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Señores

SUPERINTENDENCIA DE INDUSTRIA Y
DIRECCIÓN DE NUEVAS CREACIONES

E. _____ S. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 10-001885- -00002-0000

Fecha: 2010-05-04 18:06:50 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTE/II Evt: 379 FASENACIONALII
Act. 444 RESPUESTAREQUE Folios: 40

Ref.: Expediente N° 10-001.885

Solicitud de Patente de Invención Titulada: "N-{4-(2,2-DIMETIL-PROPIOMIL)-(5R)-5-[(2-ETILAMINO-ETANO SULFONIL AMINO)-METIL]-5-FENIL-4,5-DIHIDRO-[1,3,4]TIADIAZOL-2-IL}-2,2-DIMETIL PROPIONAMIDA"

Solicitante: ELI-LILLY AND COMPANY AND KIOWA HAKKO KIRIN CO., LTD.

Nuestra Ref.: P2009/000199

RESPUESTA AL OFICIO No. 3009 NOTIFICADO
POR FIJACION EN LISTA No. 81, DE FECHA 05 DE MARZO DE 2010
(EXAMEN DE FORMA)

CARLOS P. OLAPTE, mayor de edad y vecino de Bogotá, identificado tal como aparece al pie de mi firma, en mi carácter de apoderado de la sociedad en referencia, me permito dar respuesta al auto proferido por ese Despacho, dentro del término legal previsto en el artículo 39 de la Decisión 486, en los siguientes términos:

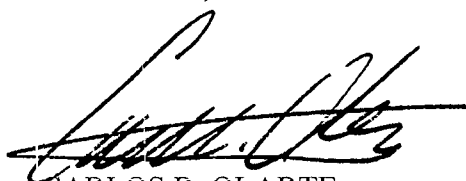
1. En respuesta a la primera observación del Examinador, me permito adjuntar la traducción del reporte del examen preliminar internacional.
2. En respuesta a la segunda observación del Examinador me permito adjuntar copia autentica del poder a mi conferido por mi representada KIOWA HAKKO KIRIN CO., LTD., según lo previsto en los Artículos 63 y subsiguientes del Código de Procedimiento Civil.
3. En respuesta a la tercera observación del Examinador, me permito presentar un nuevo título: "N-{4-(2,2-DIMETIL-PROPIOMIL)-(5R)-5-[(2-ETILAMINO-ETANO

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SULFONIL AMINO)-METIL]-5-FENIL-4,5-DIHIDRO-[1,3,4]TIADIAZOL-2-IL}-
2,2-DIMETIL PROPIONAMIDA⁷", el cual permite identificar claramente el objeto de la
solicitud de patente según lo previsto en la Regla 4.3 PCT, Artículos 26 y 27 de la Decisión
486 y Circular Única de la SIC numeral 5.2.9.

4. En respuesta a la cuarta observación del Examinador, me permito aportar junto al
presente memorial un (1) documento de cesión debidamente legalizado, según los artículos
259 y 260 del CPC, en los que consta la cesión de cinco (5) inventores al solicitante, junto
con su correspondiente traducción, según lo previsto en el Art. 26-k de la Decisión 486.

Atentamente,



CARLOS R. OLARTE
C.C. 79.782.747 de Bogotá
T.P. 74.295

Anexo: Copia de la traducción del reporte de examen preliminar
Documento de Poder
Documento de Cesión

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HOJA MODIFICADA

Reivindicamos:

1. Una composición farmacéutica la cual comprende N- [4- (2,2- dimetil- propionil) - (5R) - 5- [(2- etilamino- etanosulfonilamino) - metil]- 5- fenil- 4,5- dihidro- [1,3,4]tiadiazol- 2- il)- 2,2- dimetil- propionamida, un buffer y/o sal, y un vehículo, diluyente o excipiente farmacéuticamente aceptable en solución en donde el pH de dicha composición es inferior a 6,4 y mayor a 2,0 y contiene no más de 2.5% de N- [4- (2,2- dimetil- propionil) - (5S) - 5- [(2- etilamino- etanosulfonilamino) - metil]- 5- fenil- 4,5- dihidro- [1,3,4]tiadiazol- 2- il)- 2,2- dimetil- propionamida.

2. La composición farmacéutica de la reivindicación 1 en donde el pH de dicha composición es inferior a 6,2 y mayor a 2,0.

3. La composición farmacéutica de la reivindicación 1 en donde el pH de dicha composición es inferior a 5,4 y mayor a 2,0.

4. La composición farmacéutica de la reivindicación 1 en donde el pH de dicha composición es inferior a 4,2 y mayor a 2,0.

5. Una composición farmacéutica liofilizada la cual comprende N- [4- (2,2- dimetil- propionil) - (5R) - 5- [(2- etilamino- etanosulfonilamino) - metil]- 5- fenil- 4,5- dihidro- [1,3,4]tiadiazol- 2- il)- 2,2- dimetil- propionamida, un buffer y/o sal, y un vehículo, diluyente o excipiente farmacéuticamente aceptable dando una formulación en solución al diluirse con diluyente acuoso con un pH inferior a 6,4 y mayor a 2,0 y que contiene no más de 2.5% de N- [4- (2,2- dimetil- propionil) - (5S) - 5- [(2- etilamino- etanosulfonilamino) - metil]- 5- fenil- 4,5- dihidro- [1,3,4]tiadiazol- 2- il)- 2,2- dimetil- propionamida.

6. La composición farmacéutica liofilizada de la reivindicación 5 en donde el pH de dicha composición es inferior a 6,2 y mayor a 2,0.

7. La composición farmacéutica liofilizada de la reivindicación 5 en donde el pH de dicha composición es inferior a 5,4 y mayor a 2,0.

8. La composición farmacéutica liofilizada de la reivindicación 5 en donde el pH de dicha composición es inferior a 4,2 y mayor a 2,0.

9. Una composición farmacéutica liofilizada la cual comprende N- [4- (2,2- dimetil- propionil) - (5R) - 5- [(2- etilamino- etanosulfonilamino) - metil]- 5- fenil- 4,5- dihidro- [1,3,4]tiadiazol- 2- il)- 2,2- dimetil- propionamida, un buffer y/o sal, y un vehículo, diluyente o excipiente farmacéuticamente aceptable.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference X17500	FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/US2008/069301	International filing date (day/month/year) 07.07.2008	Priority date (day/month/year) 12.07.2007
International Patent Classification (IPC) or national classification and IPC INV. A61K9/19		
Applicant ELI LILLY AND COMPANY		
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 7 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ sent to the applicant and to the International Bureau a total of 2 sheets, as follows: ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 602 of the Administrative Instructions).		
4. This report contains indications relating to the following items: ☒ Box No. I Basis of the report ☐ 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 Article 35(2) 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		
Date of submission of the demand 2009-05-08	Date of completion of this report 14.10.2009	
Name and mailing address of the international preliminary examining authority:  European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	Authorized officer Gómez Gallardo, S Telephone No. +31 70 340-9348 	

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**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/US2008/069301

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

- ☒ 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 (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-7 as originally filed

Claims, Numbers

1-9 filed with telefax on 08.05.2009

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☒ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☒ the claims, Nos. 1-9
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

5. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 70.2 (e)).

6. ☐ Supplementary international search report(s) from Authority(ies) have been received and taken into account in drawing up this report (Rule 45bis.8(b) and (c)).

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/US2008/069301

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>3-9</u>
	No: Claims	<u>1,2</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-9</u>
Industrial applicability (IA)	Yes: Claims	<u>1-9</u>
	No: Claims	

2. Citations and explanations (Rule 70.7):

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

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/US2008/059301

Re Item I

Basis of the report

The attention of the applicant is drawn to the fact that some of the amendments introduced in the new claims, as filed with telefax on 8 May 2009, go beyond the disclosure in the application as originally filed. More particularly, said amendments are as follows:

(a) in claims 1 and 5, the following statement has been introduced "*and contains no more than 2.5% N-[4-(2,2-dimethyl-propionyl)-(5S)-5-((2-ethylamino-ethanesulfonylamino)-methyl)-5-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]-2,2-dimethyl-propionamide*". However, in the originally filed application, there is only basis for the pharmaceutical composition containing no more than 2% N-[4-(2,2-dimethyl-propionyl)-(5S)-5-((2-ethylamino-ethanesulfonylamino)-methyl)-5-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]-2,2-dimethyl-propionamide (cf. page 5, lines 1 and 2).

(b) following a lack of clarity objection, the pH feature has been removed from claim 9. However, it is to be noted that, throughout the description of the invention, it is apparent that, in order to solve the instability problem of the R enantiomer, it is necessary that the pH is controlled in a range from less than 6.4 to greater than 2 when diluting the lyophilized formulation with an aqueous diluent. The deletion of the pH range in claim 9, instead of the rewording of the pH statement so that it reads that the pH value refers to the diluted lyophilized formulation, leads, therefore, to an undue generalisation according to which any pH is possible upon dilution.

The present examination report is established as if the above-mentioned amendments would not have been made (Rule 70.2(c) PCT).

Re Item V

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

1. CITED DOCUMENTS

INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)

International application No.

PCT/US2008/069301

Reference is made to the following documents:

- D1: EP 1 616 866 A (KYOWA HAKKO KOGYO KK [JP]; FUJI PHOTO FILM CO LTD [JP])
18 January 2006 (2006-01-18), of the same family as WO 2004/092147 A (KYOWA
HAKKO KOGYO KK [JP]; FUJI PHOTO FILM CO LTD [JP]) 28 October 2004 (2004-10-
28) (cited in the application)
- D2: CA 2 602 397 A (KYOWA HAKKO KOGYO KK [JP]; FUJI PHOTO FILM CO LTD [JP])
28 September 2006 (2006-09-28), of the same family as WO 2006/101102 A (KYOWA
HAKKO KOGYO KK [JP]; FUJI PHOTO FILM CO LTD [JP]; MURAKATA CHIKA) 28
September 2006 (2006-09-28) (cited in the application)

2. NOVELTY (Art. 33(2) PCT)

2.1. It is to be noted that, in claim 5, the statement "*affording a solution formulation when diluted with aqueous diluent having a pH less than 6.4 and greater than 2*" is a **result to be achieved**. This merely amounts to a statement of the underlying problem, **without providing the technical features necessary for achieving this result (i.e. the formulation components, e.g. the particular buffers and/or salts used (tartrate, phosphate, citrate, mesylate, sodium sulfate or sodium chloride (cf. page 4, lines 17 and 18)))**. Furthermore, the nature of the aqueous diluent may have a strong influence on the final pH obtained upon dilution. In view of this, the above-mentioned statement is, at present, considered as not limiting when assessing the novelty of the present application.

2.2. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1 and 2 is not new in the sense of Article 33(2) PCT.

Document D1 discloses (cf. page 37, table 9, compound 176; page 50 - page 51, example 9) an injection composition comprising (A) N-[4-(2,2-dimethyl-propionyl)-5-((2-ethylamino-ethanesulfonylamino)-methyl)-5-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]-2,2-dimethyl-propionamide, (B) D-mannitol, (C) HCl, (D) NaOH and (E) distilled water for injection. HCl and NaOH are known to produce NaCl, which is one of the possible buffers and/or salts mentioned in the present application. The pH of the composition of D1 is adjusted to 6. It is construed that said composition comprises at least a fraction of the

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/US2008/069301

R enantiomer of the thiadiazole derivative. Furthermore, it is stated in the description of D1 that optical isomers also fall within the scope of the family of compounds claimed (cf. page 22, paragraph 82). Therefore, the subject-matter of claims 1 and 2 is not new in view of D1.

3. INVENTIVE STEP (Art. 33(3) PCT)

3.1. Claims 1 and 2 being not new are also not inventive (Art. 33(3) PCT).

3.2. Dependent claims 3 and 4 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step. The reason for this is that no unexpected effect seems to be related to the pH being as defined in these claims (Art. 33(3) PCT).

3.3. Due to the reasoning disclosed in section 2.1., the statement "*affording a solution formulation when diluted with aqueous diluent having a pH less than 6.4 and greater than 2*", in claim 5, is, at present, considered as not limiting when assessing the inventive step of the present application (Art. 33(3) PCT).

3.4. The document D2 is regarded as being the closest prior art to the subject-matter of claims 5 and 9, and discloses (cf. page 37, table 1, compound 9; page 38, table 2, compound I; page 56, example 5; page 60 - page 61, example 13) an injection composition comprising (A) N-[4-(2,2-dimethyl-propionyl)-(5R)-5-((2-ethylamino-ethanesulfonylamino)-methyl)-5-phenyl-4,5-dihydro-1,3,4-thiadiazol-2-yl]-2,2-dimethyl-propionamide, (B) D-mannitol, (C) HCl, (D) NaOH and (E) distilled water for injection. HCl and NaOH are known to produce NaCl, which is one of the possible buffers and/or salts mentioned in the present application.

The subject-matter of claims 5 and 9, therefore, differs from D2 in that the thiadiazole derivative composition is lyophilized. This comes, however, within the scope of the customary practice followed by persons skilled in the art of formulating injectable compositions and the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of claims 5-9 also lacks an inventive step (Art. 33(3) PCT).

4. INDUSTRIAL APPLICABILITY (Art. 33(4) PCT)

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/US2008/069301

Claims 1-9 satisfy the criterion of industrial applicability set forth in Article 33(4) PCT.

Re Item VIII

Certain observations on the international application

CLARITY (Art. 6 PCT)

Although claims 5 and 9 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT. In the telefax received on 8 May 2009, the applicant alleges that claims 5 and 9 are directed to different subject-matter because claim 5 refers to a lyophilized formulation that is later diluted with an aqueous diluent and claim 9 refers to a lyophilized formulation. It is to be noted that even if the lyophilized formulation of claim 5 is later diluted, claim 5 still refers to a lyophilized formulation. Therefore, claims 5 and 9 indeed relate to the same subject-matter.

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We claim:

1. A pharmaceutical composition comprising *N*-(4-(2,2-dimethyl-propionyl)-(5*R*)-5-[(2-ethylamino-ethanesulfonylamino)-methyl]-5-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2,2-dimethyl-propionamide, a buffer and/or salt, and a pharmaceutically acceptable carrier, diluent, or excipient in solution wherein the pH of said composition is less than 6.4 and greater than 2.0 and contains no more than 2.5% *N*-(4-(2,2-dimethyl-propionyl)-(5*S*)-5-[(2-ethylamino-ethanesulfonylamino)-methyl]-5-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2,2-dimethyl-propionamide.
2. The pharmaceutical composition of Claim 1 wherein the pH of said composition is less than 6.2 and greater than 2.0.
3. The pharmaceutical composition of Claim 1 wherein the pH of said composition is less than 5.4 and greater than 2.0.
4. The pharmaceutical composition of Claim 1 wherein the pH of said composition is less than 4.2 and greater than 2.0.
5. A lyophilized pharmaceutical composition comprising *N*-(4-(2,2-dimethyl-propionyl)-(5*R*)-5-[(2-ethylamino-ethanesulfonylamino)-methyl]-5-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2,2-dimethyl-propionamide, a buffer and/or salt, and a pharmaceutically acceptable carrier, diluent, or excipient affording a solution formulation when diluted with aqueous diluent having a pH less than 6.4 and greater than 2.0 and contains no more than 2.5% *N*-(4-(2,2-dimethyl-propionyl)-(5*S*)-5-[(2-ethylamino-ethanesulfonylamino)-methyl]-5-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2,2-dimethyl-propionamide.
6. The lyophilized pharmaceutical composition of Claim 5 wherein the pH is less than 6.2 and greater than 2.0.

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7. The lyophilized pharmaceutical composition of Claim 5 wherein the pH is less than 5.4 and greater than 2.0.

8. The lyophilized pharmaceutical composition of Claim 5 wherein the pH is less than 4.2 and greater than 2.0.

9. A lyophilized pharmaceutical composition comprising *N*-(4-(2,2-dimethyl-propionyl)-(5*R*)-5-[(2-ethylamino-ethanesulfonylamino)-methyl]-5-phenyl-4,5-dihydro-[1,3,4]thiadiazol-2-yl)-2,2-dimethyl-propionamide, a buffer and/or salt, and a
10 pharmaceutically acceptable carrier, diluent, or excipient.

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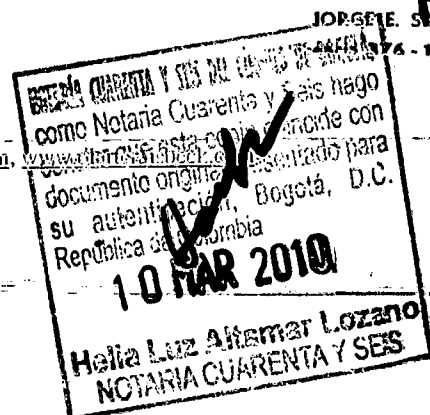
Traducción oficial de un documento cuyo original está en inglés

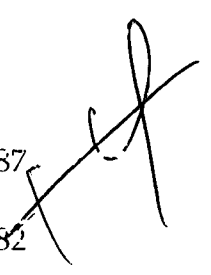
DELEGACIÓN DE AUTORIDAD
con respecto a
CIERTOS ASUNTOS SOBRE PATENTES

En nombre de Kyowa Hakko Kirin Co. Ltd., una compañía japonesa con sede comercial principal en 1-6-1 Othemachi, Chiyoda-ku, Tokyo 100-8185 Japón, delego a cada una de las siguientes personas:

Arvie J. Anderson	45,263	Robert E. Lee	27,919
Lynn D. Apelgren	45,341	James P. Leeds	35,241
Robert A. Armitage	27,417	Nelsen L. Lentz	38,537
Brian P. Barrett	39,597	Elizabeth A. McGraw	44,646
Gary M. Birch	48,881	Alejandro Martinez	53,163
Steven P. Caltrider	36,467	Douglas Norman	33,267
Paul R. Cantrell	36,470	Arleen Palmberg	40,422
Donald L. Corneglio	30,741	Edward J. Prein	37,212
Gregory A. Cox	47,504	Mark J. Stewart	43,936
Paula K. Davis	47,517	Robert D. Titus	40,206
John C. Demeter	30,167	R. Craig Tucker	45,165
Manisha A. Desai	43,585	Tina M. Tucker	47,145
Paul J. Gaylo	36,808	MaCharri Vorndran-Jones	36,711
Francis O. Ginah	44,712	Gilbert T. Voy	43,972

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Amy E. Hamilton	33,894	Lawrence T. Welch	29,487
Danica Hostettler	51,820	Alexander Wilson	45,782
Gerald P. Keleher	43,707	Mark A. Winter	53,782
Danica Hostettler	51,820	MaryAnn Wiskerchen	45,511
James J. Kelley	41,888	Dan L. Wood	48,613
Paul J. Koivuniemi	31,533	Congping Xie	57,817

todos ellos registrados para ejercer ante la Oficina de Patentes y Marcas Registradas de los Estados Unidos y empleados de Eli Lilly and Company, la autoridad para aprobar y ejecutar en nombre de la compañía Nyowa Hallo Kirin Co. Ltd., documentos con respecto a asuntos de patentes en relación con la siguiente solicitud de patente:

Registro: X17500

Solicitud No. PCT/US2008/069301

Título: FORMULACIONES ESTABLES DE DERIVADOS DE TIADIAZOLE

Incluyendo equivalentes globales y solicitudes en la fase nacional relacionadas con lo mismo.

- (i) la institución, seguimiento y completa realización de acciones dirigidas a la expedición de patentes; y
- (ii) el otorgamiento y la revocatoria de facultades de abogado en conexión con cualquiera de los anteriores.

Fechado el 29 de enero de 2010.

Tel + 57 1 601-7700, Fax + 57 1 601-7799, office@elancrafibres.com, www.elancrafibres.com


Traductor Oficial
JORGE E. GUERRA REYES
Código 378 - 1993 Minjusticia

BOGOTÁ CUARENTA Y SEIS DEL CURSO DE BOGOTÁ
constar que esta copia coincide con
documento original presentado para
su autenticación en Bogotá, D.C.
República de Colombia
10 MAR 2010
Helia Luz Aitsmar Lozano
NOTARIA CUARENTA Y SEIS

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(Firmado) /Yuzuru Matsuda/ Presidente y Director General

Kyowa Hakko Kirin Co. Ltd.

Sello

CERTIFICACIÓN NOTARIAL

Se certifica que el señor Kazuyo Saito, representante de Yuzuru Matsuda, Presidente y Director General de Kyowa Hakko Kirin Co. Ltd., ha declarado en mi presencia que dicho Yuzuru Matsuda ha reconocido haber firmado el documento adjunto.

Fechado este día 29 de enero de 2010.

(Signed) Hiroaki Sasaki, Notario

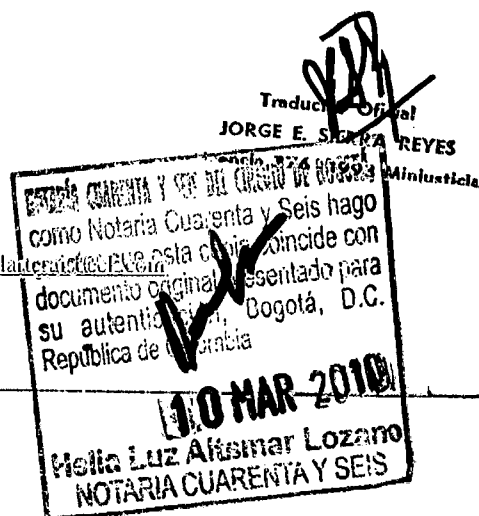
3-1, Marunouchi 3-chome, Chiyoda-ku, Tokio, adscrito a la Oficina de Asuntos Legales de Tokio.

Sello:

Sello redondo: "Notario. 3-1, Marunouchi 3-chome, Chiyoda-ku, Tokio, adscrito a la Oficina de Asuntos Legales de Tokio"

Apostilla adjunta:

Tel + 57 1 601-7700, Fax + 57 1 601-7799, office@olanteraibeck.com, www.olanteraibeck.com



Oficina del Secretario de Estado
Estado de Indiana
Todd Rokita, Secretario de Estado

APOSTILLA:

(Convention de La Haye du 5 octobre 1961)

1. País: Estados Unidos de América
2. El presente documento público ha sido firmado por: Debra E. Smith
3. Actuando en calidad de: Notario Público de y para el Condado de Marion
4. Lleva el sello/estampilla de: Notario Público de y para el Estado de Indiana
5. En: Indianápolis, Indiana
6. El: Once de febrero de 2010
7. Por: Secretario del Estado de Indiana
8. Bajo el No.: A2010-2644
9. Sello / estampilla: Sello del Estado de Indiana - 1816
10. Firma: Todd Rokita, Secretario del Estado de Indiana

CERTIFICADO

A partir de Mayo 1º de 2003 todas las Apostillas del Secretario de Estado de Indiana tendrán un sello impreso electrónicamente.

"FIN DE LA TRADUCCIÓN"

Certificación:

Certifico que la presente es una traducción auténtica y completa del inglés al español del documento adjunto, la cual he elaborado según mi leal saber y entender.

Documento: "Eli Lilly Company - Delegación de Autoridad"

Fecha: 25 de febrero de 2010.

Traductor: Jorge Enrique Sierra Reyes (Sello y firma digital debidamente registrados ante el Ministerio de Relaciones Exteriores de Colombia)

Licencia # 376 de 1993, expedida por el Ministerio de Justicia.

Dirección: Carrera 15 # 99-13 Of. 411, Bogotá, D.C.

Teléfonos: (571) 218 2303, (571) 623 2925.

E-mail: tresorer1@yahoo.com

Traducción # 14-617

Traductor Oficial

JORGE E. SIERRA REYES

Licencia-376 de 1993 Alinjusticia

Tel + 57 1 601-7700, Fax + 57 1 601-7799, office@olarteraisback.com, www.olarteraisback.com

Como Notaria Cuarenta y Seis hago constar que esta copia concide con documento original presentado para su autenticación en Bogotá, D.C. Republica de Colombia

10 MAR 2010

Hella Luz Altamir Lozano
NOTARIA CUARENTA Y SEIS

OLARTE RAISBECK
OLARTE, RAISBECK MOURE & CASTRO LTDA.

X17500 Colombia

Carlos R. Olarte
J. Ian Raisbeck
Juan Guillermo Moure
Natalia Castro

Alexander Agudelo
Catalina Barbastefano
Ángela Correa
Erika Rico
Carlos A. Parra
Andrés Alvarado
Gina Arias
Juan Felipe Acosta
Andrés Rincón
Grace García
Mariana Franco

Of Counsel
Guillermo Chahín
Graciela Melo
Jacqueline Chaparro
Cruz B. de Moncaleano

Power of Attorney

The undersigned,

domiciled in

KYOWA HAKKO KIRIN CO., LTD.

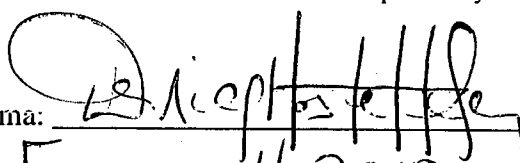
1-6-1 Ohtemachi Chiyoda-ku, Tokyo 100-8185 Japan

by means of these presents hereby grants to **Carlos R. Olarte and/or J. Ian Raisbeck and/or Juan Guillermo Moure and/or Natalia Castro** full and sufficient Power of Attorney to file, prosecute, obtain, defend and enforce any and all of the company's Patents for Inventions, Utility Models, Layout-Designs (topographies) of Integrated Circuits, Industrial Designs, Trademarks, Advertising Slogans, Trade Names, Commercial Emblems, Geographical Indications, Protection of Trade Secrets, Obtainer's Certificates, Copyrights, Registration of Domain Names, Health Registrations, or any other intellectual property right in the Republic of Colombia, to which end it empowers them to take all steps necessary before any administrative or judicial authority of any class for the objects stated, to file petitions, recourses, replies and oppositions, pay taxes and annuities, request testimonies, receive documents and securities, abandon applications, collect refunds, desist, settle, conciliate or negotiate. Sufficient power is hereby granted to receive notifications on behalf of the Company, to confer powers on those who are to represent the company judicially and extrajudicially, to answer in court in the matter of all claims and demands that may be presented in connection with the objects stated, giving them likewise power to substitute these presents and revoke such substitutions.

El suscrito,

domiciliado en

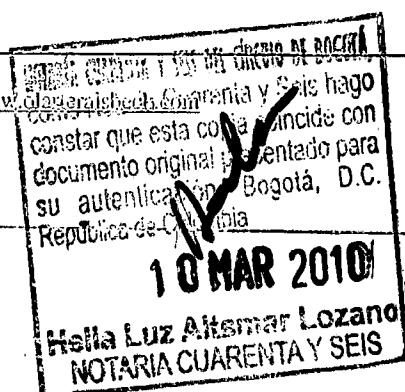
por medio del presente otorga a **Carlos R. Olarte y/o J. Ian Raisbeck y/o Juan Guillermo Moure y/o Natalia Castro** poder amplio y suficiente para presentar, tramitar, obtener, defender y hacer respetar todas y cualquiera de las Patentes de Invención, Modelos de Utilidad, Esquemas de Trazados de Circuitos Integrados, Diseños Industriales, Marcas, Lemas Comerciales, Nombres Comerciales, Enseñas Comerciales, Denominaciones de Origen, Protección de Secretos Empresariales, Certificados de Obtentor, Derechos de Autor, Registro de Nombres de Dominio, Registros Sanitarios, o cualquier otro bien de propiedad intelectual de la compañía en la República de Colombia, a cuyo efecto lo faculta para dar todos los pasos necesarios ante cualquier autoridad administrativa o judicial de cualquier jerarquía para cumplir con lo encomendado, elevar solicitudes, recursos, respuestas y oposiciones, pagar impuestos y anualidades, solicitar testimonios, recibir documentos y valores, desistir, transigir, y percibir. Se concede poder bastante para recibir notificaciones a nombre de la compañía, otorgar poderes a quienes vayan a representar a la compañía judicial y extrajudicialmente, responder en juicio a todas las reclamaciones o demandas que por motivo de lo encomendado se presentaren, dándoles asimismo facultad para sustituir el presente y revocar dichas sustituciones.

Signature/Firma: 

Date/Fecha: **FEBRUARY 4, 2010**

City/Country/Ciudad,País: **INDIANAPOLIS, INDIANA, USA**

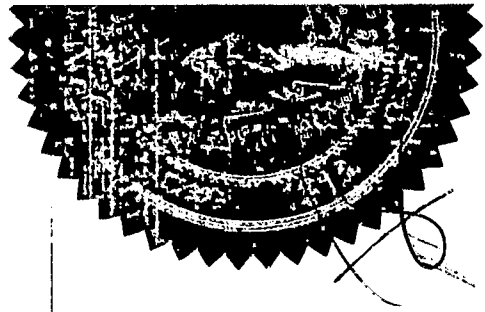
Diagonal 24 N° 5 - 28, Bogotá D.C., Colombia
Tel + 57 1 601-7700, Fax + 57 1 601-7799, office@olarteraisbeck.com, www.olarteraisbeck.com





Todd Rokita
Secretary of State

SECRETARY OF STATE
STATE OF INDIANA



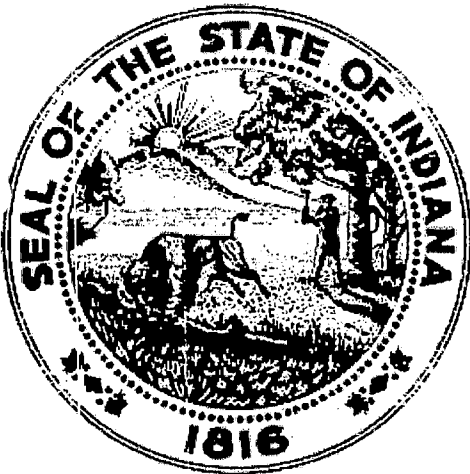
APOSTILLE

(Convention de la Haye du 5 Octobre 1961)

1. Country: United States of America
2. This public document has been signed by *Debra E. Smith*
3. acting in the capacity of notary public in & for *Marion* County
4. and bears the seal/stamp of notary public in & for the State of Indiana

CERTIFIED

5. at Indianapolis, Indiana
6. this the *Eleventh* day of *February*, 2010
7. by Secretary of State of Indiana
8. No. A2010 - 2644
9. Seal/Stamp:
10. Signature:

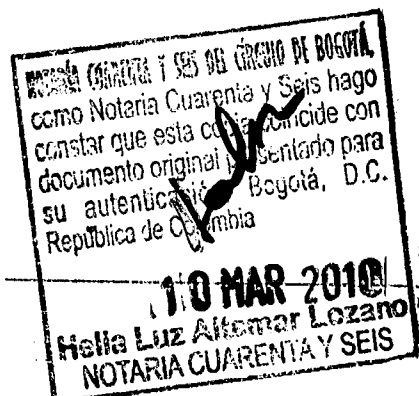


Todd Rokita

Todd Rokita
Indiana Secretary of State

Effective May 1, 2003 all apostilles from the Indiana Secretary of State will have an electronically printed seal.

TDOVE



MODEL OF NOTARIAL CERTIFICATION

Notarial Certification

Certificación Notarial

On this date,
February 4, 2010

The undersigned Notary Public certifies:

1. That

of legal age and domiciled in

signed the foregoing document.

2. That the grantor has executed the foregoing document as Patent Counsel of ELI LILLY AND COMPANY.

3. That KYOWA HAKKO KIRIN CO., LTD, having its principal place of business located in 1-6-1 Ohtemachi, Chiyoda-ku, Tokyo 100-8185, Japan is duly incorporated, is currently in existence, and that the purposes for which the Power of Attorney is granted are within the scope of its corporate purposes.

4. That the grantor has the authority to execute the Power of Attorney and that his/her representation is legal.

5. The foundation for my certifications contained in points 2, 3 and 4 was the exhibition of the following authentic document(s):

Delegation of Authority Concerning Certain Patent Matters, Dated: January 29, 2010

En esta fecha,

el Notario Público suscrito certifica:

1. Que

Danica Hostettler

mayor de edad y domiciliado

Lilly Corporate Center
Indianapolis, Indiana 46285

suscribió el documento que antecede.

2. Que el otorgante ha suscrito el referido documento en su carácter de de

3. Que

con sede principal ubicada en

está legalmente constituida, que tiene existencia legal vigente y que los propósitos para los cuales se otorga el poder se encuentra dentro de los que comprenden su objeto social.

4. Que el otorgante tiene la representación para suscribir el poder, y que ésta es legítima.

5. El fundamento de mis certificaciones contenidas en los puntos 2, 3 y 4 fue la exhibición de los (del) siguiente(s) documento(s) auténtico(s):

NOTARY PUBLIC (Signature):

[Handwritten Signature]

SEAL (optional)

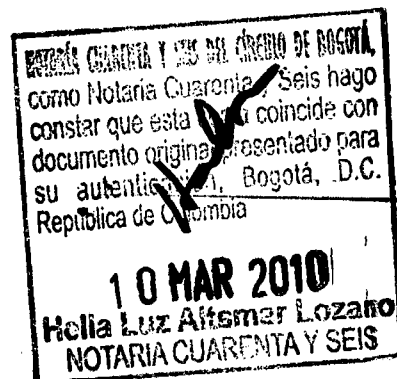


Debra E. Smith, Notary Public

Commission No. 000394

My Commission Expires: January 18, 2017

Resident of Marion County



89

**Delegation of Authority Concerning
Certain Patent Matters**

On behalf of Kyowa Hakko Kirin Co., Ltd., a Japanese corporation with a principal place of business at 1-6-1 Othemachi, Chiyoda-ku, Tokyo 100-8185 Japan, I delegate to each of the following persons:

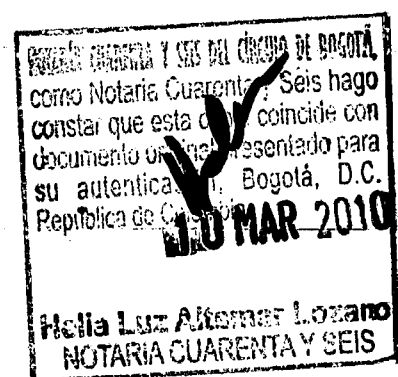
Name	Reg. No.	Name	Reg. No.
Arvie J. Anderson	45,263	Robert E. Lee	27,919
Lynn D. Apelgren	45,341	James P. Leeds	35,241
Robert A. Armitage	27,417	Nelsen L. Lentz	38,537
Brian P. Barrett	39,597	Elizabeth A. McGraw	44,646
Gary M. Birch	48,881	Alejandro Martinez	58,163
Steven P. Caltrider	36,467	Douglas Norman	33,267
Paul R. Cantrell	36,470	Arleen Palmberg	40,422
Donald L. Corneglio	30,741	Edward J. Prein	37,212
Gregory A. Cox	47,504	Mark J. Stewart	43,936
Paula K. Davis	47,517	Robert D. Titus	40,206
John C. Demeter	30,167	R. Craig Tucker	45,165
Manisha A. Desai	43,585	Tina M. Tucker	47,145
Paul J. Gaylo	36,808	MaCharri Vorndran-Jones	36,711
Francis O. Ginah	44,712	Gilbert T. Voy	43,972
Amy E. Hamilton	33,894	Lawrence T. Welch	29,487
Danica Hostettler	51,820	Alexander Wilson	45,782
Gerald P. Keleher	43,707	Mark A. Winter	53,782
Danica Hostettler	51,820	MaryAnn Wiskerchen	45,511
James J. Kelley	41,888	Dan L. Wood	48,613
Paul J. Koivuniemi	31,533	Congping Xie	57,817

all of whom are registered to practice before the United States Patent and Trademark Office and are employees of Eli Lilly and Company, the authority to approve and execute for and on behalf of Kyowa Hakko Kirin Co., Ltd., documents in connection with the following patent application:

Docket: X17500
Application No.: PCT/US2008/069301
Title: STABLE FORMULATIONS OF THIADIAZOLE
DERIVATIVE

including global equivalents and national phase applications related thereof:

- (i) the institution, prosecution, and completion of proceedings directed towards the issuance of patents; and
- (ii) the granting and the revocation of powers of attorney in connection with any of the foregoing.



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gt

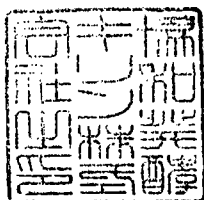
Dated: January 29, 2010

Yuzuru Matsuda

Yuzuru Matsuda

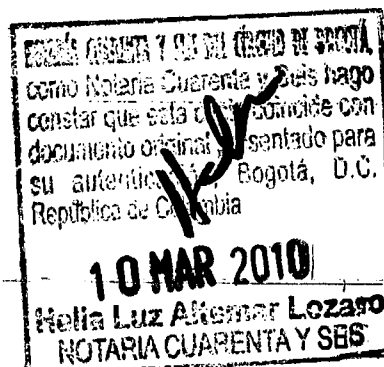
President and C.E.O.

Kyowa Hakko Kirin Co., Ltd.



NOTARY

(SEAL)



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27

NOTARIAL CERTIFICATE

This is to certify that Kazuyo Saito, an agent of Yuzuru Matsuda, President and C.E.O. of Kyowa Hakko Kirin Co., Ltd., has stated in my presence that said Yuzuru Matsuda has acknowledged to have signed the attached document.

Dated this 29th day of January, 2010.



Hiroaki Sasaki

Hiroaki Sasaki

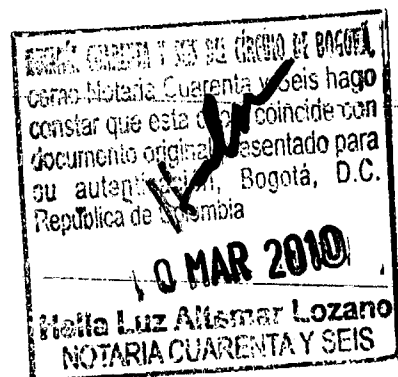
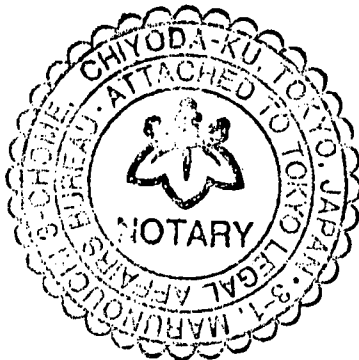
NOTARY

3-1, Marunouchi 3-chome,

Chiyoda-ku, Tokyo

ATTACHED TO

Tokyo Legal Affairs Bureau



[Handwritten signature]

(1)	平成 2 2 年 登 簿 第 0 0 5 4 号
(2)	添付書面における作成名義人協和発酵キリン株式会社
(3)	代表取締役松田譲の代理人斉藤和代は、当職の面前で、
(4)	本人が作成名義人の署名を自認していると陳述した。
(5)	よって、これを認証する。
(6)	平成 2 2 年 1 月 2 9 日、本職役場において
(7)	東京都千代田区丸の内三丁目 3 番 1 号
(8)	東京法務局所属
(9)	公証人 佐々木博章
(10)	
(11)	
(12)	
(13)	
(14)	
(15)	
(16)	
(17)	
(18)	
(19)	
(20)	

NOTARIA CUARENTA Y SEIS DEL CIRCUITO DE BOGOTÁ,
como Notaria Cuarenta y Seis hago
constar que esta copia coincide con
documento original presentado para
su autenticación en Bogotá, D.C.
República de Colombia
10 MAR 2010
Hellen Luz Altamir Lozano
NOTARIA CUARENTA Y SEIS

CESIÓN

Dado que

Hiroko-Kusano, de Kyowa Hakko Kogyo Co., Ltd.

1-6-1, Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón, ciudadano japonés.

Dinesh Shyamdeo Mishra, de 2504 Sutton Avenue, Carmel, Indiana 46032

1-6-Estados Unidos de América, ciudadano de los Estados Unidos.

Yoshikazu Tashiro, de Kyowa Hakko Kogyo Co., Ltd.

1-6-1, Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón, ciudadano japonés.

Yosuke Watanabe, de Kyowa Hakko Kogyo Co., Ltd.

1-6-1, Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón, ciudadano japonés.

Hong Zhuang de 3887 Branch Creek Court, Zionsville 46077. Estados Unidos de América, ciudadano de la República Popular de China.

son co-inventores de una invención que es el tema de una solicitud de patente ("Solicitud") que lleva por título "FORMULACIONES ESTABLES DE DERIVADO DE TIADIAZOLE" que contiene diez (10) páginas y ninguna hoja de dibujos y la cual:

(X) fue radicada

(X) como una Solicitud Internacional, según el Tratado de Cooperación sobre Patentes ("PCT") con la Oficina de Patentes y Marcas Registradas de Estados Unidos en la función de Oficina de Recepción
el 7 de julio de 2008 y número serial acordado PCT/US2008/069301; y

Dado que KYOWA HAKKO KOGYO CO., LTD., que tiene su sede principal de negocios en 1-6-1 Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón y ELI LILLY AND COMPANY, una compañía de Indiana que tiene su sede comercial principal en Lilly Corporate Center, Indianapolis, Indiana 46285 desea adquirir la totalidad del interés en todos los inventos que se desvelan en dicha Solicitud;

ENTONCES, por lo tanto en consideración de mi empleo, los acuerdos relacionados con el mismo, u otra buena y valiosa consideración, de lo cual estoy acusando recibo, por el presente cedo a KYOWA HAKKO KOGYO CO., LTD., y ELI LILLY AND COMPANY, sus sucesores y cesionarios (colectivamente "Kyowa" y "Lilly") la totalidad de mi derecho título e interés sobre la Solicitud, incluyendo todos los derechos de prioridad para los demás países que surjan de allí, todos los inventos revelados allí y cualquier solicitud de patente presente o futura para dichos inventos que pueda radicarse en cualquier país, incluyendo pero no solamente, continuaciones, continuaciones parciales, divisiones, sustituciones, reexámenes, reexpediciones, solicitudes internacionales radicadas bajo el PCT, solicitudes provisionales de patente de los Estados Unidos, solicitudes provisionales de patente de los Estados Unidos subsiguientes que reclamen algo o la totalidad de este invento, certificados de adición, modelos de utilidad, patentes

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"petty", así como la demás propiedad intelectual relacionada con la Solicitud, inclusive pero no solamente, certificados de protección suplementaria y cualquier extensión de término de patente relacionada que se pueda otorgar para Cartas de Patente con respecto a la Solicitud; todo lo anterior para que sea poseído y disfrutado por Kyowa y Lilly para su propio uso y disfrute hasta el final del término o términos para los cuales dichas cartas de patente y derechos de propiedad intelectual relacionados puedan otorgarse, de forma tan completa y total como pudiera haber sido poseído y disfrutado por mí si esta Cesión y venta a Kyowa y Lilly no se hubiera realizado.

Por mí y por mis herederos, sucesores y representantes legales, convengo en que no se ha hecho ni se hará ninguna cesión, venta, acuerdo o gravamen ni se hará nada con lo que esta Cesión pueda entrar en conflicto.

Por mí y mis herederos, sucesores y representantes legales, convengo y acuerdo además con Kyowa y Lilly en que por solicitud yo y ellos, sin consideración adicional que la ya pagada, pero a costa de Kyowa y Lilly: (i) ejecutaremos solicitudes originales, provisionales, sustitutos, de continuación, de división, de continuación parcial, reexaminadas o reexpedidas, correcciones de especificaciones o declaraciones o declaraciones juramentadas para dicha solicitud; (ii) comunicaremos a Kyowa y Lilly cualquier hecho conocido por nosotros relacionado con dicho invento o la historia del mismo; (iii) ejecutaremos declaraciones preliminares y testificaremos en cualquier caso de interferencia, proceso y declaración de descubrimiento de litigio, oposición, proceso de


Traductor Oficial

JORGE E. SIERRA REYES

Licencia 376 • 1993 Minjusticia

cancelación, concurso de prioridad, proceso de uso público, proceso de agencia administrativa, litigio y demás acciones judiciales y similares; (iv) ejecutaremos y entregaremos cualquier documento de solicitud, declaración juramentada, declaración, cesión u otros instrumentos; y (v) haremos las demás acciones que en opinión del Asesor Jurídico de Kyowa y Lilly puedan necesitarse o desearse para asegurar el otorgamiento de las Cartas de Patente y propiedad intelectual relacionada con Kyowa y Lilly o sus nominados en los Estados Unidos y en todos los demás países en donde Kyowa y Lilly pueda desear hacer patentar dichos inventos, o alguno de ellos, con especificaciones y reclamos de forma tal que sea aprobado por el Asesor Jurídico de Kyowa y Lilly e invertir y confirmar a Kyowa y Lilly o sus nominados en el título total y completo, legal y equitativo, para todas las dichas cartas de patente y propiedad intelectual relacionada.

He ejecutado esta cesión en la fecha indicada más adelante.

Fecha: 11 de agosto de 2008	(Firmado) Hiroko-Kusano, Inventor
Fecha: 18 de agosto de 2008	(Firmado) Yoshikazu, Tashiro, Inventor
Fecha: 1 de agosto de 2008	(Firmado) Watanabe, Inventor

CESIÓN

Dado que

Hiroko-Kusano, de Kyowa Hakko Kogyo Co., Ltd.

1-6-1, Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón, ciudadano japonés.

Dinesh Shyamdeo Mishra, de 2504 Sutton Avenue, Carmel, Indiana 46032


Traductor Oficial
JORGE E. SIERRA REYES
Licencia 376 • 1993 Minjusticia

1-6-Estados Unidos de América, ciudadano de los Estados Unidos.

Yoshitazu Tashiro, de Kyowa Hakko Kogyo Co., Ltd.

1-6-1, Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón, ciudadano japonés.

Yosuke Watanabe, de Kyowa Hakko Kogyo Co., Ltd.

1-6-1, Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón, ciudadano japonés.

Hong Zhuang de 3887 Branch Creek Court, Zionsville 46077. Estados Unidos de América, ciudadano de la República Popular de China.

son co-inventores de una invención que es el tema de una solicitud de patente ("Solicitud") que lleva por título "FOPMULACIONES ESTABLES DE DERIVADO DE TIADIAZOLE" que contiene diez (10) páginas y ninguna hoja de dibujos y la cual:

(X) fue radicada

(X) como una Solicitud Internacional, según el Tratado de Cooperación sobre Patentes ("PCT") con la Oficina de Patentes y Marcas Registradas de Estados Unidos en la función de Oficina de Recepción

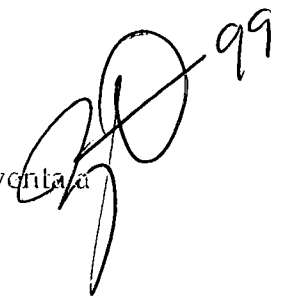
el 7 de julio de 2008 y número serial acordado PCT/US2008/069301; y

Dado que KYOWA HAKKO KOGYO CO., LTD., que tiene su sede principal de negocios en 1-6-1 Ohtemachi, Chiyoda-ku, Tokio, 100-8185, Japón y ELI LILLY AND COMPANY, una compañía de Indiana que tiene su sede comercial principal

en Lilly Corporate Center, Indianapolis, Indiana 46285 desea adquirir la totalidad del interés en todos los inventos que se desvelan en dicha Solicitud;

ENTONCES, por lo tanto en consideración de mi empleo, los acuerdos relacionados con el mismo, u otra buena y valiosa consideración, de lo cual estoy acusando recibo, por el presente cedo a KYOWA HAKKO KOGYO CO., LTD., y ELI LILLY AND COMPANY, sus sucesores y cesionarios (colectivamente "Kyowa" y "Lilly") la totalidad de mi derecho título e interés sobre la Solicitud, incluyendo todos los derechos de prioridad para los demás países que surjan de allí, todos los inventos revelados allí y cualquier solicitud de patente presente o futura para dichos inventos que pueda radicarse en cualquier país, incluyendo pero no solamente, continuaciones, continuaciones parciales, divisiones, sustituciones, reexámenes, reexpediciones, solicitudes internacionales radicadas bajo el PCT, solicitudes provisionales de patente de los Estados Unidos, solicitudes provisionales de patente de los Estados Unidos subsiguientes que reclamen algo o la totalidad de este invento, certificados de adición, modelos de utilidad, patentes "petty", así como la demás propiedad intelectual relacionada con la Solicitud, inclusive pero no solamente, certificados de protección suplementaria y cualquier extensión de término de patente relacionada que se pueda otorgar para Cartas de Patente con respecto a la Solicitud; todo lo anterior para que sea poseído y disfrutado por Kyowa y Lilly para su propio uso y disfrute hasta el final del término o términos para los cuales dichas cartas de patente y derechos de propiedad intelectual relacionados puedan otorgarse, de forma tan completa y

total como pudiera haber sido poseído y disfrutado por mí si esta Cesión y venta a Kyowa y Lilly no se hubiera realizado.



Por mí y por mis herederos, sucesores y representantes legales, convengo en que no se ha hecho ni se hará ninguna cesión, venta, acuerdo o gravamen ni se hará nada con lo que esta Cesión pueda entrar en conflicto.

Por mí y mis herederos, sucesores y representantes legales, convengo y acuerdo además con Kyowa y Lilly en que por solicitud yo y ellos, sin consideración adicional que la ya pagada, pero a costa de Kyowa y Lilly: (i) ejecutaremos solicitudes originales, provisionales, sustitutos, de continuación, de división, de continuación parcial, reexaminadas o reexpedidas, correcciones de especificaciones o declaraciones o declaraciones juramentadas para dicha solicitud; (ii) comunicaremos a Kyowa y Lilly cualquier hecho conocido por nosotros relacionado con dicho invento o la historia del mismo; (iii) ejecutaremos declaraciones preliminares y testificaremos en cualquier caso de interferencia, proceso y declaración de descubrimiento de litigio, oposición, proceso de cancelación, concurso de prioridad, proceso de uso público, proceso de agencia administrativa, litigio y demás acciones judiciales y similares; (iv) ejecutaremos y entregaremos cualquier documento de solicitud, declaración juramentada, declaración, cesión u otros instrumentos; y (v) haremos las demás acciones que en opinión del Asesor Jurídico de Kyowa y Lilly puedan necesitarse o desearse para asegurar el otorgamiento de las Cartas de Patente y propiedad intelectual relacionada con Kyowa y Lilly o sus nominados en los Estados Unidos y en todos



los demás países en donde Kyowa y Lilly pueda desear hacer patentar dichos inventos, o alguno de ellos, con especificaciones y reclamos de forma tal que sea aprobado por el Asesor Jurídico de Kyowa y Lilly e invertir y confirmar a Kyowa y Lilly o sus nominados en el título total y completo, legal y equitativo, para todas las dichas cartas de patente y propiedad intelectual relacionada.

He ejecutado esta cesión en la fecha indicada más adelante.

Fecha: 2 de julio de 2008 (Firmado) Dinesh Shyamdeo Mishra, Inventor

Fecha: 2 de julio de 2008 (Firmado) Hong Zhuang, Inventor

CERTIFICADO DE CONFORMIDAD

Estado de Indiana

Condado de Marion

Yo, Debra E. Smith, Notario Público debidamente nombrado en el Condado de Marion, Estado de Indiana, Estados Unidos de América, certifico por el presente documento que el documento adjunto, identificado como una cesión entre los cedentes Hiroko-Kusano, Dinesh Shyamdeo Mishra, Yoshikazu Tashiro, Yosuke Watanabe, Hong Zhuang y el Cesionario ELI LILLY AND COMPANY, es una copia exacta del documento original.

Firmado este 29 de marzo de 2010.

(Firmado) Debra E. Smith, Notario Público. Mi nombramiento vence el 18 de enero de 2017. Residente en el Condado de Marion.

Sello: "Notario Público de Indiana"



Apostilla adjunta:

Oficina del Secretario de Estado
Estado de Indiana
Todd Rokita, Secretario de Estado
APOSTILLA:
(Convention de La Haye du 5 octobre 1961)

1. País: Estados Unidos de América
2. El presente documento público ha sido firmado por: Debra E. Smith
3. Actuando en calidad de: Notario Público de y para el Condado de Marion
4. Lleva el sello/estampilla de: Notario Público de y para el Estado de Indiana
Certificado
5. En: Indianápolis, Indiana
6. El: 30 de marzo de 2010
7. Por: Secretario del Estado de Indiana
8. Bajo el No.: A2010-4474
9. Sello / estampilla: Sello del Estado de Indiana - 1816
10. Firma: Todd Rokita, Secretario del Estado de Indiana

A partir de Mayo 1º de 2003 todas las Apostillas del Secretario de Estado de Indiana tendrán un sello impreso electrónicamente.

FIN DE LA TRADUCCIÓN

Certificación:

Certifico que la presente es una traducción auténtica y completa del inglés al español del documento adjunto, la cual he elaborado según mi leal saber y entender.

Documento: "El Lilly and Company -- Cesión"

Fecha: 14 de abril de 2010.

Traductor: Jorge Enrique Sierra Reyes (Sello y firma digital debidamente registrados ante el Ministerio de Relaciones Exteriores de Colombia)

Licencia # 376 de 1993, expedida por el Ministerio de Justicia.

Dirección: Carrera 15 # 99-13 Of. 411, Bogotá, D.C.

Teléfonos: (571) 218 2308, (571) 623 2925.

E-mail: jesus1@yahoo.com

Traducción # 14-853

Traductor Oficial

JORGE E. SIERRA REYES

Licencia 376 - 1993 Minjusticia



SECRETARY OF STATE
STATE OF INDIANA

23 102



Todd Rokita
Secretary of State

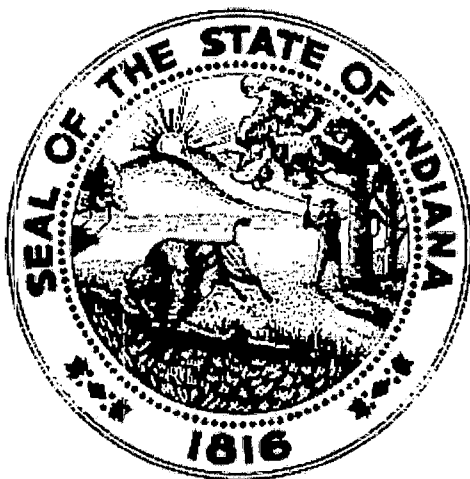
APOSTILLE

(Convention de la Haye du 5 Octobre 1961)

1. Country: United States of America
2. This public document has been signed by *Debra E. Smith*
3. acting in the capacity of notary public in & for *Marion* County
4. and bears the seal/stamp of notary public in & for the State of Indiana

CERTIFIED

5. at Indianapolis, Indiana
6. this the *Thirtieth* day of *March, 2010*
7. by Secretary of State of Indiana
8. No. A2010 - 4474
9. Seal/Stamp:
10. Signature:



Todd Rokita

Todd Rokita
Indiana Secretary of State

Effective May 1, 2003 all apostilles from the Indiana Secretary of State will have an electronically printed seal.

34/103

CERTIFICATE OF CONFORMITY

STATE OF INDIANA
COUNTY OF MARION

I, Debra E. Smith, a Notary Public duly commissioned in the county of Marion, State of Indiana, United States of America, do hereby certify that the attached document identified as an assignment between assignor Hiroko KUSANO, Dinesh Shyamdeo MISHRA, Yoshikazu TASHIRO, Yosuke WATANABE, Hong ZHUANG and assignee, ELI LILLY AND COMPANY, is an exact copy of the original document.

Signed this 29 day of March 2010



A handwritten signature of Debra E. Smith in cursive script, written over a horizontal line.

NOTARY PUBLIC
Debra E. Smith
My Commission Expires
January 18, 2017
Resident of Marion County

(SEAL)

104
2/3

ASSIGNMENT

WHEREAS,

Hiroko KUSANO
Kyowa Hakko Kogyo Co., Ltd.
1-6-1, Ohtemachi, Chiyoda-ku,
Tokyo, 100-8185, Japan
Japanese Citizenship

Dinesh Shyamdeo MISHRA
2504 Sutton Avenue
Carmel, Indiana 46032
United States of America
United States Citizenship

Yoshikazu TASHIRO
Kyowa Hakko Kogyo Co., Ltd.
1-6-1, Ohtemachi, Chiyoda-ku,
Tokyo, 100-8185, Japan
Japanese Citizenship

Yosuke WATANABE
Kyowa Hakko Kogyo Co., Ltd.
1-6-1, Ohtemachi, Chiyoda-ku,
Tokyo, 100-8185, Japan
Japanese Citizenship

Hong ZHUANG
3887 Branch Creek Court
Zionsville, IN 46077
United States of America
P.R. China Citizenship

are co-inventors of an invention that is the subject of a patent application ("Application")
which is entitled **STABLE FORMULATIONS OF THIADIAZOLE DERIVATIVE**,
containing 10 pages and 0 sheets of drawings, and which:

☒ is being filed:
☐ was filed:

- ☐ in the United States Patent and Trademark Office
- ☐ in the United Kingdom Patent Office
- ☐ in the European Patent Office
- ☐ in the Spanish Patent Office as a European Application
- ☒ as an international application under the Patent Cooperation Treaty ("PCT"),
with United States Patent and Trademark Office acting as Receiving Office

on 7 JULY 2008 and accorded serial number PCT/JP2008/069301:

and

WHEREAS KYOWA HAKKO KOGYO CO., LTD., having its principal place of business at 1-6-1 Ohtemachi, Chiyoda-ku, Tokyo 100-8185 JAPAN and **ELI LILLY AND COMPANY**, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire the entire interest in all inventions disclosed in such Application;

NOW, THEREFORE, in consideration of my employment, any agreements related thereto, or other good and valuable consideration, the receipt of which is hereby acknowledged, I hereby assign to Kyowa Hakko Kogyo Co., Ltd., and Eli Lilly and Company, its successors and assigns (collectively "Kyowa" and "Lilly") my entire right, title and interest in, to and under the Application, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all present or future patent applications to such inventions that may be filed in any country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications filed under the PCT, United States provisional patent applications, subsequent United States provisional patent applications claiming some or all of this invention, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates; and any related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Kyowa and Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by me had this Assignment and sale to Kyowa and Lilly not been made.

For myself and for my heirs, successors and legal representatives, I covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For myself and for my heirs, successors and legal representatives, I further covenant and agree with Kyowa and Lilly that upon request I and they will, without further consideration than that now paid, but at the expense of Kyowa and Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Kyowa and Lilly any facts known to me or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Kyowa and Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Kyowa and Lilly or its nominees, in the United States and in all other countries where Kyowa and Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Kyowa and Lilly and to vest and confirm in Kyowa and Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.

27/106

I have executed this assignment on the date indicated below.

August 11, 2008
Date

H. Kusano
Hiroko KUSANO, Inventor

August 18, 2008
Date

Y. Tashiro
Yoshikazu TASHIRO, Inventor

August 1, 2008
Date

Yosuke Watanabe
Yosuke WATANABE, Inventor

256/109

ASSIGNMENT

WHEREAS,

Hiroko KUSANO
Kyowa Hakko Kogyo Co., Ltd.
1-6-1, Ohtemachi, Chiyoda-ku,
Tokyo, 100-8185, Japan
Japanese Citizenship

Dinesh Shyamdeo MISHRA
2504 Sutton Avenue
Carmel, Indiana 46032
United States of America
United States Citizenship

Yoshikazu TASHIRO
Kyowa Hakko Kogyo Co., Ltd.
1-6-1, Ohtemachi, Chiyoda-ku,
Tokyo, 100-8185, Japan
Japanese Citizenship

Yosuke WATANABE
Kyowa Hakko Kogyo Co., Ltd.
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Tokyo, 100-8185, Japan
Japanese Citizenship

Hong ZHUANG
3887 Branch Creek Court
Zionsville, IN 46077
United States of America
P.R. China Citizenship

are co-inventors of an invention that is the subject of a patent application ("Application") which is entitled **STABLE FORMULATIONS OF THIADIAZOLE DERIVATIVE**, containing 10 pages and 0 sheets of drawings, and which:

☒ is being filed:
☐ was filed:

- ☐ in the United States Patent and Trademark Office
- ☐ in the United Kingdom Patent Office
- ☐ in the European Patent Office
- ☐ in the Spanish Patent Office as a European Application
- ☒ as an international application under the Patent Cooperation Treaty ("PCT"), with United States Patent and Trademark Office acting as Receiving Office

on 7 July 2008 and accorded serial number PCT/JP2008/067201;

and

WHEREAS KYOWA HAKKO KOGYO CO., LTD., having its principal place of business at 1-6-1 Ohtemachi, Chiyoda-ku, Tokyo 100-8185 JAPAN and **ELI LILLY AND COMPANY**, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire the entire interest in all inventions disclosed in such Application;

NOW, THEREFORE, in consideration of my employment, any agreements related thereto, or other good and valuable consideration, the receipt of which is hereby acknowledged, I hereby assign to Kyowa Hakko Kogyo Co., Ltd., and Eli Lilly and Company, its successors and assigns (collectively "Kyowa" and "Lilly") my entire right, title and interest in, to and under the Application, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all present or future patent applications to such inventions that may be filed in any country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications filed under the PCT, United States provisional patent applications, subsequent United States provisional patent applications claiming some or all of this invention, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates; and any related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Kyowa and Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by me had this Assignment and sale to Kyowa and Lilly not been made.

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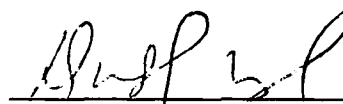
For myself and for my heirs, successors and legal representatives, I further covenant and agree with Kyowa and Lilly that upon request I and they will, without further consideration than that now paid, but at the expense of Kyowa and Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Kyowa and Lilly any facts known to me or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Kyowa and Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Kyowa and Lilly or its nominees, in the United States and in all other countries where Kyowa and Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Kyowa and Lilly and to vest and confirm in Kyowa and Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.



I have executed this assignment on the date indicated below.

2-Jul-2008

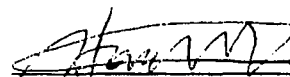
Date



Dinesh Shyamdeo MISHRA, Inventor

02-July-2008

Date



Hong ZHUANG, Inventor