

Marcas – Patentes
Modelos – Diseños
Nombres Comerciales – Enseñas
Propiedad Intelectual
Registros en el Exterior
Registros Sanitarios INVIMA – ICA
Acciones Judiciales – Administrativas
Derecho Comercial – Industrial
Asesoría – Contratos – Otros
Corresponsalia a Nivel Mundial

MDE



Mario Delgado Echeverry e Hijos Ltda.

Abogados Consultores – Marcas y Patentes

Bogotá D.C. – Colombia
Avda. Kra. 24 Park Way No. 37 – 31 Of.
202
Tels. (571) 2444096 – 3690624
Fax (571) 2442496 A.A. No. 6207
E-mail: mde@mdelaw.com
mdelawof@cablenet.co
mdeabogados@cablenet.co

Miembros ACPI – ASIP – AIPPI

**SEÑOR
SUPERINTEDENTE DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
E. S. D.**

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 14-158889- -00002-0000

Fecha: 2014-09-17 17:02:01 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 379 FASENACIONALII
Act. 444 RESPUESTAREQUE Folios: 14

Ref.: Expediente No.: 14 158.889

Patente de Invención: FORMULACIONES DE ANTIBIÓTICOS.

Atentamente se dirige a usted **JAIME EDUARDO DELGADO VILLEGAS**, Abogado, mayor y vecino de Bogotá D.C., e identificado como aparece al pie de mi firma, me dirijo a su Digno Despacho para manifestarle lo siguiente:

1. En mi condición de apoderado de la sociedad Bayer New Zealand Limited domiciliada Auckland, New Zealand presenté ante su Digno Despacho la solicitud de registro de la Patente de Invención mencionada en la referencia.
2. Debido a lo anterior, y con el fin de dar cumplimiento al requerimiento hecho por su Despacho mediante Oficio No. 10047 del 19 de agosto de 2014, me permito aclarar que:
 - Las reivindicaciones modificadas SI fueron presentadas en fase Internacional ante el PCT el día 3 de mayo de 2013, tal y como consta en el Informe Internacional de Patentabilidad Capítulo II del 23 de junio de 2014, el cual se adjunta.

Con la documentación adjunta, doy cumplimiento dentro de término hábil a lo requerido por su Digno Despacho, por lo que comedidamente solicito se continúe con el trámite normal de registro de la Patente de Invención que se enuncia en la referencia.

Atentamente,

JAIME EDUARDO DELGADO VILLEGAS

C.C. No. 19'270.955 de Bogotá

T.P. No. 43.308 del Consejo Superior de la Judicatura.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY		International Application No. PCT/NZ2012/000245
Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement	
1. Statement		
Novelty (N)	Claims 1-22	YES
	Claims NONE	NO
Inventive step (IS)	Claims 1-22	YES
	Claims NONE	NO
Industrial applicability (IA)	Claims 1-22	YES
	Claims NONE	NO
2. CITATIONS AND EXPLANATIONS:		
<u>CITATIONS</u>		
D1: CN 101401787 A (XILONG XIAO et al.,) 08 April 2009		
D2: CN 1517090 A (WANG YUWAN) 04 August 2004		
D3: EP 0391369 A2 (YISSUM RESEARCH DEVELOPMENT COMPANY OF THE HEBREW UNIVERSITY OF JERUSALEM) 10 October 1990		
D4: WO 2009/032843 A2 (AUSPEX PHARMACEUTICALS, INC.) 12 March 2009		
<u>NOVELTY (N)</u>		
D1 discloses a Ceftiofur suspension formulation used as an injection for preventing bacterial diseases in livestock (abstract; description). The Ceftiofur formulation is described to include an oil (such as soybean oil) and glycerol triacetate or diacetin (abstract; Claim 4). The concentration of Ceftiofur in the formulation is described to be between 5-30% w/v (abstract; Claim 9). Example 10 describes a Ceftiofur injection containing Ceftiofur suspended in hydrogenated castor oil and the antibiotic injection made up in soybean oil and glycerol triacetate. It is noted that hydrogenated castor oil in which Ceftiofur is suspended is also known to be a non-ionic surfactant. Ceftiofur is described to be administered once to an animal at a dose of 5-7 mg/kg and an effective blood concentration of the administered antibiotic can be maintained for 5.5 days (description). The animal can be reinjected in 5-7 days if necessary. D2 discloses a cephalosporin suspension formulation used for treating animal bacterial infections including bovine and swine respiratory diseases (description). Veterinary injections containing 5-50% (w/v) cephalosporin, glycerol triacetate (triacetin), triglyceride and surfactant such as sorbitan are described by D2 (description). Example 17 describes a formulation that includes Cefoperozone, hydrogenated castor oil and triacetin. Example 30 describes a Cefotaxime formulation — a third generation cephalosporin antibiotic. Furthermore, D2 describes triacetin to be a good biocompatible solvent that is widely used for pharmaceutical preparations and provides a suspension formulation with good stability (description). None of the identified prior art citations discloses a cephalosporin suspension formulation that comprises an oil and 0.05-5% w/v glycerol acetate. There is no explicit disclosure of a cephalosporin suspension formulation comprising cotton seed oil and glycerol acetate in the identified prior art citations. The identified prior art citations also do not disclose a cephalosporin suspension formulation with a dispersing agent as claimed in the claims. A cephalosporin suspension formulation contained in a container made substantially of PET (polyethylene terephthalate) is not disclosed by the identified prior art citations. A method of preparing a cephalosporin suspension formulation as defined by the claims is also not disclosed by the identified prior art citations. Therefore, the invention claimed in each of amended Claims 1-22 meets the requirements of Article 33(2) of the PCT for novelty.		
<u>INVENTIVE STEP (IS)</u>		
None of the identified prior art citations obviously suggest to a person skilled in the art a cephalosporin suspension formulation that comprises an oil and 0.05-5% w/v glycerol acetate or a method of preparing a cephalosporin suspension formulation as claimed in amended Claims 20-22. Therefore, the invention claimed in each of amended Claims 1-22 meets the requirements of Article 33(3) of the PCT for inventive step.		
Form PCT/IPEA/409 (Box V) (July 2011)		

International Application No.

PCT/NZ2012/000245

INDUSTRIAL APPLICABILITY (IA)

The invention defined in each of amended Claims 1-22 is considered to meet the requirements of industrial applicability under Article 33(4) of the PCT because it can be made by, or used in, industry.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY	International application No. PCT/NZ2012/000245
Box No. VII Certain defects in the international application	
The following defects in the form or contents of the international application have been noted: Amended Claims 23 and 24 do not comply with Rule 6.2(a) because they rely on references to the description and examples.	

UNIT 3 | 422 INNES ROAD, RAINBOW, CHRISTCHURCH 8052
PO BOX 2201, CHRISTCHURCH 8140, NEW ZEALAND
PHONE: +64 3 941 2460 | FAX: +64 3 941 2461 | WWW.JAMA.CO.NZ



FACSIMILE TRANSMISSION

From: 0064 7 957 5660
To: 0061 2 6283 7999

Total Pages: 16

This facsimile transmission and any accompanying documentation may contain legally privileged and confidential information intended for the addressee only. If you are not the addressee your use of this information is strictly prohibited. If you have received this transmission in error, please notify us immediately by collect telephone call on +64 7 957 5660. If you did not receive all the pages please call us as soon as possible.

3 May 2013
HAMILTON OFFICE

IP Australia
Discovery House
47 Bowes Street
Woden
ACT 2606
Australia

LODGEMENT UNIT	
A	\$ 796 Payable
B	\$ 796 Received
C	\$ 796 Underpaid
D	\$ Overpaid
FANG BATCH No.	
601960	

Confirmation by Courier

IP Australia
- 3 MAY 2013
RECEIVED FEP FAX

Bayer New Zealand Limited
PCT Application No. PCT/NZ2012/000245
"Antibiotic Formulations"
Our ref: 132887PCT/76 AMM

Please find enclosed a Demand for further examination of this PCT application.

With the Demand, please also find enclosed replacement pages 25 - 28 in marked up and clean format. We request that further examination be undertaken using the amended claims as submitted with this response.

Summary of claim amendments

In brief, the claim set has been amended such that the limitations of claim 10 have been incorporated into independent claim 1. Claim 10 specifies that the glycerol acetate solvent is included in the formulation in the range of 0.05-5% w/v. In the Written Opinion, claim 10 was considered novel and inventive over the cited prior art documents. Therefore, we trust that the current amendment to claim 1 will be sufficient to render all claims both novel and inventive.

Accordingly, claim 10 has been deleted from the claim set and the remaining claims have been renumbered.

In addition, the Applicant has also discussed the two prior art documents which were considered by the Examiner to be particularly relevant to previous claim 1.

Discussion of D1 and D2

The present invention is easily distinguished from the cited documents.

D1 uses gelled triacetin as a long-acting depot formulation, whilst the present invention uses an oil as the carrier for the suspended cephalosporin with, importantly as now claimed, a small quantity of triacetin as the re-suspendability enhancer/anti-caking agent. In D1, triacetin is used

JAMES & WELLS
INTELLECTUAL PROPERTY

as a solvent to dissolve polyvinylpyrrolidone, which forms a 'transparent gel polymer compound'. Other examples of 'organogels' using triacetin are described in US 6331311. The purpose of the gelling is to increase viscosity, which can help with storage stability of the suspension, but also provide a long-acting composition. According to the disclosure, the gel formulation is directed at forming a depot of drug in the body that lasts for 5 days.

Considering the different direction of D1 compared to the present invention, it does not disclose or teach towards the features of previous claim 10, which are considered novel and inventive in the Written Opinion.

D2 uses triacetin as a carrier, with thickeners to adjust viscosity. D2 discloses various suspended antibiotic formulations using triacetin as the main carrier, which seems to have been chosen not only for its biocompatibility but also as a carrier with a density similar to the solid suspended drug particles.

D2 mentions that, if the densities do not match, then the suspended particles will either sink to the bottom or float on top. None of the particular examples read on to the previous claim 1 since none include an oil. Hydrogenated castor oil is included in the compositions, but it is a solid wax, rather than an oil. One of the inventors suggests that the release characteristics of triacetin as the main carrier would be quite different to an oil based suspension. The release from triacetin would likely be much more rapid since it is more readily dispersed into the body (its solubility is about 7% in water). The release could be modified with thickeners, which may be one of the reasons for adding hydrogenated castor oil in the examples of D2.

Similarly, D2 does not disclose or teach towards the features of previous claim 10, which are considered novel and inventive in the Written Opinion.

We also enclose a credit card payment form for AU\$796.00 as payment for the Demand.

We look forward to issuance of the second Written Opinion.

Please confirm receipt of this Demand.

If there are any material errors in the preparation and filing of this Demand please email/fax/telephone us at your earliest convenience.

Yours sincerely

James & Wells Intellectual Property



Peter Brown
Associate
peterb@laws.co.nz

Enclosure: Demand Request
Amended pages 25-28 (marked up and replacement copies)
Credit card payment form

James & Wells Ref: 132887PCT/76 AMM

WHAT WE CLAIM IS:

1. A suspension formulation for administration to an animal, the suspension formulation including:
 - a) at least one cephalosporin antibiotic or a pharmaceutically similar salt thereof;
 - b) an oil; and
 - c) a glycerol acetate solvent,characterised in that the glycerol acetate solvent is included in the formulation in the range of 0.05 – 5% w/v.
2. The suspension formulation as claimed in claim 1 wherein the cephalosporin antibiotic is selected from the group consisting of third generation cephalosporin antibiotics.
3. The suspension formulation as claimed in claim 2 where the cephalosporin antibiotic is ceftiofur.
4. The suspension formulation as claimed in any one of the above claims wherein the concentration of the cephalosporin antibiotic is between 1 – 30% w/v.
5. The suspension formulation as claimed in any one of the above claims wherein the concentration of the cephalosporin antibiotic is between 5 – 6 % w/v.
6. The suspension formulation as claimed in any one of the above claims wherein the oil is selected from the group consisting of canola oil, corn oil, cottonseed oil, olive oil, peanut oil, sesame oil, soybean oil, safflower oil,

PCT/NZ2012/000245

Received 03/05/2013

James & Wells Ref: 132887PCT/76 AMM

coconut oil, sunflower oil, palm oil, monoglyceride, diglyceride and triglyceride medium chain succinic acid triglyceride.

- 7. The suspension formulation as claimed in claim 6 wherein the oil is cottonseed oil.**
- 8. The suspension formulation as claimed in any of the above claims wherein the glycerol acetate solvent is selected from the group consisting of acetin, diacetin and triacetin.**
- 9. The suspension formulation as claimed in claim 8 wherein the glycerol acetate solvent is triacetin.**
- 10. The suspension formulation as claimed in any of the above claims wherein the glycerol acetate solvent is included in the formulation in the range of 0.5% w/v.**
- 11. The suspension formulation as claimed in any of the above claims wherein the formulation includes a surfactant.**
- 12. The suspension formulation as claimed in claim 11, wherein the surfactant is sorbitan monooleate.**
- 13. The suspension formulation as claimed in any of the above claims, wherein the formulation includes a dispersing agent.**
- 14. The suspension formulation as claimed in claim 13, wherein the dispersing agent is hydrogenated phosphatidylcholine.**
- 15. A container including an amount of a suspension formulation as claimed in any one of the above claims characterised in that the container is made substantially of PET (polyethylene terephthalate).**

James & Wells Ref: 132887PCT/76 AMM

16. A method of administering a suspension formulation as claimed in any one of the above claims, to an animal for the treatment or prevention of a bacterial infection or resulting condition.
17. The method of claim 16 wherein the suspension formulation is administered at a rate of between 0.5 to 5 mg/kg animal/day.
18. The use in the manufacture of a medicament including a suspension formulation as claimed in any of claims 1 to 14 for the treatment or prevention of a bacterial infection or condition in an animal.
19. The use as claimed in the claim 18 wherein the bacterial infection or condition to be treated or prevented is bovine bacterial respiratory disease, swine bacterial respiratory disease, foot rot or metritis.
20. A method of preparing a suspension formulation as claimed in any one of claims 1 to 14 wherein the method includes the steps of
 - a. adding an amount of an oil to a first container;
 - b. adding an amount of an oil to a second container, and heating to a temperature between room temperature and 100°C;
 - c. adding an amount of a dispersing agent to the second container;
 - d. adding an amount of a surfactant to a third container;
 - e. adding the glycerol acetate solvent to the third container;
 - f. mixing the contents of the first, second and third containers together;
 - g. adding the cephalosporin antibiotic to the mixed contents; and
 - h. optionally, making the mixture up to a desired volume with an oil.

PCT/NZ2012/000245

Received 03/05/2013

James & Wells Ref: 132887PCT/76 AMM

21. A method as claimed in claim 20 wherein the heating step in (b) comprises heating the oil to between 15-90°C.
22. A method as claimed in either claim 20 or 21 wherein the mixture resulting from step b) is incubated for between 5 minutes and 60 minutes.
23. A suspension formulation as herein described and with reference to Example 1 in the Best Modes section.
24. A method of manufacture of the suspension formulation as herein described and with reference to Example 2 in the Best Modes section.

James & Wells Ref: 132887PCT/76 AMM

WHAT WE CLAIM IS:

1. A suspension formulation for administration to an animal, the suspension formulation including:
 - a) at least one cephalosporin antibiotic or a pharmaceutically similar salt thereof;
 - b) an oil; and
 - c) a glycerol acetate solvent,

characterised in that the glycerol acetate solvent is included in the formulation in the range of 0.05 – 5% w/v.
2. The suspension formulation as claimed in claim 1 wherein the cephalosporin antibiotic is selected from the group consisting of third generation cephalosporin antibiotics.
3. The suspension formulation as claimed in claim 2 where the cephalosporin antibiotic is ceftiofur.
4. The suspension formulation as claimed in any one of the above claims wherein the concentration of the cephalosporin antibiotic is between 1 – 30% w/v.
5. The suspension formulation as claimed in any one of the above claims wherein the concentration of the cephalosporin antibiotic is between 5 – 6 % w/v.
6. The suspension formulation as claimed in any one of the above claims wherein the oil is selected from the group consisting of canola oil, corn oil, cottonseed oil, olive oil, peanut oil, sesame oil, soybean oil, safflower oil.

James & Wells Ref: 132867PCT/76 AMM

coconut oil, sunflower oil, palm oil, monoglyceride, diglyceride and triglyceride medium chain succinic acid triglyceride.

7. The suspension formulation as claimed in claim 6 wherein the oil is cottonseed oil.
8. The suspension formulation as claimed in any of the above claims wherein the glycerol acetate solvent is selected from the group consisting of acetin, diacetin and triacetin.
9. The suspension formulation as claimed in claim 8 wherein the glycerol acetate solvent is triacetin.
- ~~10.~~ The suspension formulation as claimed in any of the above claims wherein the glycerol acetate solvent is included in the formulation in the range of 0.05 — 5% w/v.
- ~~11.~~ 10. The suspension formulation as claimed in any of the above claims wherein the glycerol acetate solvent is included in the formulation in the range of 0.5% w/v.
- ~~12.~~ 11. The suspension formulation as claimed in any of the above claims wherein the formulation includes a surfactant.
- ~~13.~~ 12. The suspension formulation as claimed in claim ~~11~~12, wherein the surfactant is sorbitan monooleate.
- ~~14.~~ 13. The suspension formulation as claimed in any of the above claims, wherein the formulation includes a dispersing agent.
- ~~15.~~ 14. The suspension formulation as claimed in claim ~~13~~14, wherein the dispersing agent is hydrogenated phosphatidylcholine.

James & Wells Ref: 132887PCT/78 AMM

46.15. A container including an amount of a suspension formulation as claimed in any one of the above claims characterised in that the container is made substantially of PET (polyethylene terephthalate).

47.16. A method of administering a suspension formulation as claimed in any one of the above claims, to an animal for the treatment or prevention of a bacterial infection or resulting condition.

48.17. The method of claim ~~16~~47 wherein the suspension formulation is administered at a rate of between 0.5 to 5 mg/kg animal/day.

49.18. The use in the manufacture of a medicament including a suspension formulation as claimed in any of claims 1 to ~~14~~15 for the treatment or prevention of a bacterial infection or condition in an animal.

20.19. The use as claimed in the claim ~~18~~19 wherein the bacterial infection or condition to be treated or prevented is bovine bacterial respiratory disease, swine bacterial respiratory disease, foot rot or metritis.

24.20. A method of preparing a suspension formulation as claimed in any one of claims 1 to ~~14~~15 wherein the method includes the steps of

- a. adding an amount of an oil to a first container;
- b. adding an amount of an oil to a second container, and heating to a temperature between room temperature and 100°C;
- c. adding an amount of a dispersing agent to the second container;
- d. adding an amount of a surfactant to a third container;
- e. adding the glycerol acetate solvent to the third container;
- f. mixing the contents of the first, second and third containers together;

James & Wells Ref: 132887PCT/78 AMM

g. adding the cephalosporin antibiotic to the mixed contents; and

h. optionally, making the mixture up to a desired volume with an oil.

~~22-21.~~ A method as claimed in claim ~~2024~~ wherein the heating step in (b) comprises heating the oil to between 15-90°C.

~~23-22.~~ A method as claimed in either claim ~~2024~~ or ~~2122~~ wherein the mixture resulting from step b) is incubated for between 5 minutes and 60 minutes.

~~24-23.~~ A suspension formulation as herein described and with reference to Example 1 in the Best Modes section.

~~25-24.~~ A method of manufacture of the suspension formulation as herein described and with reference to Example 2 in the Best Modes section.