptible of industrial application.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 2006/042099 (**D3**)	20.04.2006	07.10.2005	08.10.2004

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/US2006/019513

Re Item VII
Certain defects in the application (form or content)

4.1 References to other documents may relate directly to the disclosure of the invention. If the matter the documents refer to is essential to satisfy the requirements of Article 5 PCT, this matter should be incorporated *expressis verbis* in the description because the patent specification should be self-contained regarding the essential features of the invention, i.e. capable of being understood without reference to any document. As a consequence, the sentence with the expression "*incorporated by reference*" from *page 4, lines 30-31* should not be used (PCT Guidelines 4.26).

4.2 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents **D1**, **D2** and **D4** is not mentioned in the description, nor are these documents identified therein.

4.3 Contrarily to the statement given on *page 4, last paragraph*, the patent application US 2004/0122075 does not relate to metaflumizone.

Re Item VIII
Certain observations on the international application (clarity)

5.1 The use of the term "*about*" in claims 1, 2, 9 and 12 and in the description renders the subject-matter unclear within the meaning of Article 6 PCT (see also PCT Guidelines 5.38).

5.2 In claims 4 and 12, the relative term "*low*" in the expression "*non-ionic low foam surfactant*" does not have a generally accepted meaning. Such a term is ambiguous and therefore not suitable for clearly defining the subject-matter for which protection is sought (see also PCT Guidelines 5.34).

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PATENT COOPERATION TREATY PCT/US2006/019513

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

RENDA, Barbara, L.
Wyeth
Patent Law Department
Five Giralda Farms
Madison, New Jersey 07940
ETATS-UNIS D'AMERIQUE

Date of mailing *(day/month/year)* 31 August 2006 (31.08.2006)	
Applicant's or agent's file reference AM102089	**IMPORTANT NOTIFICATION**
International application No. PCT/US2006/019513	International filing date *(day/month/year)* 19 May 2006 (19.05.2006)
International publication date *(day/month/year)* **Not yet published**	Priority date *(day/month/year)* 24 May 2005 (24.05.2005)
Applicant WYETH et al	

1. By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR", in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. *(If applicable)* The **letters "NR"** appearing in the right-hand column denote **a priority document which, on the date of mailing of this Form, had not yet been received by the International Bureau** under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

3. *(If applicable)***An asterisk (*)** appearing next to a date of receipt, in the right-hand column, denotes **a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b)** (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as the priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
24 May 2005 (24.05.2005)	60/683,950	US	17 July 2006 (17.07.2006)

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
EXTRACTO PARA PUBLICACIÓN
SOLICITUD DE PATENTE DE INVENCIÓN PCT

(21) N° de solicitud:	(51) Int Cl: **A01P 5/00, A01N 43/90, A01N 47/34, A01P 7/02, A01P 7/04**
22) Fecha de solicitud:	(71)Solicitante(s) **WYETH**
(30) Prioridad (31) ***No.*** **60/683,950** 32) ***Fecha*** **24/05/05** (33) ***País*** **US**	(72) Inventor(es) **ALBRIGHT, Robert B.**
	(74) Apoderado: **ALVARO CORREA ORDOÑEZ**
(85) Fecha límite inicio fase nacional: ***24/12/07***	(87) Publicación internacional
(86) Datos relativos a la presentación de la solicitud PCT	Fecha: ***30/11/06***
Fecha de presentación de la solicitud: ***19/05/06***	N° publicación: **WO/2006/127487**
No. de solicitud **PCT/US2006/019513**	

(54) Título: **COMPOSICIONES CONCENTRADAS DE ALTA CARGA ÚTILES PARA EL CONTROL DE ECTO Y ENDO PARÁSITOS**

Reivindicación(es):

1. Una composición para la administración tópica que comprende en una base peso a volumen de desde aproximadamente 0.1 a aproximadamente 10% de un compuesto macrólido antiparasítico sustancialmente insoluble en agua, aproximadamente 5% a aproximadamente 40% de metaflumizona; aproximadamente 0% a aproximadamente 15% de un agente penetrante; aproximadamente 2 a aproximadamente 8% de un tensoactivo; y aproximadamente 50% a aproximadamente 80% de un disolvente portador.

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
TARJETA ARCHIVO PROPIETARIOS

PATENTE DE INVENCION ___ PCT X MODELO DE UTILIDAD ___ DISEÑO INDUSTRIAL ___

(21) N° de solicitud: (22) Fecha de solicitud:

(51) Clasificación Internacional : A01P 5/00, A01N 43/90, A01N 47/34, A01P 7/02, A01P 7/04

(71)Solicitante(s) **WYETH**

(72) Inventor(es) ALBRIGHT, Robert B.

(74) Apoderado: ALVARO CORREA ORDOÑEZ

(30) Prioridad	(31) ***No. Prioridad***	32) ***Fecha***	(33) ***País***
	60/683,950	**24/05/05**	**US**

(85) Fecha inicio fase nacional:**24/12/07**

(86) Datos relativos a la presentación de la solicitud PCT
Fecha de presentación de la solicitud: **19/05/06**
No. de solicitud **PCT/US2006/019513**

(87) Publicación internacional
Fecha: ***30/11/06***
N° publicación: **WO/2006/127487**

(54) Titulo:
COMPOSICIONES CONCENTRADAS DE ALTA CARGA ÚTILES PARA EL CONTROL DE ECTO Y ENDO PARÁSITOS

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
TARJETA ARCHIVO TEMATICO

SUPERINTENDENCIA PATENTE DE INVENCION ____ PCT _X_ MODELO DE UTILIDAD ____ DISEÑO INDUSTRIAL ___

(21) N° de solicitud: (22) Fecha de solicitud:

(51) Clasificación Internacional : A01P 5/00, A01N 43/90, A01N 47/34, A01P 7/02, A01P 7/04

(71)Solicitante(s) **WYETH**

(72) Inventor(es) ALBRIGHT, Robert B.

(74) Apoderado: ALVARO CORREA ORDOÑEZ

(30) Prioridad	(31) *No. Prioridad*	32) *Fecha*	(33) *País*
	60/683,950	**24/05/05**	**US**

(85) Fecha límite inicio fase nacional: **24/12/07**

(86) Datos relativos a la presentación de la solic. PCT
Fecha de presentación de la solicitud: **19/05/06**
No. de solicitud **PCT/US2006/019513**

(87) Publicación internacional:
Fecha: ***30/11/06***
No. Publicación : **WO/2006/127487**

(54) Titulo:
COMPOSICIONES CONCENTRADAS DE ALTA CARGA ÚTILES PARA EL CONTROL DE ECTO Y ENDO PARÁSITOS

(57) Resumen: Se preparan composiciones concentradas de alta carga que comprenden metaflumizona, un compuesto macrólido antiparasitico sustancialmente insoluble en agua, tal como moxidectina, un agente puente opcional, un tensoactivo y un disolvente portador adecuado. Estas composiciones pueden ser tópicamente administradas a animales, y son útiles para evitar o tratar infestaciones ectoparasiticas en animales de de sangre caliente durante periodos prolongados de tiempo. Adicionalmente, ellas pueden ser adicionalmente diluidas para suministrar otros tipos de formulaciones utilizables tanto para administración tópica como oral.

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 07-123146- -00000-0000

Fecha: 2007-11-21 16:07:00 Dep: 2020 NUECREACION
Tra: 11 PATENTEIYII Eve: 378 PASENACIONAL
Act: 411 PRESENTACION Folios: 69

Industria y Comercio
SUPERINTENDENCIA

REQUISITOS MINIMOS PARA ADMISION A TRAMITE PCT

PATENTE DE INVENCION [X] MODELO DE UTILIDAD [ ]

- Indicación de que se solicita la concesión de una patente [X]
- Datos de identificación del solicitante o de la persona que presenta la solicitud [X]
- Descripción de la invención [X]
- Dibujos de ser estos pertinentes [ ]
- Comprobante de pago de las tasas establecidas [X]

COMPLETA [ ] INCOMPLETA [ ]

DISEÑO INDUSTRIAL [ ]

- Indicación de que se solicita el registro de Diseño Industrial [ ]
- Datos de identificación del solicitante o de la persona que presenta la solicitud [ ]
- Representación gráfica y fotográfica del Diseño Industrial o muestra del material que incorpora el diseño [ ]
- Comprobante de pago de las tasas establecidas [ ]

COMPLETA [ ] INCOMPLETA [ ]

ESQUEMA DE TRAZADO [ ]

- Indicación de que se solicita el registro de un Esquema de Trazado [ ]
- Datos de identificación del solicitante o de la persona que presenta la solicitud [ ]
- Representación gráfica del esquema trazado [ ]
- Comprobante de pago de las tasas establecidas [ ]

COMPLETA [ ] INCOMPLETA [ ]

REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

71
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Bogotá,
2020

Doctor(a)
CORREA ORDOÑEZ ALVARO

REFERENCIA	Radicación No.	07 123146
	Solicitud internacional	PCT/US2006/019513
	Fecha inicio fase nacional	24/12/2007
	Trámite	11
	Evento	378
	Actuación	430
	Oficio No.	16745

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

1. La solicitud no contiene el poder debidamente otorgado, con el lleno de los requisitos exigidos por los artículos 63 y subsiguientes del Código de Procedimiento Civil. Adicionalmente, deberá presentar el documento que acredita la existencia y representación legal de la sociedad solicitante, cuando ésta fuere persona jurídica.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Unica No.10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista de fecha 28 DIC. 2007
adpall