

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 13-158446-00012-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 851 DIVISIONAL Folios: 7-8



Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 15-222394-00000-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 7-8

ntf

DELEGATURA DE PROPIEDAD INDUSTRIAL
DIRECCIÓN DE NUEVAS CREACIONES

SOLICITUD DIVISIONAL
DE PATENTE DE
INVENCION

TITULO: FORMAS CRISTALINAS DE 5-CLORO-N2-(2-ISOPROPOXI-5-METIL-
4-PIPERIDIN-4-IL-FENIL)-N4-[2-(PROPAN-2-SULFONIL)-FENIL]-PIRIMIDIN-2,4-
DIAMINA.

SOLICITANTE: NOVARTIS AG

EXPEDIENTE No. 13-158.446

DIRECCIÓN: Lichtstrasse 35, CH-4056 Basel, Suiza.

APODERADO: CARLOS R. OLARTE

BOGOTÁ: 18 de septiembre de 2015

P2013/000093A



No. 13-158446-00012-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
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No. 15-222394-00000-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 7-8

DIRECCIÓN DE NUEVAS CREACIONES
CONVERSIÓN, DIVISIÓN Y FUSIÓN DE SOLICITUDES

1. Identificación del Trámite

☐

Conversión

☒

División

☐

Fusión

☒

Patente de Invención

☐

Patente de Modelo de Utilidad

2. Datos del solicitante

☐

Persona Natural

☒

Persona Jurídica

NOVARTIS AG

Nombre o denominación / Nombre o razón social

Nombre del representante legal

Tipo de empresa

☐

Micro

☐

Pequeña

☐

Mediana

☐

Otra

Documento de identificación

☐

C.C.

☐

C.E.

☒

NIT

☐

Otro

Número

Nacionalidad/Pais de constitución	Dirección del titular	Ciudad
Suiza	Lichtstrasse 35, CH-4056 Basel, Suiza	Basel
Dirección electrónica	No. Fax	Número telefónico

☐

Autorizo expresamente a la Superintendencia de Industria y Comercio para que todas las comunicaciones sean enviadas a través de la dirección de correo electrónico

3. Datos del apoderado:

CARLOS R. OLARTE

Apellidos y Nombre

79.782.747 Bta

Documento de identificación

74.295

Tarjeta profesional

Dirección y domicilio	Dirección del titular	Ciudad
Carrera 5 No 34-03 Bogotá D.C.		
Dirección electrónica	No. Fax	Número telefónico
office@mourer.com	601-7799	601-7700

En caso de haber presentado poder general para asuntos que se adelanten ante la Delegatura de Propiedad Industrial, sirvase indicar el número de su radicación o protocolo de poder general

4. Datos del trámite:

CONVERSION

Expediente No.

De:

A:

DIVISION

Expediente No.

13-158.446

No. de divisionales

FUSION

Expediente No.

Expediente No.

2

5. Comprobante de Pago No	Fecha
---------------------------	-------

6. Anexos	
☒	Comprobante de pago de la tasa para la presentación de la corrección y/o modificación
☒	Poder, si fuere el caso con el que se acredita la representación
☒	Número de documento que ordena la comisión o fusión o división
☐	Documento que contiene la conversión, división o fusión de la solicitud
☒	Copia de la solicitud y sus anexos en formato magnético

7. Firma	
CARLOS R. OLARTE	
Nombre y apellidos	Firma
79.782.747	74.295
C.C.	Tarjeta Profesional

OLARTEMOURE

OLARTE MOURE & ASOCIADOS LTDA.



Espacio reservado para el adhesivo de radicación.

PETITORIO - FORMULARIO ÚNICO DE SOLICITUD DIVISIONAL DE PATENTE PCT

ENTRADA EN FASE NACIONAL

P2013/000093A

SOLICITUD DE:

1

☒

Patente de Invención.

☐

Patente de Modelo de Utilidad.

☒

Capítulo I.

☐

Capítulo II.

2

**SOLICITANTE
(71)**

Nombre: Novartis AG

Dirección: Lichtstrasse 35, CH-4056 Basel,
Suiza

Nacionalidad o Domicilio: Suiza

Lugar de Constitución: Suiza

Teléfono: _____

Fax: _____

E-mail: _____

IDENTIFICACIÓN

C.C.

☐

NIT

☐

C.E.

☐

Otro

☐

Cual

Número

**REPRESENTANTE
O APODERADO**

Nombre: CARLOS R. OLARTE

Dirección: Carrera 5 No 34-03 Bogotá D.C.

Teléfono: 601-7700 **Fax:** 601-7799

E-mail: office@olartemoure.com

IDENTIFICACIÓN

C.C.

☒

NIT

☐

C.E.

☐

Otro

☐

Cual

Número 79782747Bta
TP 74.295

**INVENTOR (ES)
(72)**

Nombre: VER PAGINA ADJUNTA

Dirección: VER PAGINA ADJUNTA

Nacionalidad o Domicilio: VER PAGINA ADJUNTA

5

PCT (86)

Solicitud Internacional No. PCT/US2011/065030

Fecha Diciembre 15, 2011

Publicación Internacional No. WO 2012/082972 A1

Fecha Junio 21, 2012

6

Título (54) FORMAS CRISTALINAS DE 5-CLORO-N2-(2-ISOPROPOXI-5-METIL-4-PIPERIDIN-4-IL-FENIL)-N4-[2-(PROPAN-2-SULFONIL)-FENIL]-PIRIMIDIN-2,4-DIAMINA.

Clasificación Internacional (51) C07D 401/12; A61K 31/506; A61P 35/00.

Prioridad

SI

☒

NO

☐

(33) País de Origen

US

(32) Fecha

Diciembre 17, 2010

(31) Número de
Solicitud

61/424,194

9

Comprobante de pago No. 14-

Fecha



ANEXOS



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. Adjunto copia simple ver expediente No. 08-102.832



Documento de cesión del inventor al solicitante o a su causante.



Declaraciones. Declaración bajo la regla 4.17 (ii) del PCT.



Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos).



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.



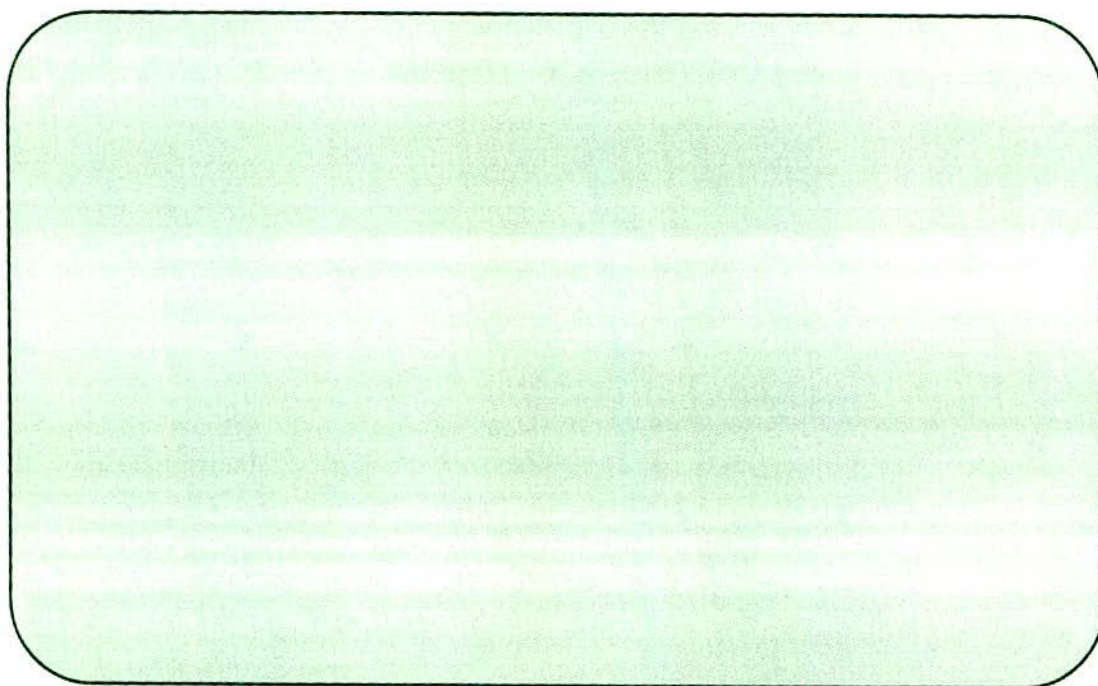
De ser el caso, modificaciones efectuadas a la solicitud internacional.



Otros. Búsqueda Internacional



FIGURA CARACTERÍSTICA:



Solicito la concesión de la patente,

NOMBRE: CARLOS R. OLARTE

FIRMA:

C.C. 79.782.747 Btá T.P. 74.295

LISTA DE INVENTORES

PCT/US2011/065030

FENG, Lili

Novartis Pharmaceuticals Corporation,
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New Jersey 07936-1080
Estados Unidos de América
Nacionalidad: China

GONG, Baoqing

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Estados Unidos de América
Nacionalidad: Estadounidense

KARPINSKI, Piotr H.

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Estados Unidos de América
Nacionalidad: Estadounidense

WAYKOLE, Liladhar Murlidhar

Novartis Pharmaceuticals Corporation,
One Health Plaza, East Hanover,
New Jersey 07936-1080
Estados Unidos de América
Nacionalidad: Estadounidense

 Industria y Comercio SUPERINTENDENCIA	TESTIGO DOCUMENTAL	Folio: <u>6</u>
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Dependencia Jerárquica: DEL PROPIEDAD INDUSTRIAL		Código: 2000
Dependencia Productora: GRUPO DE NUEVAS CREACIONES		Código: 2020
Tipo de Radicación: Entrada: ☒ Salida: ☐ Traslado: ☐ Convenio: ☐		
Radicator:		
DESCRIPCIÓN DE LA PRUEBA		
Nombre de la Serie / Subserie:		Código:
Expediente: 13-158446-12 15-222394-0	Solicitante / Quejoso / Demandante / otros.	
Prueba excluida: <u>cd</u>		
Nº. de Pruebas excluidas: <u>1</u>		
Fecha de emisión de la Prueba:		
UBICACIÓN DE LA PRUEBA EN LA SECCIÓN DE MATERIAL GRÁFICO		
Nº. de bloque:		Otras especificaciones:
Nº. de rodante:		
Nº. de estante:		
Nº. de archivador:		
Nº. de entrepaño:		
Nº. de gaveta:		
Nº. de caja:		
IMPORTANTE: - El material gráfico o especial que se encuentra dentro o anexo a las unidades documentales o expedientes, debe extraerse y llevarse a aquella sección del archivo que se haya dispuesto para conservar documentos en distintos formatos. - Entiéndase por material gráfico todos aquellos dibujos, croquis, mapas, planos, fotografías, ilustraciones, pictografías, códigos, prensa, objetos tridimensionales, entre otros.		
Observaciones: <u>El CD contiene</u> <u>10 archivos en formato PDF</u> <u>procesados y cargados al sistema</u> <u>Andrés</u>		Unidad de Conservación ☐ Bolsa ☐ Caja ☐ Libro ☐ Sobre ☐ Tomo ☐ Otro Soporte Documental ☒ CD ☐ Disquete ☐ DVD ☐ Folleto ☐ Periódico ☐ Plano ☐ Publicación Periódica ☐ USB ☐ Otro

ruf

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800.176.089-2

- / -



RECIBO DE CAJA

No. 15 - 103001

Bogotá D.C., Septiembre 18 de 2015 - 16:17:56

RECIBIDO DE : OLARTE MOURE & ASOCIADOS

NI 830.122.870

RE

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR. PAGO
RECIBO DE CA	SIC ** RECIBO **	999999999	97590	04/09/2015	32.000.00
RECIBO DE CA	SIC ** RECIBO **	999999999	97614	04/09/2015	132.000.00
RECIBO DE CA	SIC ** RECIBO **	999999999	97625	04/09/2015	109.000.00
RECIBO DE CA	SIC ** RECIBO **	999999999	97626	04/09/2015	109.000.00
RECIBO DE CA	SIC ** RECIBO **	999999999	97627	04/09/2015	109.000.00

*** Conceptos Pagados ***

CANT. RENTISTICO	CONCEPTO	Vr. UNIDITARIO	Vr. CONCEPTO
1 50005-01-01 SOLICITUDES	2205 DIVISIONAL SOLICITUD DE PATENTE DE INVENCIÓN CONT. DERE	478.000.00	478.000.00
			\$478.000.00

SON: **CUATROCIENTOS SETENTA Y OCHO MIL PESOS MONEDA CORRIENTE***

Responsable: _____

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 13-158446-00012-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 15-222394-00000-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 7-8

Sede Centro: Carrera 13 No. 27 - 00 Pisos 3,4,5 y 10 Bogotá, D.C.- Colombia

Web: www.sic.gov.co e-mail: info@sic.gov.co Conmutador: (571) 5870000 Fax: (571) 5870284 Línea: 018000-910165 Call Center: (571) 6513240

Septiembre 18 de 2015 - 16:17:57



No. 15-222394-00000-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
 Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
 Act. 411 PRESENTACION Folios: 7-8

ADMISI



No. 13-158448-00012-0000

Fecha: 2015-09-18 17:01:09 Dep. 2020 DIR.NUEVASCR
 Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
 Act. 851 DIVISIONAL Folios: 7-8

PATENTE DE INVENCION ☐MODELO DE UTILIDAD ☐

Art 33 Decisión 486/00

- ☐ Indicación que se solicita una patente.
 - ☐ Datos de identificación del solicitante o de la persona que presenta la solicitud
 - ☐ Descripción de la invención
 - ☐ Dibujos de ser estos pertinentes
 - ☐ Comprobante de pago de las tasas establecidas (De ser el caso formato de descuento)
- Completa ☐ Incompleta ☐

PATENTE DE INVENCION PCT ☐MODELO DE UTILIDAD PCT ☐

Art.33 Decisión 486/00, Circular Única

- ☐ Indicación que se solicita una PCT
 - ☐ Copia de la solicitud en español, tal como fue presentada inicialmente (capítulo descriptivo, reivindicatorio, resumen)
 - ☐ Dibujos de ser estos pertinentes
 - ☐ Comprobante de pago de las tasas establecidas (de ser el caso formato de descuento)
- Completa ☐ Incompleta ☐

DISEÑO INDUSTRIAL ☐

(Art. 119 Decisión 486/00)

- ☐ Indicación que se solicita 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 ☐

(Art. 92 Decisión 486/00)

- ☐ Indicación que se solicita un esquema de trazado
 - ☐ Datos de identificación del solicitante o de la persona que presenta la solicitud
 - ☐ Representación gráfica de un esquema de trazado
 - ☐ Comprobante de pago de las tasas establecidas
- Completa ☐ Incompleta ☐

	Espacio reservado para el adhesivo de radicación
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DIRECCIÓN DE NUEVAS CREACIONES
CONVERSIÓN, DIVISIÓN Y FUSIÓN DE SOLICITUDES

1. Identificación del Trámite

☐ Conversión	☒ División	☐ Fusión
☒ Patente de Invención		
☐ Patente de Modelo de Utilidad		

2. Datos del solicitante

☐ Persona Natural	☒ Persona Jurídica
--	--

NOVARTIS AG

Nombre o denominación / Nombre o razón social

Nombre del representante legal

Tipo de empresa ☐ Micro ☐ Pequeña ☐ Mediana ☐ Otra

Documento de Identificación ☐ C.C. ☐ C.E. ☒ NIT ☐ Otro Número _____

Nacionalidad/Pais de constitución	Dirección del titular	Ciudad
Suiza	Lichtstrasse 35, CH-4056 Basel, Suiza	Basel
Dirección electrónica	No. Fax	Número telefónico

☐	Autorizo expresamente a la Superintendencia de Industria y Comercio para que todas las comunicaciones sean enviadas a través de la dirección de correo electrónico
--------------------------	--

3. Datos del apoderado:

CARLOS R. OLARTE	79.782.747 Bta	74.295
Apellidos y Nombre	Documento de identificación	Tarjeta profesional

Dirección y domicilio	Dirección del titular	Ciudad
Carrera 5 No 34-03 Bogotá D.C.		
Dirección electrónica	No. Fax	Número telefónico
office@mour.com	601-7799	601-7700

En caso de haber presentado poder general para asuntos que se adelanten ante la Delegatura de Propiedad Industrial, sírvase indicar el número de su radicación o protocolo de poder general _____

4. Datos del trámite:

CONVERSION Expediente No. _____ De: _____ A: _____	DIVISION Expediente No. 13-158.446 No. de divisionales _____	FUSION Expediente No. _____ Expediente No. _____
--	---	---

5. Comprobante de Pago No	_____	Fecha	<table><tr><td> </td><td> </td><td> </td></tr></table>			

6. Anexos						
<table><tr><td>X</td></tr><tr><td>X</td></tr><tr><td>X</td></tr><tr><td> </td></tr><tr><td>X</td></tr></table>	X	X	X		X	Comprobante de pago de la tasa para la presentación de la corrección y/o modificación Poder, si fuere el caso con el que se acredita la representación Número de documento que ordena la comisión o fusión o división Documento que contiene la conversión, división o fusión de la solicitud Copia de la solicitud y sus anexos en formato magnético
X						
X						
X						
X						

7. Firma	
CARLOS R. OLARTE	_____
Nombre y apellidos	Firma
79.782.747	74.295
C.C.	Tarjeta Profesional



Espacio reservado para el adhesivo de radicación.

PETITORIO - FORMULARIO ÚNICO DE SOLICITUD DIVISIONAL DE
PATENTE PCT
ENTRADA EN FASE NACIONAL

P2013/000093A

SOLICITUD DE:

1

☒

Patente de Invención.

☐

Patente de Modelo de Utilidad.

☒

Capítulo I.

☐

Capítulo II.

2

SOLICITANTE
(71)

Nombre: NOVARTIS AG

Dirección: Lichtstrasse 35, CH-4056 Basel,
Suiza

Nacionalidad o Domicilio: Suiza

Lugar de Constitución: Suiza

Teléfono: Fax:

E-mail:

IDENTIFICACIÓN

C.C. NIT

C.E. Otro

Cual

Número

REPRESENTANTE
O APODERADO

Nombre: CARLOS R. OLARTE

Dirección: Carrera 5 No 34-03 Bogotá D.C.

Teléfono: 601-7700 Fax: 601-7799

E-mail: office@olartemoure.com

IDENTIFICACIÓN

C.C. X NIT

C.E. Otro

Cual

Número 79782747Bta
TP 74.295

INVENTOR (ES)
(72)

Nombre: VER PAGINA ADJUNTA

Dirección: VER PAGINA ADJUNTA

Nacionalidad o Domicilio: VER PAGINA ADJUNTA

5

PCT (86)

Solicitud Internacional No. PCT/US2011/065030

Fecha Diciembre 15, 2011

Publicación Internacional No. WO 2012/082972 A1

Fecha Junio 21, 2012

6

Título (54) FORMAS CRISTALINAS DE 5-CLORO-N2-(2-ISOPROPOXI-5-METIL-4-PIPERIDIN-4-IL-FENIL)-N4-[2-(PROPAN-2-SULFONIL)-FENIL]-PIRIMIDIN-2,4-DIAMINA.

Clasificación Internacional (51) C07D 401/12; A61K 31/506; A61P 35/00.

Prioridad

SI

☒

NO

☐

(33) País de Origen

US

(32) Fecha

Diciembre 17, 2010

(31) Número de
Solicitud

61/424,194

9

Comprobante de pago No. 14-

Fecha



ANEXOS



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. Adjunto copia simple ver expediente No. 08-102.832



Documento de cesión del inventor al solicitante o a su causante.



Declaraciones. Declaración bajo la regla 4.17 (ii) del PCT.



Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos).



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.



Otros. Búsqueda Internacional



FIGURA CARACTERÍSTICA:



Solicito la concesión de la patente,

NOMBRE: CARLOS R. OLARTE FIRMA: _____
C.C. 79.782.747 Btá T.P. 74.295



Espacio reservado para el adhesivo de radicación.

PETITORIO - FORMULARIO ÚNICO DE SOLICITUD DIVISIONAL DE
PATENTE PCT
ENTRADA EN FASE NACIONAL

P2013/000093A

SOLICITUD DE:

1

☒

Patente de Invención.

☐

Patente de Modelo de Utilidad.

☒

Capítulo I.

☐

Capítulo II.

2

SOLICITANTE
(71)

Nombre: NOVARTIS AG

Dirección: Lichtstrasse 35, CH-4056 Basel,
Suiza

Nacionalidad o Domicilio: Suiza

Lugar de Constitución: Suiza

Teléfono: Fax:

E-mail:

IDENTIFICACIÓN

C.C.

☐

NIT

☐

C.E.

☐

Otro

☐

Cual

Número

REPRESENTANTE
O APODERADO

Nombre: CARLOS R. OLARTE

Dirección: Carrera 5 No 34-03 Bogotá D.C.

Teléfono: 601-7700 Fax: 601-7799

E-mail: office@olartemoure.com

IDENTIFICACIÓN

C.C.

☒

NIT

☐

C.E.

☐

Otro

☐

Cual

Número 79782747Bta
TP 74.295

INVENTOR (ES)
(72)

Nombre: VER PAGINA ADJUNTA

Dirección: VER PAGINA ADJUNTA

Nacionalidad o Domicilio: VER PAGINA ADJUNTA

5

PCT (86)

Solicitud Internacional No. PCT/US2011/065030

Fecha Diciembre 15, 2011

Publicación Internacional No. WO 2012/082972 A1

Fecha Junio 21, 2012

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Título (54) FORMAS CRISTALINAS DE 5-CLORO-N2-(2-ISOPROPOXI-5-METIL-4-PIPERIDIN-4-IL-FENIL)-N4-[2-(PROPAN-2-SULFONIL)-FENIL]-PIRIMIDIN-2,4-DIAMINA.

Clasificación Internacional (51) C07D 401/12; A61K 31/506; A61P 35/00.

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NO

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(33) País de Origen

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(32) Fecha

Diciembre 17, 2010

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61/424,194

9

Comprobante de pago No. 14-

Fecha



ANEXOS



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. Adjunto copia simple ver expediente No. 08-102.832



Documento de cesión del inventor al solicitante o a su causante.



Declaraciones. Declaración bajo la regla 4.17 (ii) del PCT.



Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos).



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.



Otros. Búsqueda Internacional



FIGURA CARACTERÍSTICA:



Solicito la concesión de la patente,

NOMBRE: CARLOS R. OLARTE FIRMA: _____
C.C. 79.782.747 Btá T.P. 74.295

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Nota del traductor:

El documento adjunto de poder de Novartis AG a Carlos R. Olarte y/o J. Ian Raisbeck y/o Ana Maria Frieri y/o Juan Guillermo Moure y/o Natalia Castro lleva los siguientes datos en inglés.

CERTIFICACIÓN NOTARIAL

1. En esta fecha, día 30 de Agosto de 2006, yo, el suscrito Notario Público certifico por medio del presente la autenticidad de las firmas del señor Arthur Canonica, ciudadano de Corticiasca, Suiza, residente en Wisen/SO, Suiza, y del Sr. Pascal Traub, ciudadano de Riehen, Suiza, residente en Basilea, Suiza, ambos personas mayores de edad y con dirección comercial en Lichstrasse 35, 4056, Basilea, Suiza. La autenticidad de la firmas fue establecida por medio de la comparación.
2. Además, yo, el Notario Público, certifico por el presente que las anteriores personas han ejecutado el anterior documento como apoderados de Novartis AG.
3. Además, yo, el Notario Público certifico por el presente que Novartis AG, con su principal lugar de negocios en Basilea, Suiza, está debidamente constituida, está actualmente vigente y que los propósitos para los cuales se otorgó el Documento de Poder están dentro del alcance de sus propósitos corporativos.



4. Además, yo, el Notario Público, certifico por el presente que las anteriores personas tienen la autoridad para ejecutar el documento de Poder y que por este instrumento, su representación es legal.

La base para mis certificaciones de los puntos 2, 3 y 4 fue la exhibición de los siguientes documentos auténticos:

- Documento de Poder de Novartis AG fechado el 19 de junio de 2006 y
- Extracto del Registro de Comercio del Cantón de la ciudad de Basilea para Novartis AG, en Basilea, fechado el 25 de enero de 2006.

Basilea, Suiza, este día 30 de Agosto de 2006.

(Firmado) Dr. Matthias Staehelin, Notario Público del Cantón de la ciudad de Basilea, Suiza.

Mi licencia vence el 11 de Marzo de 2009.

Hay una Apostilla de Suiza, firmada por Heidi Fischer, bajo el No. 8049/13584.



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

Certificación:

Certifico que la presente es una traducción verdadera y completa del documento adjunto: "Novartis"

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Power of Attorney

The undersigned,

domiciled in

NOVARTIS AG

Lichtstrasse 35, CH-4056 Basel / Switzerland

by means of these presents hereby grants to **Carlos R. Olarte and/or J. Ian Raisbeck and/or Ana María Frieri 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 and collect refunds. 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.

Signature/Firma:

Date/Fecha: June 27, 2006

City/Country/Ciudad,País: Basel, Switzerland

Poder

El suscrito,

domiciliado en

por medio del presente otorga a **Carlos R. Olarte y/o J. Ian Raisbeck y/o Ana María Frieri y/o Juan Guillermo Moure y/o Natalia Castro** poder especial, 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 los 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 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.


Arthur Canonica


Pascal Traub

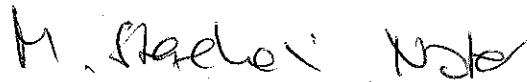
Attestation

- 1 On this date, the 30th (thirtieth) day of August 2006 (two thousand and six), I, the undersigned Notary Public certify herewith the authenticity of the signatures of **Mr. Arthur Canonica**, citizen of Corticiasca, Switzerland, residing in Wisen/SO, Switzerland and of **Mr. Pascal Traub**, citizen of Riehen, Switzerland, residing in Basel, Switzerland, both of legal age and with business address at, Lichtstrasse 35, 4056 Basel, Switzerland. The authenticity of the signatures was established by means of comparison.
- 2 Further, I, the Notary Public certify herewith that the foregoing persons have executed the foregoing document as proxy holders for Novartis AG.
- 3 Further, I, the Notary Public certify herewith that Novartis AG, having its principal place of business located in Basel / Switzerland, 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 Further, I, the Notary Public certify herewith that the foregoing persons have the authority to execute the Power of Attorney and that for this instrument their representation is legal.

The foundation for my certifications contained in points 2 (two), 3 (three) and 4 (four) was the exhibition of the following authentic documents:

- Power of Attorney by Novartis AG dated June 19 (nineteen), 2006 (two thousand and six); and
- Extract from the Register of Commerce of the Canton of Basel-City for Novartis AG, in Basel, dated January 25 (twenty-five), 2006 (two thousand and six).

BASEL, Switzerland, this 30th (thirtieth) day of August 2006 (two thousand and six)



Dr. Matthias Staehelin, Notary Public
in the Canton of Basel-City, Switzerland

My license expires on March 11 (eleven),
2009 (two thousand and nine).

APOSTILLE

(Hague Convention of October 5th, 1961)

1. Country: Switzerland (Schweiz / Suisse)

This official document

2. is signed by *P. in*

3. in his/her function as *St. Stettelin*

4. and certified by the seal of the *St. Stettelin*

Certified 20. Aug. 2006

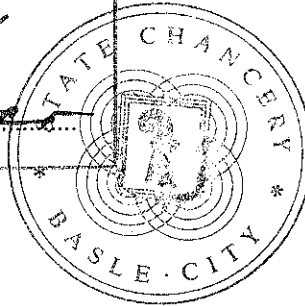
5. in Basel (Bâle) 6. on

7. by the State Chancery of the Canton of Basel-Stadt

8. no. *2009/18584*

9. Seal / stamp: 10. Signature: *Fischer*

Heidi Fischer





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

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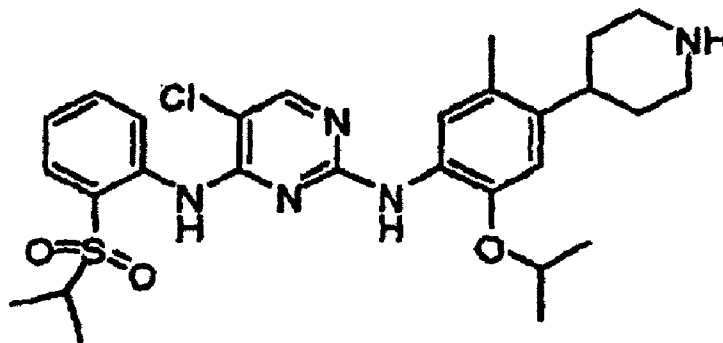
Declarations under Rule 4.17:

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))

Published:

— with international search report (Art. 21(3))

(54) Title: CRYSTALLINE FORMS OF 5-CHLORO-N2-(2-ISOPROPOXY-5-METHYL-4-PIPERIDIN-4-YL-PHENYL)-N4[2-(PROPANE-2-SULFONYL)-PHENYL]-PYRIMIDINE-2,4-DIAMINE



(57) Abstract: The present invention describes specific crystalline forms of 5-chloro-N2-(2-isopropoxy-5-methyl-4-(piperidin-4-yl)-phenyl)-N4[2-(isopropylsulfonyl)phenyl]-2,4-diamine. The present invention further relates to methods for preparing said crystalline forms, pharmaceutical compositions comprising said crystalline forms, and methods of using said crystalline forms and pharmaceutical compositions to treat disease.

CRYSTALLINE FORMS OF 5-CHLORO-N2-(2-ISOPROPOXY-5-METHYL-4-PIPERIDIN-4-YL-PHENYL)-N4-[2-(PROPANE-2-SULFONYL)-PHENYL]-PYRIMIDINE-2, 4-DIAMINE

5

Field of the Invention

The present invention is directed to crystalline forms of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine, methods of making the same, pharmaceutical compositions comprising the same and methods of treatment using the same.

10

Background

Polymorphism denotes the existence of more than one crystalline form of a substance. This ability of a chemical substance to crystallize in more than one crystalline form can have a profound effect on the shelf life, solubility, formulation properties, and processing properties of a drug. In addition, the action of a drug can be affected by the polymorphism of the drug molecule. Different polymorphs can have different rates of uptake in the body, leading to lower or higher biological activity than desired. In extreme cases, an undesired polymorph can even show toxicity. The occurrence of an unknown crystalline form during manufacture can have a significant impact.

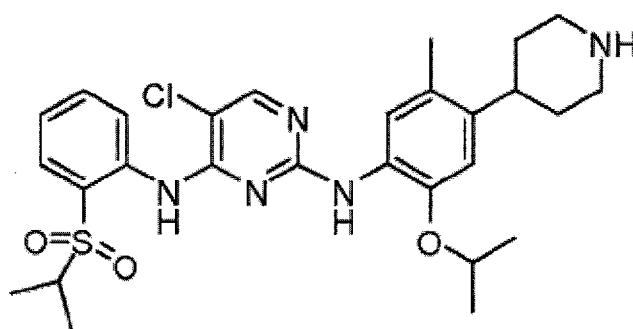
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Understanding and controlling polymorphism, then, gives a decided advantage in bringing new drugs to the marketplace. First and foremost, predicting any possible polymorphs for a drug product can be used to diminish the possibility of contamination during a drug's manufacture or storage by other polymorphic forms. Failure to catch contamination can have life-threatening consequences in some cases. Crystallizing an unintended polymorph during manufacture can mean weeks or even months of production downtime while scientists find and correct the cause of the new crystalline form or go through another round of testing to obtain approval for the new crystalline form.

25

Second, understanding which crystalline forms of a drug are possible in certain cases allows researchers to maximize the desired properties of a compound, such as solubility, formulation properties, processing properties, and shelf life. Understanding these factors early in the development of a new drug may mean a more active, more stable, or more cheaply manufactured drug.

The compound 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine, in the form of a free base, of formula



(I)

is an anaplastic lymphoma kinase (ALK) inhibitor, a member of the insulin receptor super family of receptor tyrosine kinases. Compound I was originally described in WO 2008/073687 A1 as Example 7, compound 66.

WO 2008/073687 A1, however, provides no information about crystalline forms of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine or its corresponding salts. Crystalline forms of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine have been discovered, which are useful in treating diseases which respond to inhibition of anaplastic lymphoma kinase activity, focal adhesion kinase (FAK), zeta-chain-associated protein kinase 70 (ZAP-70) insulin-like growth factor (IGF-1R or a combination thereof. The crystalline forms exhibit new physical properties that may be exploited in order to obtain new pharmacological properties, and that may be utilized in the drug

product development of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Summary of the Invention

5 The present invention provides substantially pure crystalline forms of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

The present invention also provides a pharmaceutical composition comprising: (a) a therapeutically effective amount of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-
10 2, 4-diamine; and (b) at least one pharmaceutically acceptable carrier.

The present invention also provides a method for the preparation of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine which comprises the step of: reacting 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-
15 phenyl]-pyrimidine-2, 4-diamine dihydrochloride in a solvent with at least two equivalents of aqueous sodium hydroxide.

The present invention also provides a method for the preparation of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine which comprises the step of: heating a
20 mixture of two crystalline forms of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine in a solvent.

The present invention also provides a method for the treatment of disorders mediated by anaplastic lymphoma kinase, comprising administering to a patient in need of such treatment an effective amount of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.
25

The present invention also provides the use of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-

phenyl]-pyrimidine-2, 4-diamine for the preparation of a medicament for the treatment of disorders mediated by anaplastic lymphoma kinase.

The present invention also provides a method for the treatment of disorders selected from benign or malignant tumor; a cancer selected from anaplastic large cell lymphoma; non-Hodgkin's lymphoma; an inflammatory myofibroblastic tumor; a neuroblastoma; sarcoma; lung, non-small cell lung cancer; bronchus; prostate; breast (including sporadic breast cancers and sufferers of Cowden disease); pancreas; gastrointestinal cancer; colon; rectum; colon carcinoma; colorectal adenoma; thyroid; liver; intrahepatic bile duct; hepatocellular; adrenal gland; stomach; gastric; glioma; glioblastoma; endometrial; melanoma; kidney; renal pelvis; urinary bladder; uterine corpus; uterine cervix; vagina; ovary; multiple myeloma; esophagus; a leukaemia; acute myelogenous leukemia; chronic myelogenous leukemia; lymphocytic leukemia; myeloid leukemia; brain; a carcinoma of the brain; oral cavity and pharynx; larynx; small intestine; and melanoma, comprising administering to a patient in need of such treatment an effective amount of a crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Brief Description of the Drawings

Figure 1 depicts X-ray powder diffraction pattern for crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Figure 2 depicts the differential scanning calorimetry curve for crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Figure 3 depicts the thermogravimmetric plot for crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Figure 4 depicts X-ray powder diffraction pattern for crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Figure 5 depicts the differential scanning calorimetry curve for crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Figure 6 depicts the thermogravimetric plot for crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine.

Detailed Description of the Invention

The compound 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine is obtained in distinct crystalline forms. These "crystalline form(s)" (or "crystalline modification(s)" or "polymorphic form(s)" or "polymorph(s)", as the terms will be used interchangeably herein) differ with respect to thermodynamic stability, physical parameters, x-ray structure and methods of preparation. In addition, "amorphous" refers to a disordered solid state. It should be noted that different samples of a particular crystalline form will share the same major X-ray powder diffraction (XRPD) peaks, but that there can be variation in powder patterns with regard to minor peaks. In addition, the term "about" with regard to XRPD maxima values (in degrees) generally means within 0.3°, more preferably within 0.2°, and most preferably within 0.1° of the given value. Alternatively, the term "about" means (in this and all contexts) within an accepted standard of error of the mean, when considered by one of ordinary skill in the art. As used herein, the term "substantially pure" means that more than 80% of one crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine or salt thereof is present or isolated, preferably at least 85%, more preferably at least 90%, and most preferably at least 95% of one of the crystalline forms described herein is present.

In one embodiment, a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine is isolated, referred to as crystalline form A. Form A of the free base is relatively non-hygroscopic at 84% relative humidity (RH) and exhibits minor increase in moisture uptake at 93% RH. It has good solubility at pH 1, fair solubility in water and good solubility in organic solvents (11 mg/mL in pH 1, 0.21 mg/mL in water and 40 mg/mL in methanol, respectively). It is converted to a hydrochloride salt (non-stoichiometric) in pH 1 (0.1N HCl) solution over 72 hour. The pH of 1% suspension in water is 6.86.

The XRPD of crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibits diffraction peaks having maxima at diffraction angles 7.2°, 8.1°, 10.8°, 12.0°, 12.4°, 13.4°, 14.4°, 14.8°, 15.7°, 16.9°, 17.7°, 18.5°, 19.0°, 19.5°, 20.0°, 20.3°, 21.1°, 21.6°, 22.4°, 22.6°, 23.0°, 24.1°, 24.5°, 25.5°, 26.0°, 26.2°, 27.0°, 27.3°, 28.3°, 29.0°, 29.1°, 30.6°, 31.3°, 32.8°, 33.5°, 34.2° and 36.4° (2θ degrees), as summarized by the XRPD pattern in Figure 1.

Crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibits the following thermal parameters: melting point, T_m (onset) 174° C as determined by differential scanning calorimetry at a scanning rate of 10° C/min. (Figure 2), decomposition point, T > 250° C, and a weight loss on drying of 0.1% at 200° C, as determined by thermogravimetric analysis and summarized in Figure 3.

The Fourier Transform Infrared (FT-IR) spectrum of crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibits main bands (in units of wavenumbers, cm⁻¹) at 3440.4, 3318.9, 2973.7, 2931.3, 2921.7, 1596.8, 1562.1, 1498.4, 1442.5, 1409.7, 1382.7, 1311.4, 1284.4, 1270.9, 1251.6, 1224.6, 1139.7, 1126.2, 1139.7, 1126.2, 1105.0, 1081.9, 1049.1, 1020.2, 1012.5, 952.7, 937.3, 894.8, 877.5, 860.1, 848.5, 817.7, 798.4, 781.0, 763.7, 756.0, 732.8, 686.6, 665.3, 644.1, 586.3 and 543.8.

In another embodiment, a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine is isolated, referred to as crystalline form B.

The XRPD of crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibits diffraction peaks having maxima at diffraction angles 5.1°, 5.5°, 5.6°, 9.5°, 9.6°, 10.1°, 11.0°, 11.8°, 12.1°, 12.6°, 13.7°, 14.5°, 14.9°, 15.2°, 16.1°, 16.6°, 16.7°, 17.0°, 17.1°, 17.5°, 17.7°, 18.0°, 18.8°, 19.0°, 19.3°, 19.5°, 20.5°, 20.9°, 21.5°, 21.9°, 22.1°, 22.4°, 22.8°, 23.2°, 23.7°, 23.9°, 24.3°, 24.5°, 24.8°, 25.1°, 25.4°, 25.9°, 26.4°, 26.8°, 27.8°, 28.1°, 28.6°, 29.1°, 29.6°, 29.8°, 30.6°, 31.6°, 32.7°, 33.5°, 34.2°, 35.4°, 35.6° and 36.8° (2θ degrees), as summarized by the XRPD pattern in Figure 4.

Crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibits the following thermal parameters: melting point, T_m (onset) 162° C as determined by differential scanning calorimetry at a scanning rate of 10° C/min. (Figure 5), decomposition point, T > 250° C, and a weight loss on drying of 0.05% at 200° C, as determined by thermogravimetric analysis and summarized in Figure 6.

The Fourier Transform Infrared (FT-IR) spectrum of crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibits main bands (wavenumbers, cm⁻¹) at 3418.7, 3309.5, 3202.3, 2976.2, 2936.3, 2806.9, 2731.8, 1683.9, 1652.8, 1598.4, 1568.9, 1507.0, 1483.5, 1447.1, 1411.0, 1314.9, 1288.1, 1261.1, 1220.8, 1195.7, 1170.8, 1140.1, 1124.6, 1083.2, 1053.3, 1010.1, 947.1, 874.5, 776.0, 758.7, 734.5, 706.5, 678.5, 652.1, 586.3, 544.7, 519.1, 472.6, and 456.8.

In an exemplary embodiment, the present invention provides a method for the preparation substantially pure crystalline forms of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine. The crystalline forms are prepared from a solvent or mixed solvents comprising a good solvent, in which the compound is readily soluble, and a poor solvent, in which it is more sparingly soluble, may also be employed provided that crystallization from the mixture is possible using the selected solvent mixture.

Examples of good solvents include methanol, ethanol and isopropanol, formic acid, acetic acid, ethyl acetate, tetrahydrofuran and acetone. An example of a poor solvent is *e.g.*, water.

In one embodiment, crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine is prepared
5 by reacting 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine dihydrochloride in aqueous acetone with at least two equivalents of aqueous sodium hydroxide. The ratio of acetone:water usefully employed in accordance with the invention ranges from 1:1 to 5:1 and 1:1 to 1:5 (volume:volume, v/v), including 1:1 and 3:1. The reaction temperature ranges from 20° to 70° C, including 55° C.

10 In one embodiment, the crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine contains less than 1% by weight total impurities. In another embodiment, the polymorph form A contains less than 0.5% by weight total impurities. In yet another embodiment, the polymorph form A contains less than 0.1 % by weight total impurities.

15 In another embodiment, crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine is prepared by reacting 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine with aqueous hydrochloric acid and subsequently adding sodium hydroxide. The reaction temperature ranges from 20° C to 70° C

20 In another embodiment, crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine is converted to crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine by adding a small amount of crystalline form A (1% by weight or less, referred to as seeding) to a suspension or solution of form B of 5-
25 Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine in aqueous acetone. The temperature usefully employed for seeding ranges from 20-40° C.

As used herein, the term “seed” can be used as a noun to describe one or more crystals of a crystalline compound of formula I. The term “seed” can also be used as a verb to describe the

act of introducing said one or more crystals of a crystalline compound of formula I into an environment (including, but not limited to *e.g.*, a solution, a mixture, a suspension, or a dispersion) thereby resulting in the formation of more crystals of the crystalline compound of formula I.

5 In another embodiment, crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine is converted to crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine by heating a suspension or solution containing crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-
10 N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine in aqueous acetone. Mixed solvents usefully employed include, for example, acetone/water and ethanol/water. In a preferred embodiment, the ratio of acetone:water usefully employed ranges from 1:1 to 5:1 (volume:volume, v/v), including 1:1 and 3:1. The reaction temperature ranges from 30° to 70° C, including 50° C.

15 In an exemplary embodiment, a pharmaceutical composition is provided comprising: (a) a therapeutically effective amount of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine; and (b) at least one pharmaceutically acceptable carrier. In a preferred
20 embodiment, the pharmaceutical composition comprises: (a) a therapeutically effective amount of a substantially pure crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine; and (b) at least one pharmaceutically acceptable carrier.

 The at least one pharmaceutically acceptable carrier is in the form of a diluent, vehicle or excipient and can readily be selected by one of ordinary skill in the art and will be determined by
25 the desired mode of administration. Illustrative examples of suitable modes of administration include oral, nasal, parenteral, topical, transdermal, and rectal. The pharmaceutical compositions of this invention may take any pharmaceutical form recognizable to the skilled artisan as being suitable. Suitable pharmaceutical forms include solid, semisolid, liquid, or lyophilized formulations, such as tablets, powders, capsules, suppositories, suspensions, liposomes, and
30 aerosols.

In an exemplary embodiment, use of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine for the preparation of a medicament for the treatment of disorders mediated by anaplastic lymphoma kinase is provided. In a preferred embodiment, the

5 medicament comprises: (a) a therapeutically effective amount of a substantially pure crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine. The medicament is useful in treating diseases which respond to inhibition of anaplastic lymphoma kinase activity, focal adhesion kinase (FAK), zeta-chain-associated protein kinase 70 (ZAP-70) insulin-like growth factor (IGF-1R and

10 combinations thereof. The diseases are selected from benign or malignant tumor; a cancer selected from anaplastic large cell lymphoma; non-Hodgkin's lymphoma; an inflammatory myofibroblastic tumor; a neuroblastoma; sarcoma; lung; bronchus; prostate; breast (including sporadic breast cancers and sufferers of Cowden disease); pancreas; gastrointestinal cancer; colon; rectum; colon carcinoma; colorectal adenoma; thyroid; liver; intrahepatic bile duct; hepatocellular; adrenal gland; stomach; gastric; glioma; glioblastoma; endometrial; melanoma; kidney; renal pelvis; urinary bladder; uterine corpus; uterine cervix; vagina; ovary; multiple myeloma; esophagus; a leukaemia; acute myelogenous leukemia; chronic myelogenous leukemia; lymphocytic leukemia; myeloid leukemia; brain; a carcinoma of the brain; oral cavity and pharynx; larynx; small intestine; and melanoma. A "therapeutically effective amount" is
15 intended to mean the amount of the inventive crystalline form that, when administered to a subject in need thereof, is sufficient to effect treatment for disease conditions alleviated by the inhibition of protein kinase activity. The amount of a given compound of the invention that will be therapeutically effective will vary depending upon factors such as the disease condition and the severity thereof, the identity of the subject in need thereof, etc., which amount may be
20 routinely determined by artisans of ordinary skill in the art. Preferably, more than 80%, more preferably at least 85%, still more preferably at least 90%, and most preferably at least 95%, of the crystalline form administered is of one of the inventive forms. As noted above, illustrative modes of administration include oral, nasal, parenteral, topical, transdermal, and rectal. Administration of the crystalline form may be accomplished by administration of a
25 pharmaceutical composition of this invention or via any other effective means.
30

Specific embodiments of the invention will now be demonstrated by reference to the following examples. It should be understood that these examples are disclosed solely by way of illustrating the invention and should not be taken in any way to limit the scope of the present invention.

5

EXAMPLE 1

Preparation of Form A of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine

10

5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine di-hydrochloride salt

15

The compound 2-isopropoxy-5-methyl-4-(piperidin-4-yl) aniline dihydrochloride (33.00 g, 85.25 mmol) and 2,5-dichloro-N-(2-(isopropyl sulfonyl)phenyl)pyrimidin-4-amine (32.53 g) was added to a 3-necked 500-mL round-bottomed flask equipped with mechanical stirring, thermocouple, reflux condenser and N₂ inlet-outlet. A solvent, 2-propanol (255.0 g, 325 mL), was added and the mixture to heated to reflux at 82±2 °C and stirred for at least 14 hours. The mixture was cooled to 22±3 °C over 1 hour and stirred at 22±3 °C for 3 hours. The resulting solids were filtered and rinsed with 3 x 40 g (3 x 51 mL) of 2-propanol. The solids were dried at 50±5 °C/10 mbar for 16 hours to yield 44.63 g of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine di-hydrochloride salt.

20

Chemical Purity (as determined by HPLC): 97.3%. Corrected yield: 71.6%. LOD = 11.60%.

25

The dihydrochloride salt was recrystallized using acetone:water (10:1,v/v). Chemical Purity (as determined by HPLC): 98.8%.

Form A of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine

7.00 g of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-yl) phenyl)-N-(2-(isopropylsulfonyl)phenyl)-2,4-diamine di-hydrochloride and 21.0 g of acetone:water (3:1, v/v) was added to a dry and clean crystallizer at ambient temperature. The mixture was heated to 55 ± 3 °C in about 20 minutes to obtain a clear solution. The hot solution was filtered and 2.6 g of acetone and water was added to the mixture. While heating was maintained, 14.69 g (about 58% by weight) of aqueous NaOH solution was added over a period of about 0.5 hour. The reaction mixture was maintained at 55 ± 3 °C for an additional 2 hours to yield an off-white slurry. An additional 10.82 g (about 58% by weight) of aqueous NaOH solution was added to the hot solution over a period of 1.5 hours to yield a thick off-white slurry. The slurry was cooled to 20 ± 3 °C over a period of about 45 minutes and 47.0 g of deionized (DI) water was added over about 30 minutes and the off-white slurry was stirred at 20 ± 3 °C for 1 hour. The slurry was filtered and rinsed with 2×25.0 g of DI water. The wet cake was dried about 17 hours in a vacuum oven at 50 ± 3 °C and 10 mbar under a N₂ purge to yield 6.06 g off-white or tan solid, 5.30 g of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-yl) phenyl)-N-(2-(isopropylsulfonyl)phenyl)-2,4-diamine. Yield: 87.5%. Form A was identified and confirmed by its corresponding XRPD pattern, FT-IR and thermal parameters.

EXAMPLE 2

Preparation of Form B of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-yl)phenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine

5.58 g of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-yl) phenyl)-N-(2-(isopropylsulfonyl)phenyl)-2,4-diamine was dissolved in 50 mL of 1.0 N HCl at 30-40° C to afford a clear solution. 200 mL of 0.3 N NaOH was added this clear solution dropwise over 20 minutes at 20-23° C. A cloudy mixture was obtained, which was heated with stirring at 40-42° C for 2 hours and subsequently heated to 50-55° C for 2 hours. The resulting slurry was cooled to room temperature and the slurry was filtered. The wet cake was washed with 3x20 mL of water and dry under vacuum to obtain 5.30 g off white solid. Yield: 95%. Form B was identified and confirmed by s corresponding XRPD pattern, FT-IR and thermal parameters.

EXAMPLE 3

Preparation of Form A of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-
(isopropylsulfonyl)phenyl)-2,4-diamine by seeding a suspension of Form B of 5-chloro-N-(2-
isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine with
Form A

A small amount of crystalline form A of 5-chloro-N-(2-isopropoxy-5-methyl-4-
 (piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine (0.1-1.0 % by weight) was
 added to a suspension of crystalline form B of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-
 4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine in aqueous acetone with stirring at
 room temperature. The crystalline form was analyzed by its corresponding turbidity profile or
 by XRPD. The amount of substantially pure form A obtained is influenced by the solvent, ratio
 of acetone to water by volume and the amount of "seed" A used, as summarized in Table 1.

Table 1. Seeding of Crystalline Form B with Form A.

Solvent System	Form A "Seed"	XRPD after 24 hours
Acetone: water (v/v)	(weight %)	
1:9	1.0	Form B + Form A
1:9	0.1	Form B
3:7	1.0	Form A
3:7	0.1	Form B + Form A
1:1	1.0	Form A (at 2 hours)
1:1	0.1	Form A (at 4 hours)

EXAMPLE 4

Conversion of Form B of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-
(isopropylsulfonyl)phenyl)-2,4-diamine to Form A of 5-chloro-N-(2-isopropoxy-5-methyl-4-

(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine by heating in an aqueous solvent

A suspension of crystalline form B of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine was heated in an aqueous solvent with stirring. The conversion of crystalline form B to crystalline form A was analyzed by its corresponding turbidity profile or by XRPD. The amount of substantially pure form A obtained and its corresponding time of conversion is influenced by the solvent system and temperature, as summarized in Table 2.

Table 2. Conversion of Crystalline Form B to Crystalline Form A.

Solvent System (v/v)	Temp. (°C)	Conv. Time (hours)	Induction Time (hours)	Yield (%)
1:1 acetone:water	35	> 3	-	-
1:1 acetone:water	40	2	1	99.1
1:1 acetone:water	50	1.5	0.1	97.6
1:1 ethanol:water	35	2	38	> 99
1:1 ethanol:water	50	1	4	> 99

Claims:

1. A crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibiting one or more X-ray powder diffraction peaks having maxima at diffraction angles selected from 7.2°, 8.1°, 10.8°, 12.0°, 12.4°, 13.4°, 14.4°, 14.8°, 15.7°, 16.9°, 17.7°, 18.5°, 19.0°, 19.5°, 20.0°, 20.3°, 21.1°, 21.6°, 22.4°, 22.6°, 23.0°, 24.1°, 24.5°, 25.5°, 26.0°, 26.2°, 27.0°, 27.3°, 28.3°, 29.0°, 29.1°, 30.6°, 31.3°, 32.8°, 33.5°, 34.2° and 36.4° (2θ degrees).
2. The crystalline form of claim 1, having a melting point of 174° C, as determined by differential scanning calorimetry.
3. The crystalline form of claim 1, having a decomposition point greater than 250° C and a weight loss on drying of 0.1% at 200° C, as determined by thermogravimetric analysis.
4. The crystalline form of claim 1, having characteristic infrared absorption bands at 3440.4, 3318.9, 2973.7, 2931.3, 2921.7, 1596.8, 1562.1, 1498.4, 1442.5, 1409.7, 1382.7, 1311.4, 1284.4, 1270.9, 1251.6, 1224.6, 1139.7, 1126.2, 1139.7, 1126.2, 1105.0, 1081.9, 1049.1, 1020.2, 1012.5, 952.7, 937.3, 894.8, 877.5, 860.1, 848.5, 817.7, 798.4, 781.0, 763.7, 756.0, 732.8, 686.6, 665.3, 644.1, 586.3 and 543.8 (in units of wavenumbers, cm⁻¹).
5. The crystalline form of claim 1, having less than 1.0 % by weight total impurities.
6. The crystalline form of claim 1, having less than 0.5% by weight total impurities.
7. The crystalline form of claim 1, having less than 0.1% by weight total impurities.
8. A crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine exhibiting one or more X-ray powder diffraction peaks having maxima at diffraction angles selected from 5.1°, 5.5°, 5.6°, 9.5°, 9.6°, 10.1°, 11.0°, 11.8°, 12.1°, 12.6°, 13.7°, 14.5°, 14.9°, 15.2°, 16.1°, 16.6°, 16.7°, 17.0°, 17.1°, 17.5°, 17.7°, 18.0°, 18.8°, 19.0°, 19.3°, 19.5°, 20.5°, 20.9°, 21.5°, 21.9°, 22.1°,

22.4°, 22.8°, 23.2°, 23.7°, 23.9°, 24.3°, 24.5°, 24.8°, 25.1°, 25.4°, 25.9°, 26.4°, 26.8°, 27.8°, 28.1°, 28.6°, 29.1°, 29.6°, 29.8°, 30.6°, 31.6°, 32.7°, 33.5°, 34.2°, 35.4°, 35.6° and 36.8° (2θ degrees).

9. The crystalline form of claim 8, having a melting point of 162° C, as determined by differential scanning calorimetry.
10. The crystalline form of claim 8, having a decomposition point greater than 250° C and a weight loss on drying of 0.05% at 200° C, as determined by thermogravimmetric analysis.
11. The crystalline form of claim 8, having characteristic infrared absorption bands at 3418.7, 3309.5, 3202.3, 2976.2, 2936.3, 2806.9, 2731.8, 1683.9, 1652.8, 1598.4, 1568.9, 1507.0, 1483.5, 1447.1, 1411.0, 1314.9, 1288.1, 1261.1, 1220.8, 1195.7, 1170.8, 1140.1, 1124.6, 1083.2, 1053.3, 1010.1, 947.1, 874.5, 776.0, 758.7, 734.5, 706.5, 678.5, 652.1, 586.3, 544.7, 519.1, 472.6, and 456.8 (in units of wavenumbers, cm⁻¹).
12. The crystalline form of claim 8, having less than 1.0% by weight total impurities.
13. The crystalline form of claim 8, having less than 0.5% by weight total impurities.
14. The crystalline form of claim 8, having less than 0.1% by weight total impurities.
15. A pharmaceutical composition comprising a crystalline form of claim 1, and a pharmaceutically acceptable carrier.
16. A pharmaceutical composition comprising a crystalline form of claim 8, and a pharmaceutically acceptable carrier.
17. A method for the preparation of a crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine which comprises the step of: reacting 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine dihydrochloride in a solvent with at least two equivalents of aqueous sodium hydroxide.
18. The method of claim 17, wherein the solvent is acetone:water (3:1) by volume.

19. The method of claim 18, further comprising heating the reactants at a temperature ranging from 30-70° C.
20. The method of claim 18, further comprising heating the reactants at a temperature of 55° C.
21. A method for converting crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine to crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine by adding a small amount of crystalline form A to a suspension of form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine in a solvent.
22. The method of claim 21, wherein the amount of form A added is 1.0 % by weight or less.
23. The method of claim 22, the solvent is acetone:water (1:1) by volume at a temperature ranging from 20-40° C.
24. A method for converting crystalline form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine to crystalline form A of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine by heating a suspension of form B of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine in a solvent.
25. The method of claim 24, the solvent is acetone:water 1:1 to 5:1 by volume at temperature ranging from 30° to 70° C.
26. The method of claim 24, the solvent is acetone:water 1:1 by volume at temperature of 50° C.
27. Use of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine

according to claim 1 for the preparation of a medicament for the treatment of disorders mediated by anaplastic lymphoma kinase.

28. A method for the treatment of disorders mediated by anaplastic lymphoma kinase,
5 comprising administering to a patient in need of such treatment an effective amount of a substantially pure crystalline form of 5-Chloro-N2-(2-isopropoxy-5-methyl-4-piperidin-4-yl-phenyl)-N4-[2-(propane-2-sulfonyl)-phenyl]-pyrimidine-2, 4-diamine according to claim 1.
29. The method of claim 28 wherein the disorder is a cancer selected from anaplastic large cell
10 lymphoma; non-Hodgkin's lymphoma; an inflammatory myofibroblastic tumor; a neuroblastoma; sarcoma; lung; bronchus; prostate; breast (including sporadic breast cancers and sufferers of Cowden disease); pancreas; gastrointestinal cancer; colon; rectum; colon carcinoma; colorectal adenoma; thyroid; liver; intrahepatic bile duct; hepatocellular; adrenal gland; stomach; gastric; glioma; glioblastoma; endometrial; melanoma; kidney;
15 renal pelvis; urinary bladder; uterine corpus; uterine cervix; vagina; ovary; multiple myeloma; esophagus; a leukaemia; acute myelogenous leukemia; chronic myelogenous leukemia; lymphocytic leukemia; myeloid leukemia; brain; a carcinoma of the brain; oral cavity and pharynx; larynx; small intestine; and melanoma.

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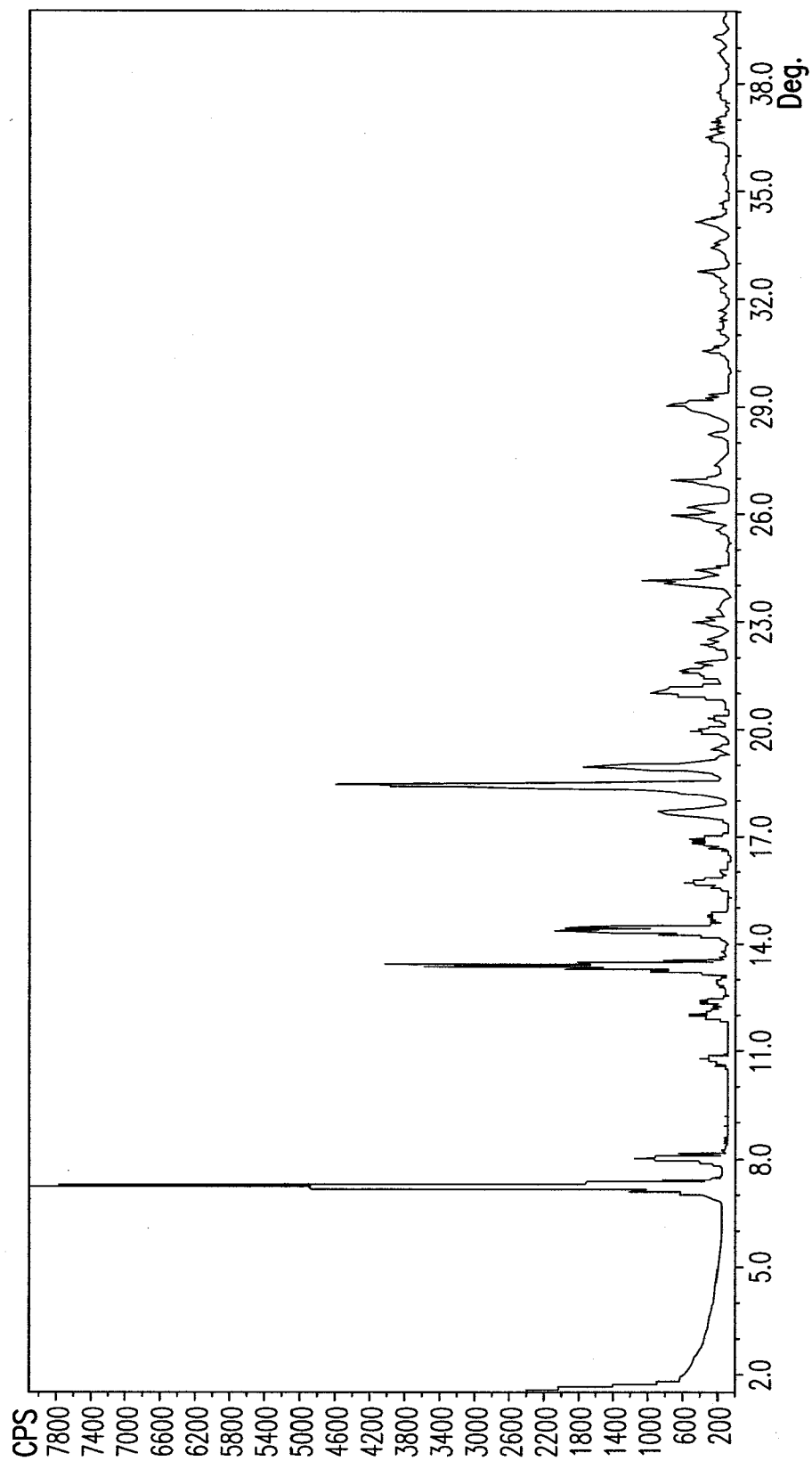


FIG.1

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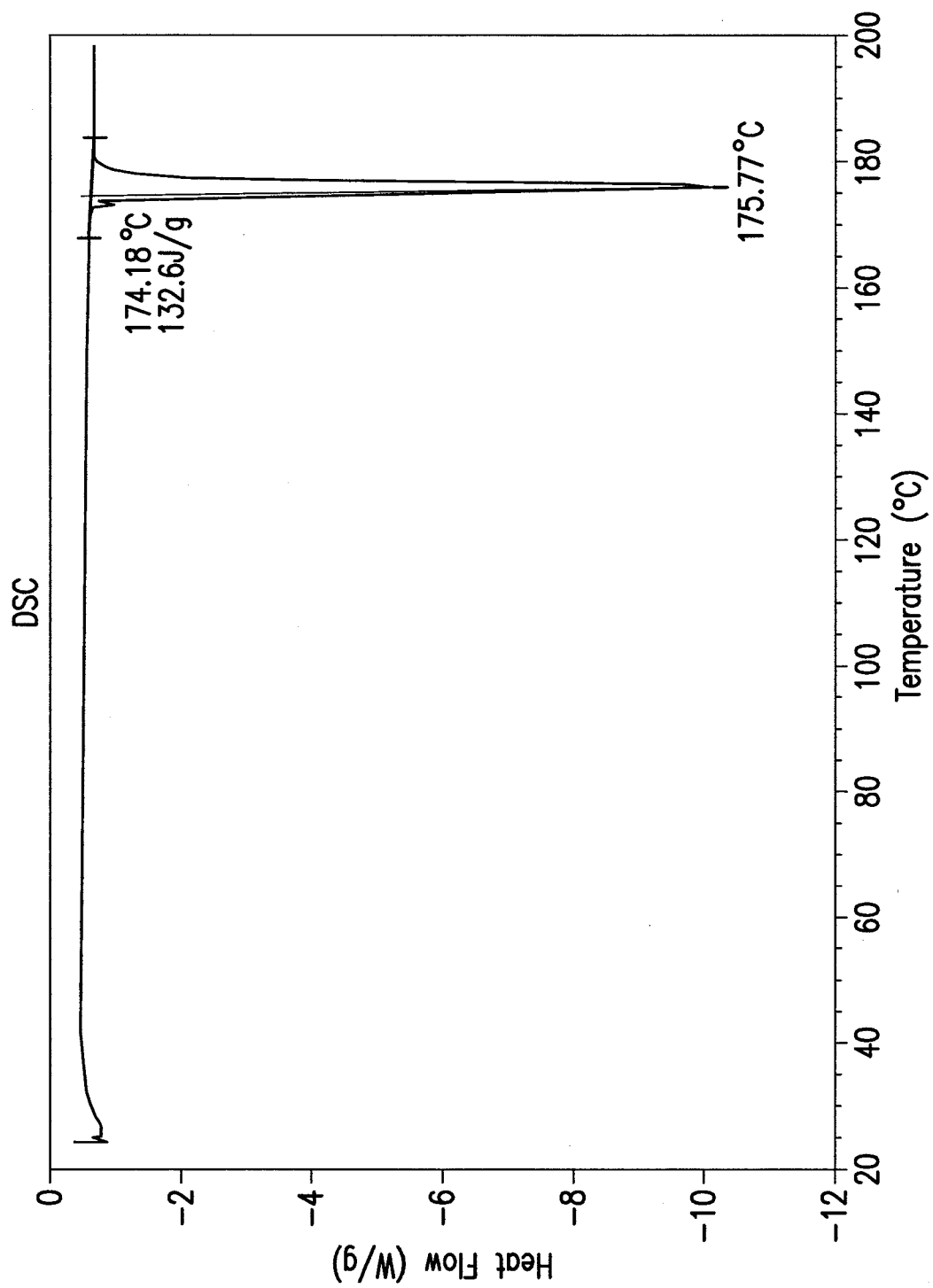


FIG.2

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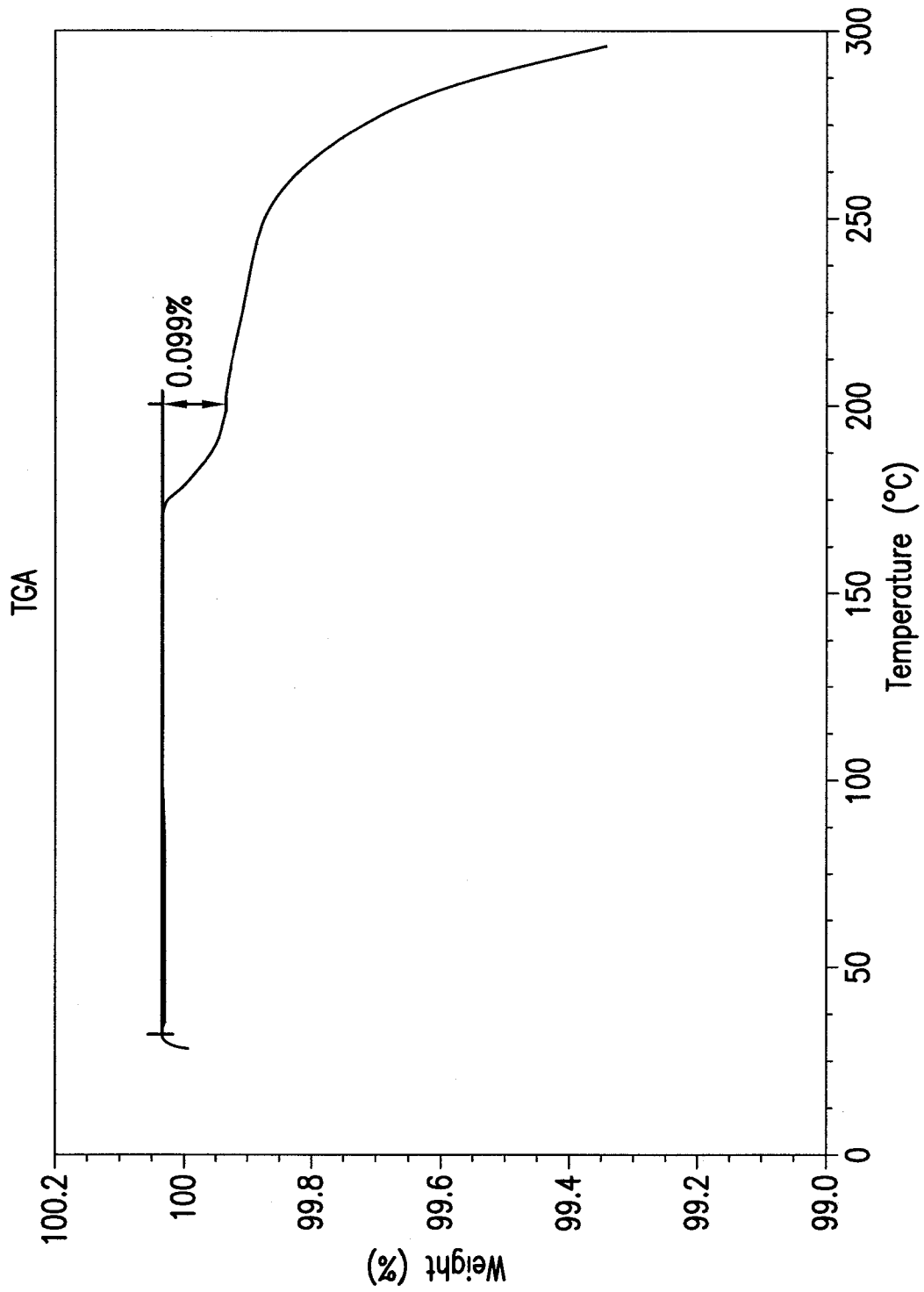


FIG.3

4/6

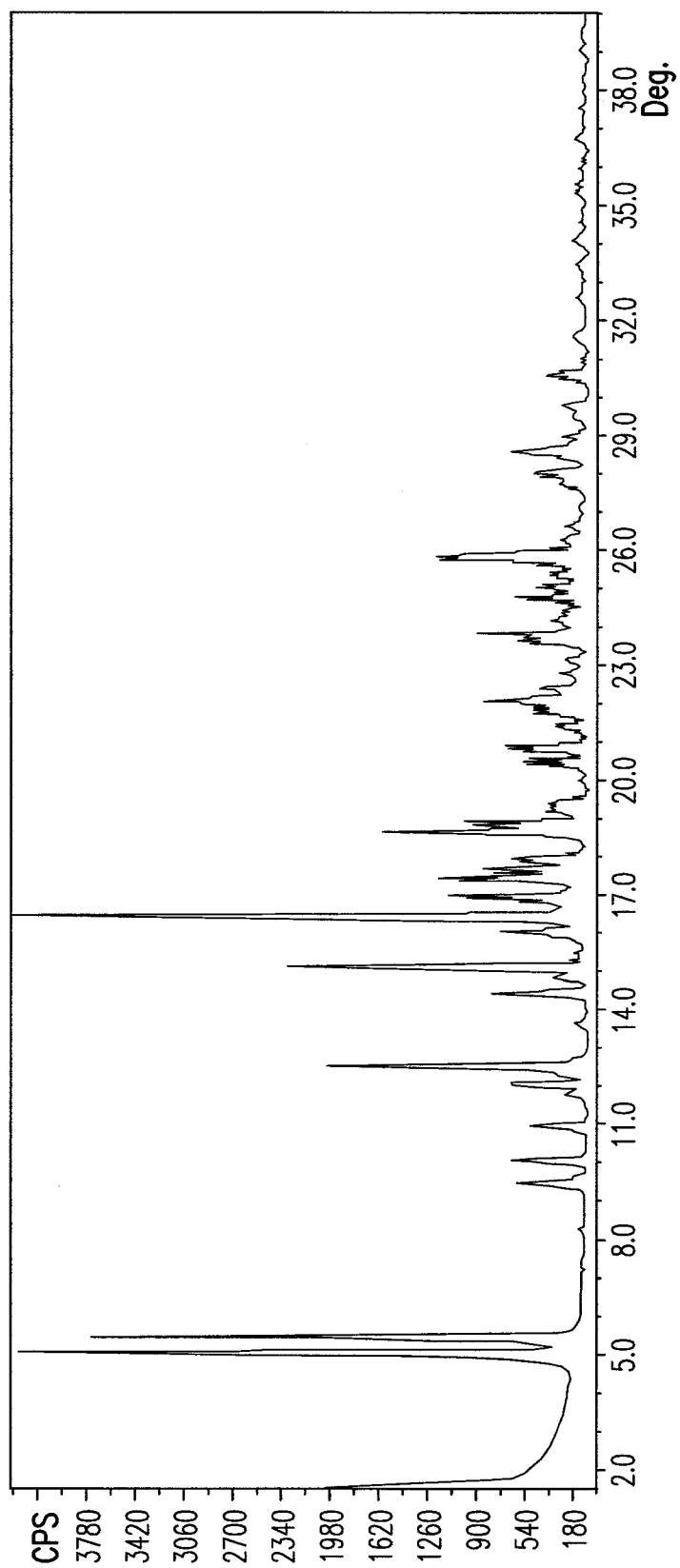


FIG.4

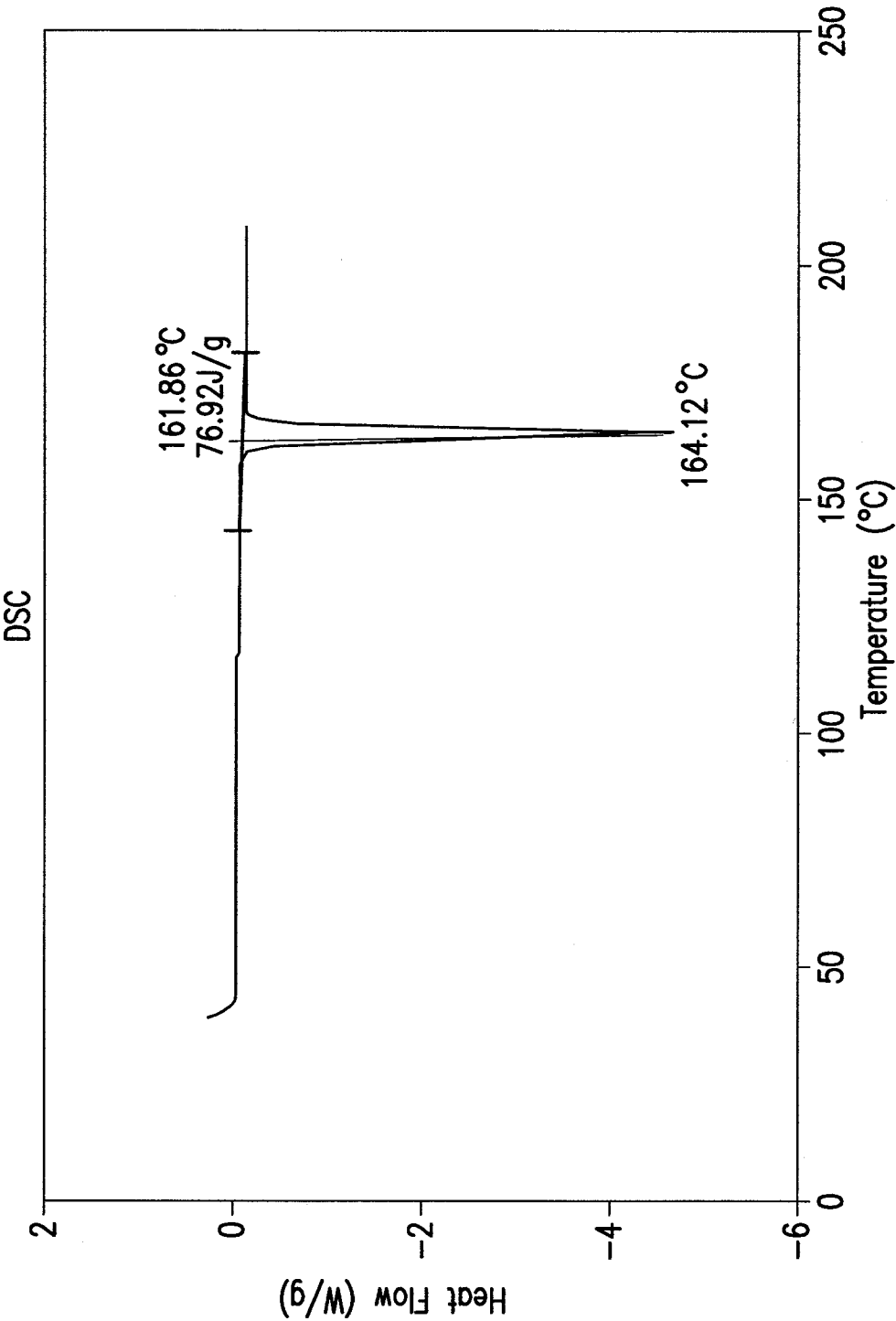


FIG.5

6/6

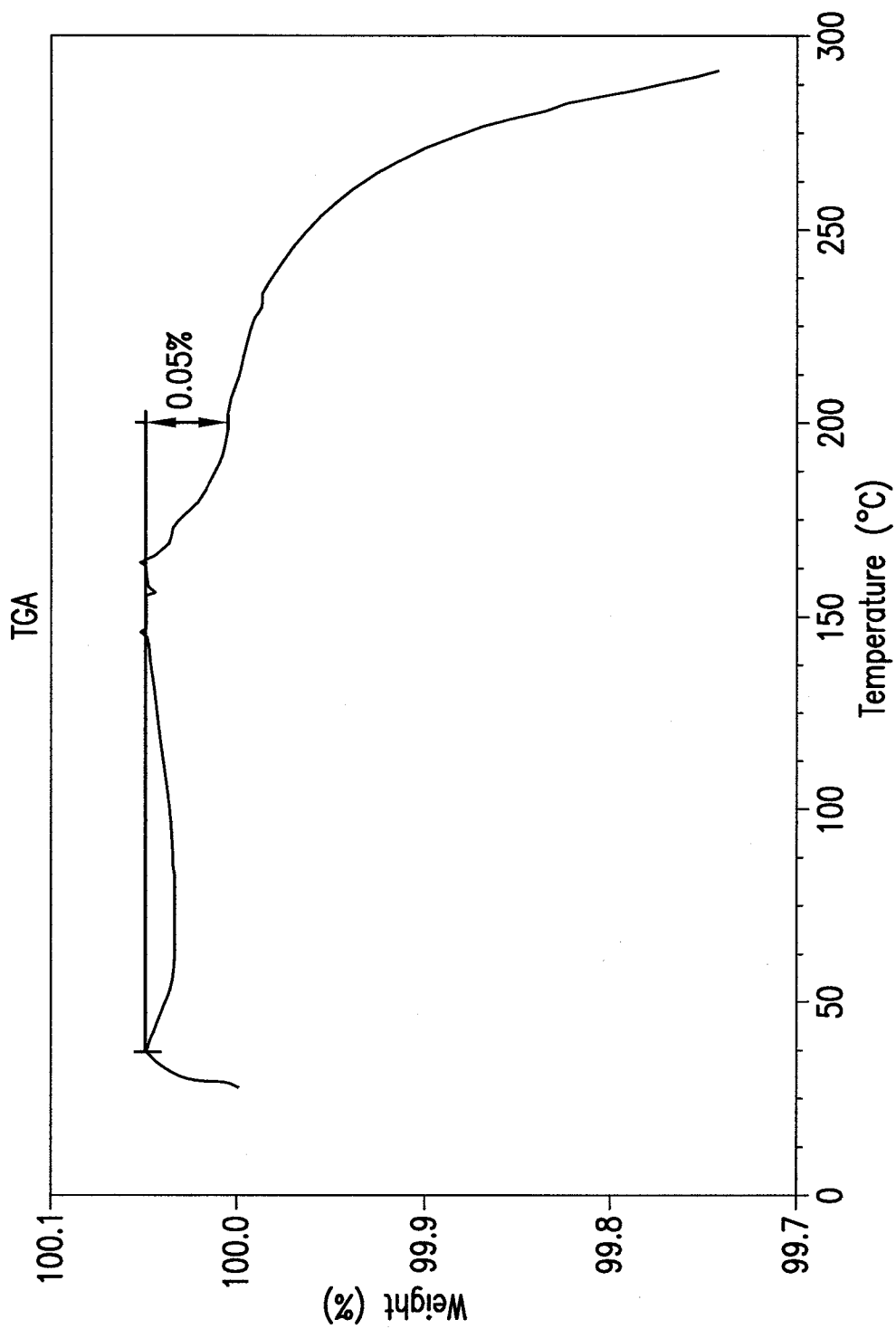


FIG. 6

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2011/065030

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D401/12 A61K31/506 A61P35/00
ADD.

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)
C07D A61K A61P

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, 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	WO 2008/073687 A2 (IRM LLC; MICHELLYS PIERRE-YVES [US]; PEI WEI [US]; MARSILJE THOMAS H []) 19 June 2008 (2008-06-19) page 45; example 7 -----	1-29



Further documents are listed in the continuation of Box C.



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

15 March 2012

Date of mailing of the international search report

30/03/2012

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Fazzi, Raffaella

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2011/065030

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008073687	A2	19-06-2008	
		AU 2007333394 A1	19-06-2008
		AU 2010210018 A1	02-09-2010
		AU 2010210019 A1	02-09-2010
		BR PI0720264 A2	10-05-2011
		CA 2671744 A1	19-06-2008
		CO 6231028 A2	20-12-2010
		CR 10832 A	14-07-2009
		EA 200970557 A1	30-12-2009
		EC SP099500 A	28-08-2009
		EP 2091918 A2	26-08-2009
		JP 2010512329 A	22-04-2010
		KR 20090087127 A	14-08-2009
		MA 30923 B1	02-11-2009
		SM AP200900058 A	19-01-2010
		SV 2009003290 A	17-08-2010
		WO 2008073687 A2	19-06-2008



CSA600262

41214

REPUBLICA DE COLOMBIA

DIVISION DE PROPIEDAD INDUSTRIAL

M A R C A S RECHAZADO

257615

Expediente No. _____

Contiene los documentos relativos a la solicitud sobre _____
UN REGISTRO DE

la marca "BER BER" Etiqueta

RECHAZADO

Clase 20 del Decreto 755 de 1.972.

Hecha por "BER BER LTDA/"

de BOGOTA, (COLOMBIA)

Apoderado, JORGE VELEZ GUTIERREZ

Bogotá, 25 JUN. 1986 de 19 _____

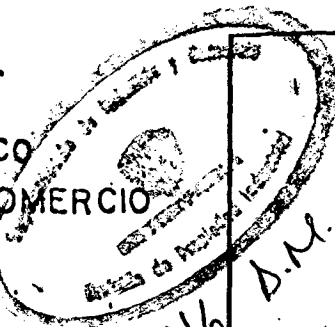
Fecha de presentación



25 JUN. 1986

REPUBLICA DE COLOMBIA

MINISTERIO DE DESARROLLO ECONOMICO
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE PROPIEDAD INDUSTRIAL



257615

- SOLICITUD -
REGISTRO DE MARCA

PRIORIDAD EXTRANJERA		
País	Nº	Fecha

☒ DE PRODUCTO	☐ COLECTIVA	☐ DE SERVICIO	☐ DEFENSIVA
Solicitante	Nombre BER BER LTDA.		
Domicilio	País COLOMBIA	Depto. o Estado y Ciudad CUNDIMARCA - BOGOTA, D.E.	
Representante Legal de la Sociedad	Nombre BERNARD GROSJEAN JOUBERT	Fecha:	
	Dirección CALLE 133 No. 40-40, Bogotá, D.E.	Resolución No.	
Apoderado	Nombre JORGE VELLEZ GUTIERREZ	Fecha:	
	Dirección Avenida Jimenez No. 149, Bogotá, D.E.	Resolución No.	
Representante Legal en Bogotá	Nombre	Fecha:	
	Dirección	Resolución No.	

CARACTERISTICAS		RECHAZADA	
Denominación de la Marca	*BERBER	Resolución No. 6059	Close
ANEXOS	Fecha: JUL 1986	LA SOLICITUD	20

- ☐ Poder Protocolo N°
- ☒ Estampillos de Timbre por \$ 1.575.00.
- ☒ Modelos (1)
- Certificados de
- ☒ Constitución de la Sociedad
- ☐ Vigencia de la Sociedad
- ☐ Representación Legal

- Comprobantes de pago por
- ☒ Derechos Fideles N° 3048742-743 105.00
- ☒ Publicación Extracto NS
- ☐ Servicios Administrativos
- Otros
- ☐
- ☐
- ☐

Apoderado - Tarjeta P. No. 33.242 de Minjusticia



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 MINISTERIO DE HACIENDA Y CREDITO PUBLICO impuestos nacionales		RECIBO OFICIAL DE PAGO				RECIBO OFICIAL No. MB-3048742			
POR CONCEPTO DE: <i>Derechos fiscales</i>		FECHA DE PAGO DIA MES AÑO 17 06 86		FORMA DE PAGO E CH B ☐ ☐ ☐		CLASE DE CONTRIBUYENTE PERSONA NATURAL JURIDICA ☐ ☐		C.C. 6 NIT. 124.631	A ☐ C ☐
APELLIDOS Y NOMBRES O RAZON SOCIAL BERNARD GROSJEAN									
EXPEDIDO EN URANO		CODIGOS ADMON DE RECAUDADORA		CON CARACTER DE ADMINISTRACION DE		CODIGO		CODIGO INTERNO	
PERIODO GRAVABLE 1986	SEMESTRE 1	REGIMEN C B S	MES 06	EXPLICACION DEL CONCEPTO DERECHOS FISCALES DE MARCA			USO OFICIAL	NUMERO 20	FECHA DIA MES AÑO
IMPUESTO \$100		INTERES MORATORIO		SANCION POR EXTEMPORANEIDAD		OTRAS SANCIONES		TOTAL INTERES Y SANCIONES	
TOTAL RECAUDADO \$100		LA SUMA DE		CIEN PESOS M.C.P.			IMP. N. 17/06/86		
SPD-IV-85-4/985.714		LIQUIDADOR				CAJERO		MH-1557	

CONTRIBUYENTE

CARVAJAL SA

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11/13

 MINISTERIO DE HACIENDA Y CREDITO PUBLICO impuestos nacionales		RECIBO OFICIAL DE PAGO				RECIBO OFICIAL No. MB-3048743					
POR CONCEPTO DE: <i>Veredas Acob</i>		FECHA DE PAGO DIA MES AÑO 27 06 86		FORMA DE PAGO E CH B ☐ ☐ ☐		CLASE DE CONTRIBUYENTE PERSONA NATURAL JURIDICA ☐ ☐		C.C. 6 NIT. 124.631		A ☐ C ☐	
APELLIDOS Y NOMBRES O RAZON SOCIAL BERNARD GROSJEAN											
EXPEDIDO EN URANO		CODIGOS ZONON OF RECAUDADORA		CON CARGO A LA ADMINISTRACION DE BBA				CODIGO		CODIGO INTERNO	
PERIODO GRAVABLE 1986		BIMESTRE F		REGIMEN C		MES 06		EXPLICACION DEL CONCEPTO LEY 1/83			
IMPUESTO		INTERES MORATORIO		SANCION POR EXTIMORANEBAD		OTRAS SANCIONES		TOTAL INTERES Y SANCIONES			
TOTAL RECAUDADO \$5-		\$5-		CINCO PESOS M.C.				17/06/86			
LA SUMA DE											
SPD-IV-85-4 085 714											
LIQUIDADOR								CAJERO			

CONTRIBUYENTE

CARVIVAL 5

11
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Señor

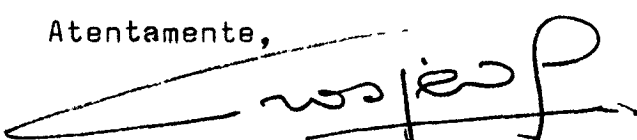
SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

- División de Propiedad Industrial -

BOGOTÁ, D.F.

Atentamente se dirige a Ud. BERNARD GROSJEAN JOUBERT, ciudadano Francés, mayor y vecino de ésta ciudad y en mi condición de Representante Legal de : BER BER LTDA., domiciliada en Bogotá, para manifestarle que confiero poder especial, amplio y suficiente al Dr. JORGE VELEZ GUTIERREZ, abogado, mayor y vecino de Bogotá, para que en nuestro nombre y representación, solicite ante Ud. el registro de la Marca de Producto "BER BER", Clase 20 del Decreto 755- de 1972, con amplias facultades para recibir, desistir, transigir, sustituir y lo demás que sea necesario en pro de nuestros intereses.

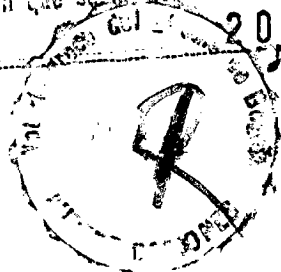
Atentamente,


BERNARD GROSJEAN JOUBERT

C.de E. # 124.631 de Bogotá

Bogotá, Mayo 15 de 1986

EDUARDO LARREA NEIRA (Notario) Troce Encargado del Oficio de
Bogotá, D.F. CONSTAR que la firma que autoriza este documento, corresponde a la que registra en la Notaría Bernard Grosjean Joubert
según la confrontación que se ha hecho de ella.
Bogotá, el 20 JUN 1986





179866 ***** 258502

CAMARA DE COMERCIO DE BOGOTA

OFICINA PRINCIPAL

FECHA JUN 03 MES 06 AÑO 86 HORA 12.40.08

CERTIFICADO DE EXISTENCIA Y REPRESENTACION

LEGAL DE: "BERBER LTDA."

EL SECRETARIO DE LA CAMARA DE COMERCIO DE

BOGOTA, CON FUNDAMENTO EN LAS MATRICULAS

E INSCRIPCIONES DEL REGISTRO MERCANTIL,

CERTIFICA:

NOMBRE: "BERBER LTDA."

DOMICILIO: BOGOTA,

CERTIFICA:

MATRICULA NO. 258502

CERTIFICA:

CONSTITUCION: ESCRITURA PUBLICA NO. 619, NOTARIA 13 DE BOGOTA DEL 17 DE MARZO DE 1986, INSCRITA EL 1 DE ABRIL DE 1986 BAJO EL NO. 187668 DEL LIBRO IX, SE CONSTITUYO LA SOCIEDAD COMERCIAL DENOMINADA: "BERBER LTDA."

CERTIFICA:

VIGENCIA: QUE LA SOCIEDAD NO SE HALLA DISUELTA. DURACION: DEL 17 DE MARZO DE 1986 AL 31 DE DICIEMBRE DEL AÑO 2.000.

CERTIFICA:

OBJETO SOCIAL: LA FABRICACION, COMPRA VENTA Y COMERCIALIZACION, IMPORTACION Y EXPORTACION DE TODA CLASE DE MUEBLES, ACCESORIOS Y IMPLEMENTOS DE DECORACION PARA LA ASesorIA Y SERVICIOS EN LAS ARTES DE FABRICACION, COMERCIALIZACION Y EN GENERAL TODO LO RELACIONADO CON LA DECORACION. PARA EL CUMPLIMIENTO DE LAS ACTIVIDADES QUE CONSTITUYEN EL OBJETO SOCIAL DESCRITO, LA SOCIEDAD PODRA CELEBRAR O EJECUTAR EN SU PROPIO NOMBRE O POR CUENTA DE TERCEROS O CON PARTICIPACION CON ELLOS, TODOS LOS ACTOS Y OPERACIONES CIVILES O MERCANTILES SOBRE LOS BIENES MUEBLES O INMUEBLES QUE SEAN NECESARIAS O CONVENIENTES PARA EL LOGRO DE LOS FINES QUE ELLA PERSIGUE.

CERTIFICA:

CAPITAL Y SOCIOS: \$2.000.000.00 DIVIDIDO EN 2.000 CUOTAS DE UN VALOR NOMINAL DE \$1.000 CADA UNA, DISTRIBUIDA ASI:

SOCIOS	DOCUMENTO IDENT.	NO. CUOTAS	VALOR
JAIMÉ ENRIQUE BERNAL SIERRA	CC. 19.063.027 BT.	1.000	\$1.000.000.00
BERNARD GROSJEAN JOUBERT	C. EXT. 124.631 BT.	1.000	1.000.000.00
TOTALS		2.000	2.000.000.00

CERTIFICA:

REPRESENTACION LEGAL: EL REPRESENTANTE LEGAL ES: EL GERENTE.

CERTIFICA:

QUE POR ESCRITURA DE CONSTITUCION CITADA FUERON NOMBRADOS CARGOS Y NOMBR
 GERENTE: BERNARD GROSJEAN JOUBERT CC. 124.631 BT.
 SUPLENTE: JAIMÉ ENRIQUE BERNAL SIERRA CC. 19.063.027 BT.

CERTIFICA:

FACULTADES DEL REPRESENTANTE LEGAL: A-REPRESENTAR LEGALMENTE A LA SOCIEDAD, JUDICIAL O EXTRAJUDICIALMENTE Y EN TODA CLASE DE AUTORIDADES Y PARTICULARES; B-USAR LA RAZON Y FIRMA SOCIAL; C-EJECUTAR Y CELEBRAR TODOS LOS ACTOS Y CONTRATOS COMPRENDIDOS DENTRO DEL OBJ

179666* * * * * 258502



* * * * *

CAMARA DE COMERCIO DE BOGOTA HORA 12.40.08

OFICINA PRINCIPAL

PAGINA 002 FECHA DIA 03 MES 06 AÑO 86

* * * * *

* * * * *

JEFE SOCIAL CUYA CUANTIA NO EXCEDE DE NOVENTA MIL P.S.S. - \$90.000- PARA NEGOCIOS QUE EXCEDE DE ESTA CUANTIA REQUERIRA AUTORIZACION PREVIA DE LA JUNTA DE SOCIOS; D-CONSTITUIR APODERADOS ESPECIALES Y CONFIARES LAS FACULTADES CIENTAS Y DETERMINADAS QUE FUERE MENESTER; E-CONVOCAR A LA JUNTA DE SOCIOS EN LAS OPORTUNIDADES PREVISTAS EN LOS ESTATUTOS Y CUANDO LO CONSIDERE NECESARIO; F-PRESENTAR A LA JUNTA DE SOCIOS EN SUS REUNIONES ORDINARIAS; EL BALANCE E INVENTARIOS DE LA SOCIEDAD LO MISMO QUE EL INFORME DE SU GESTION; G-RENDIR LAS CUENTAS E INFORMES ESPECIALES QUE LA JUNTA DE SOCIOS LE SOLICITE EN CUALQUIER TIEMPO; H-CONVOCAR A REUNIONES LA JUNTA DE SOCIOS CADA VEZ QUE LO ESTIME NECESARIO; I-EJERCER TODAS LAS DEMAS FUNCIONES QUE LEGAL Y ESTATUTARIAMENTE LE CORRESPONDAN COMO PRIMER DIRECTOR EJECUTIVO DE LA SOCIEDAD.

CERTIFICA:

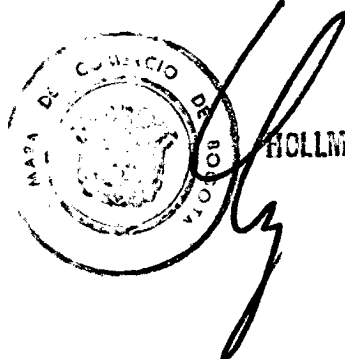
QUE NO APARECE INSCRIPCION POSTERIOR A LAS ARRIBA MENCIONADAS, DE DOCUMENTOS REFERENTES A REFORMA, DISOLUCION, LIQUIDACION O NOMBRAMIENTO DE REPRESENTANTES LEGALES DE LA EXPRESADA SOCIEDAD.

BOGOTA, D.E. FECHA DIA 03 MES 06 AÑO 86

EL SECRETARIO DE LA CAMARA DE COMERCIO DE BOGOTA

DEPLCH25: \$ 170

NO DEBES IMPUESTO DE TIMBRE



HOLLMAN ORTIZ GONZALEZ

EXTRACTO PARA PUBLICACION

SULICITUD DE MARCA

13
14

21	_____	51	20
22	_____	32	_____
		33	co. _____
		31	_____
71	"BER BER LTDA"		
	BOGOTA, COLOMBIA		
	JORGE VELEZ GUTIERREZ		
74	_____		
54	_____		

ber ber

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE PROPIEDAD INDUSTRIAL
SECCION MARCAS

EXPEDIENTE No. 257615

AUTO No.

8908/16

BOGOTA, D.E.

8 JUL 1956

Notifíquese al interesado que realizado el examen ordenado por el artículo 62 de la Decisión 85 del Acuerdo de Cartagena, la presente solicitud carece de:

- Recibo publicación \$1500-
- Recibo servicios Administrativos \$717.

De conformidad con el artículo 63 del precitado ordenamiento, en un plazo de sesenta (60) días hábiles, deberá el peticionario completar la solicitud.

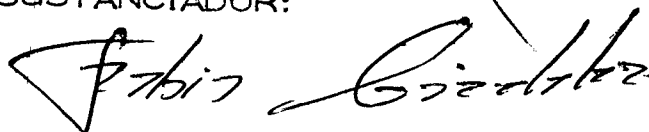
Si al vencimiento de dicho término, no se ha dado total cumplimiento a lo anteriormente ordenado, pasen las presentes diligencias al Despacho de la División de Propiedad Industrial para decidir el rechazo de esta solicitud.

NOTIFIQUESE Y CUMPLASE.


JEFE SECCION MARCAS(E).


SECRETARIO DIVISION PROPIEDAD INDUSTRIAL

SUSTANCIADOR:



SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

ESTUDIADO POR Fabio Bieda
PREPARADO POR Fabio Bieda
ELABORADO PROYECTO Fabio Bieda
BAJO RESPONSABILIDAD veena

RECEIVED
10 JUL 1986 de 1.9
Requiere por análisis en estado de este
para la
Secretaría

13 ENE. 1986

Al Despacho informando que el término con-
cedido en el auto anterior venció sin que los
interesados le hayan dado cumplimiento.

Secretaría de Propiedad Industrial

16

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE PROPIEDAD INDUSTRIAL

EXPEDIENTE No. 257.615

06059

RESOLUCION No.

FECHA

- 1. JUL 1988

" Por la cual se rechaza la solicitud de Registro de una marca:

El Jefe de la División de Propiedad Industrial,

CONSIDERANDO :

1. Que por auto de fecha Julio 8 de 1.986, ésta División inadmitió, la solicitud presentada, por deficiencia de sus requisitos formales y concedió al interesado un término de Sesenta días para subsanar los defectos señalados.
2. Que el término concedido transcurrió sin que el interesado diera cabal cumplimiento a las exigencias formuladas en dicha providencia. No cumple con el auto.
3. Que ante la situación planteada procede rechazar en forma definitiva la solicitud. presentada,

RESUELVE :

ARTICULO PRIMERO : Recházase la solicitud de Registro de la marca:
"BER BER"(Etiqueta

formulada por BER BER LTDA

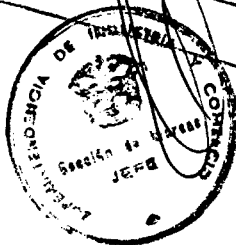
ARTICULO SEGUNDO: Contra la presente resolución proceden los recursos -
propios de la vía gubernativa. En firme ésta providen-
cia, archívese el expediente.

NOTIFIQUESE Y CUMPLASE

El Jefe de la División de Propiedad Industrial

El Secretario de la División de Propiedad Industrial

7
 SECRETARIA DE INDUSTRIA Y COMERCIO
 ESTADOS UNIDOS MEXICANOS
 DIRECCION GENERAL DE INDUSTRIA Y COMERCIO
 SECCION DE INVESTIGACION Y DESARROLLO TECNICO
 Jefe



Edicto No 789

...encar a los interesados de la providen-
 ...a las

8. NOV 1988

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22 NOV. 1988

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Secretario de Industrias y Comercio

2977 17

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE PROPIEDAD INDUSTRIAL

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CUENTA CORRIENTE 80305000

Bogotá,

2 SET. 1988

Doctor (a)

JORGE VELEZ CUTIERREZ

AVENIDA JIMENEZ NUMERO 8-49 OFICINA 406

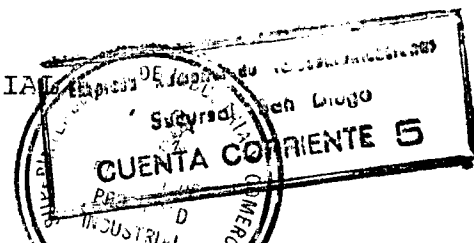
BOGOTA

SIRVASE COMPARECER A LA CARRERA 13 NUMERO 27-00 OFICINA 1027
TERMINO CINCO DIAS FIN NOTIFICARSE PROVIDENCIA EXPEDIENTE (S)
NUMERO (S) **257.615 241.855**

PUNTO DE NO PRESENTARSE SE PROCEDERA NOTIFICAR POR EDICTO PUNTO

DIANA ACOSTA CHACON

SECRETARIO DIVISION PROPIEDAD INDUSTRIAL



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SUPERINTENDENCIA DE INDUSTRIA Y
COMERCIO

EDICTO No. 789

EXPEDIENTE No. 257.615

En las diligencias adelantadas ante este Despacho por el Dr.(a) _____

JORGE VELEZ GUTIERREZ , como apoderado de _____

BER BER LTDA , domiciliado en _____

BOGOTA COLOMBIA , relacionado con la solicitud de _____

REGISTRO , se ha dictado la siguiente providencia;

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO - DIVISION PROPIEDAD INDUSTRIAL.
BOGOTA, 1 DE JULIO DE 1988 - RESOLUCION No. 006059

R E S U E L V E :

ARTICULO 1o. Recházase la solicitud de Registro de la marca: "BER BER"
(Etiqueta), formulada por BER BER LTDA.

ARTICULO 2o. Contra la presente resolución proceden los recursos propios
de la vía gubernativa. En firme esta providencia, archívese
el expediente.

NOTIFIQUESE Y CUMPLASE.

(FDO) ALVARO ATENCIA CARCAMO . Jefe Propiedad Industrial
(FDO) DIANA ALICIA ACOSTA CH . Secretario Propiedad Industrial

Contra la presente providencia proceden los recursos de reposición y apelación
interpuestos ante el Jefe de la División de Propiedad Industrial y ante el Su
perintendente de Industria y Comercio dentro de los cinco (5) días siguientes
a esta notificación.

Para notificar a los interesados de la providencia anterior, se fija este edicto
en lugar público de la Secretaría de Propiedad Industrial a las 8 A.M. de hoy : - 8. NOV 1988

SECRETARIO PROPIEDAD INDUSTRIAL

El presente edicto permanecerá fijado en la Secretaría de Propiedad Industrial
por el término de diez (10) días hábiles. Se desfija a las 5 P.M. de hoy : 27 NOV 1988

SECRETARIO PROPIEDAD INDUSTRIAL.

(12) SOLICITUD INTERNACIONAL PUBLICADA DE ACUERDO CON EL TRATADO DE COOPERACIÓN EN MATERIA DE PATENTES (TCP)

(19) Organización Mundial de la Propiedad Intelectual
Oficina Internacional

(43) Fecha de Publicación Internacional
21 de junio de 2012 (21.06.2012)

(10) Número de Publicación Internacional
PCT WO 2012/082972 A1

(51) Clasificación Internacional de Patente:
C07D 401/12 (2006.01) A61P 35/00 (2006.01)
A61K 31/506 (2006.01)

(21) Número de Solicitud Internacional:
PCT/US2011/065030

(22) Fecha de Presentación Internacional:
15 de diciembre de 2011 (15.12.2011)

(25) Idioma de Presentación: Inglés

(26) Idioma de Publicación: Inglés

(30) Información de Prioridad:
61/424,194 17-diciembre-2010 (17.12.2010) US

(71) Solicitante (para todos los Estados (Países) designados excepto US): **NOVARTIS AG** [CH/CH];
Lichtstrasse 35, CH-4056 Basilea (CH).

(72) Inventores; e

(75) Inventores/Solicitantes (para US solamente):
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(81) Estados (Países) Designados (a menos que se indique de otra manera, para cada tipo de protección nacional disponible): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Estados (Países) Designados (a menos que se indique de otra manera, para cada tipo de protección regional disponible): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasiáticos (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Europeos (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

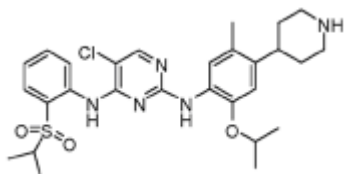
Declaraciones de acuerdo con la Regla 4.17:

-- con respecto al derecho de la solicitante d reclamar la prioridad de la solicitud anterior (Regla 4.17(iii))

Publicada:

-- con reporte de búsqueda internacional (Art. 21(3))

(54) Título : **FORMAS CRISTALINAS DE 5-CLORO-N2-(2-ISOPROPOXI-5-METIL-4-PIPERIDIN-4-IL-FENIL)-N4-[2-(PROPAN-2-SULFONIL)-FENIL]-PIRIMIDIN-2,4-DIAMINA**



(57) Resumen: La presente invención describe formas cristalinas específicas de la 5-cloro-N2-(2-isopropoxi-5-metil-4-(piperidin-4-il-fenil)-N2-(iso-propil-sulfonil)-fenil)-2,4-diamina. La presente invención se refiere además a los métodos para la preparación de estas formas cristalinas, a composiciones farmacéuticas que comprenden dichas formas

cristalinas, y a los métodos para utilizar las formas cristalinas y las composiciones farmacéuticas para tratar enfermedades.

WO 2012/082972 A1

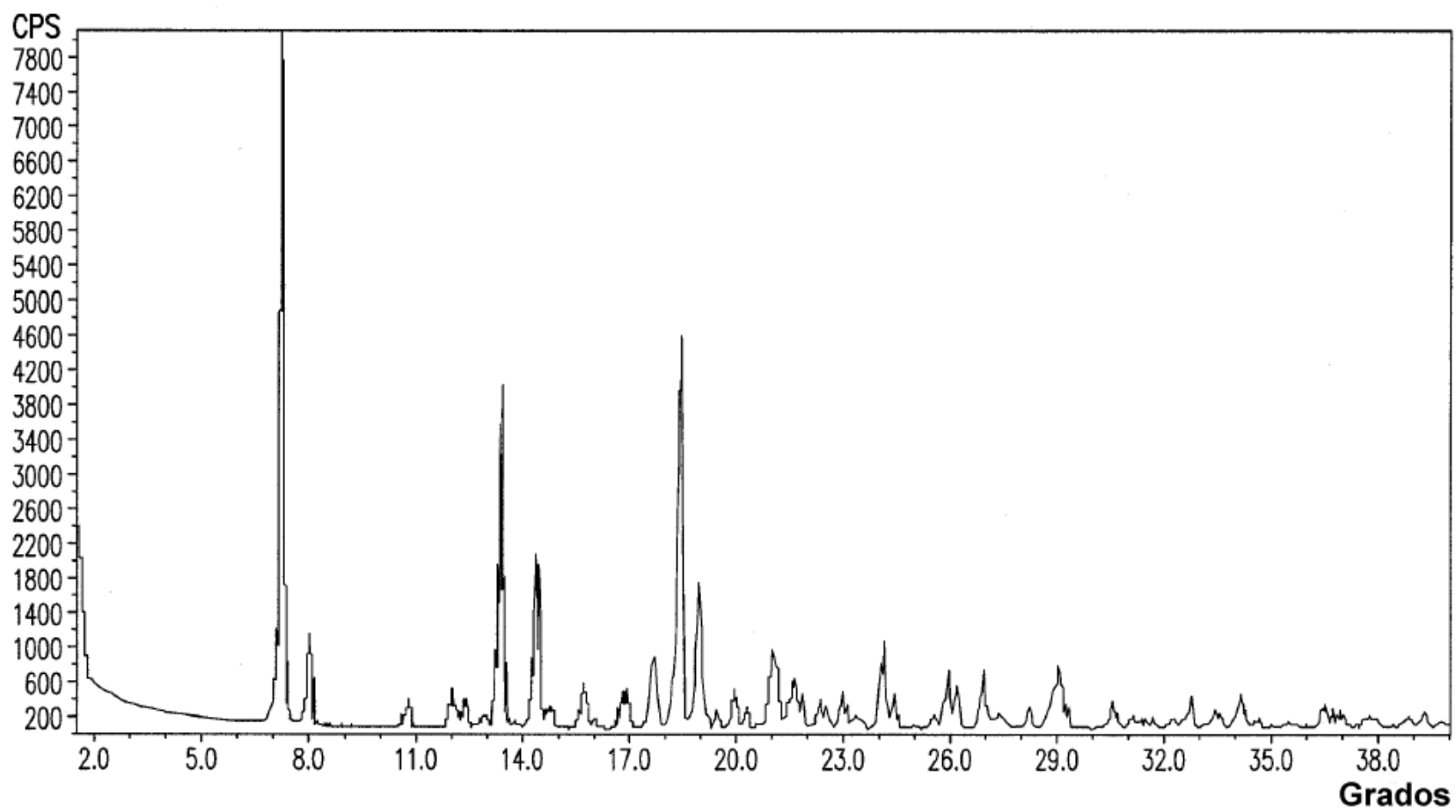


FIG. 1

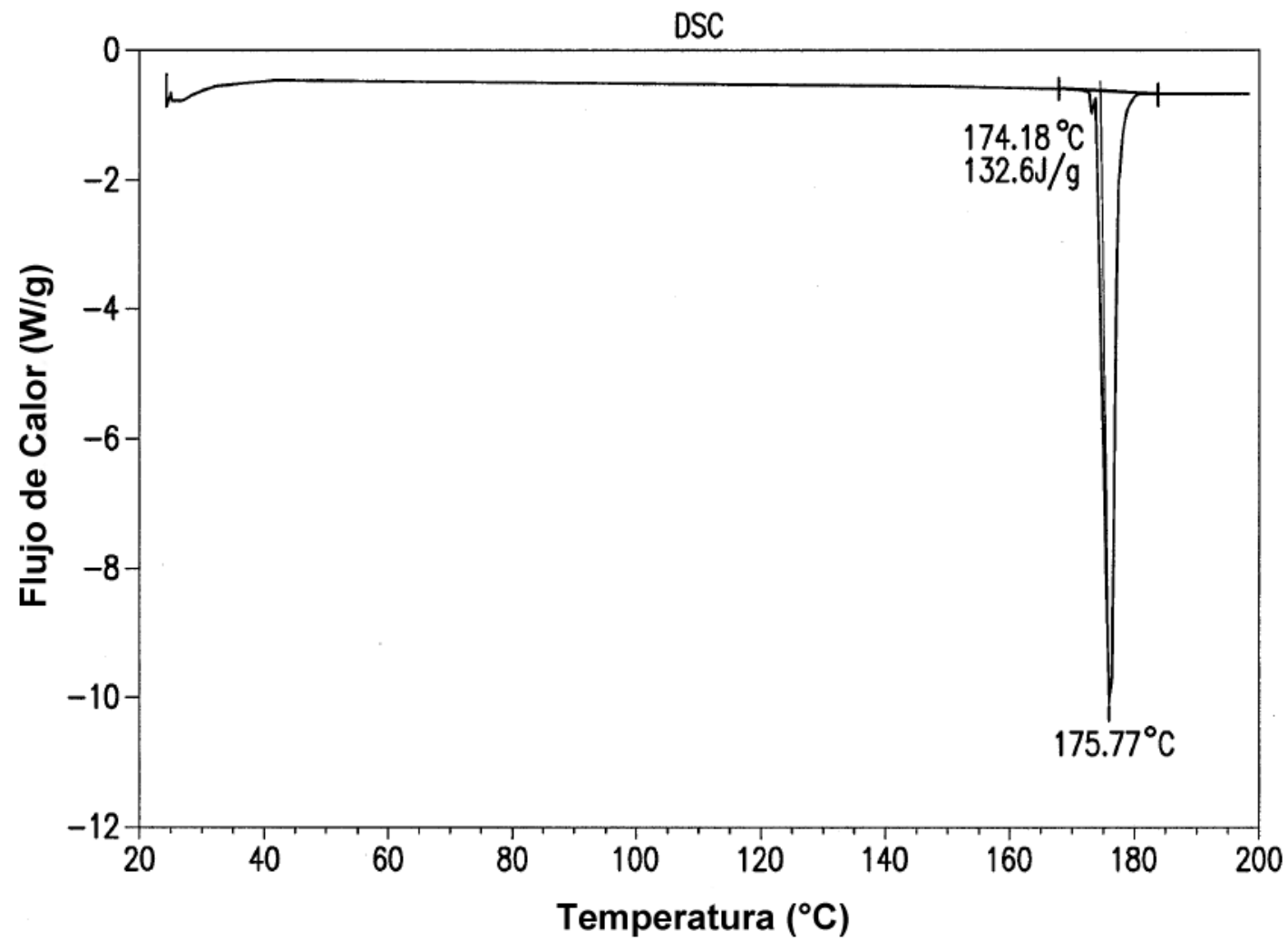


FIG. 2

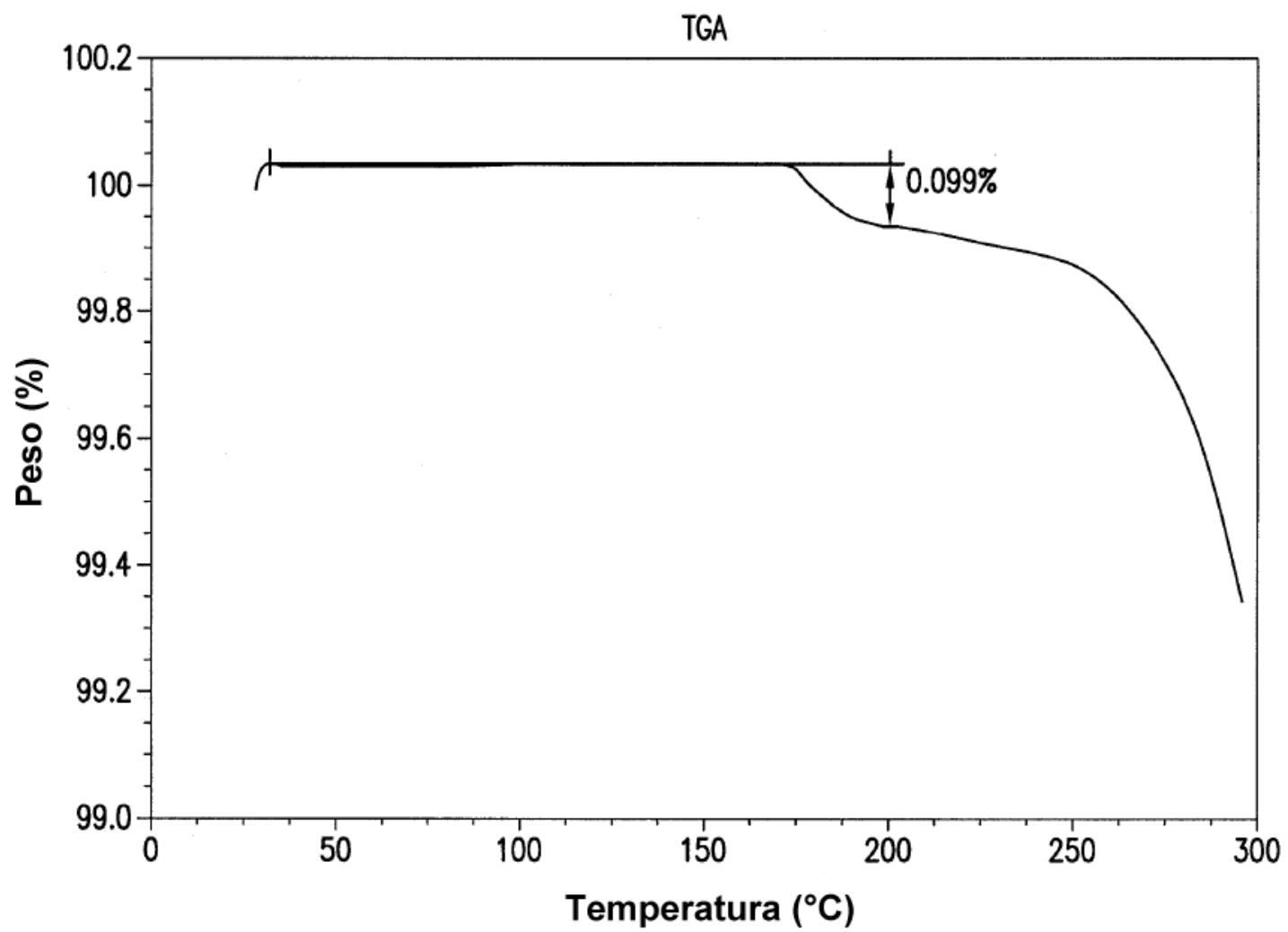


FIG. 3

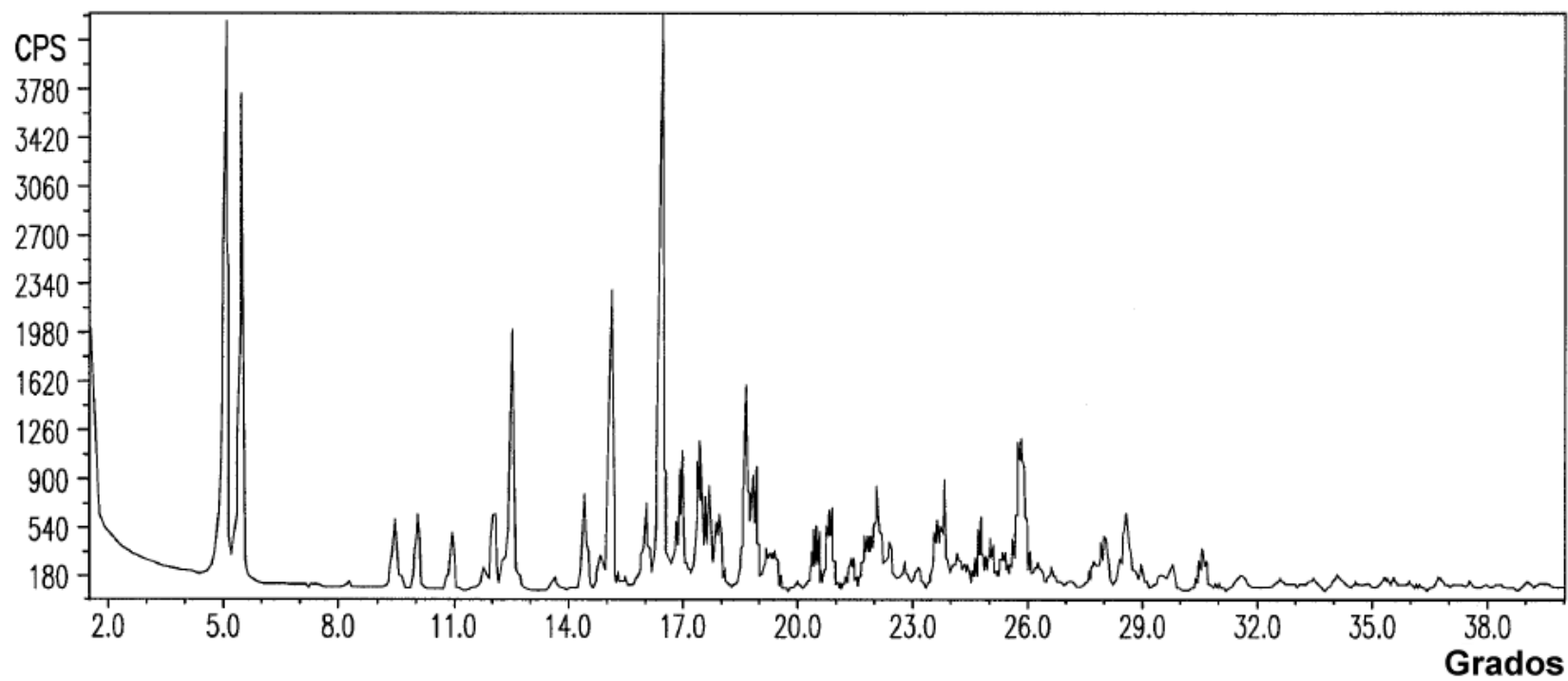


FIG. 4

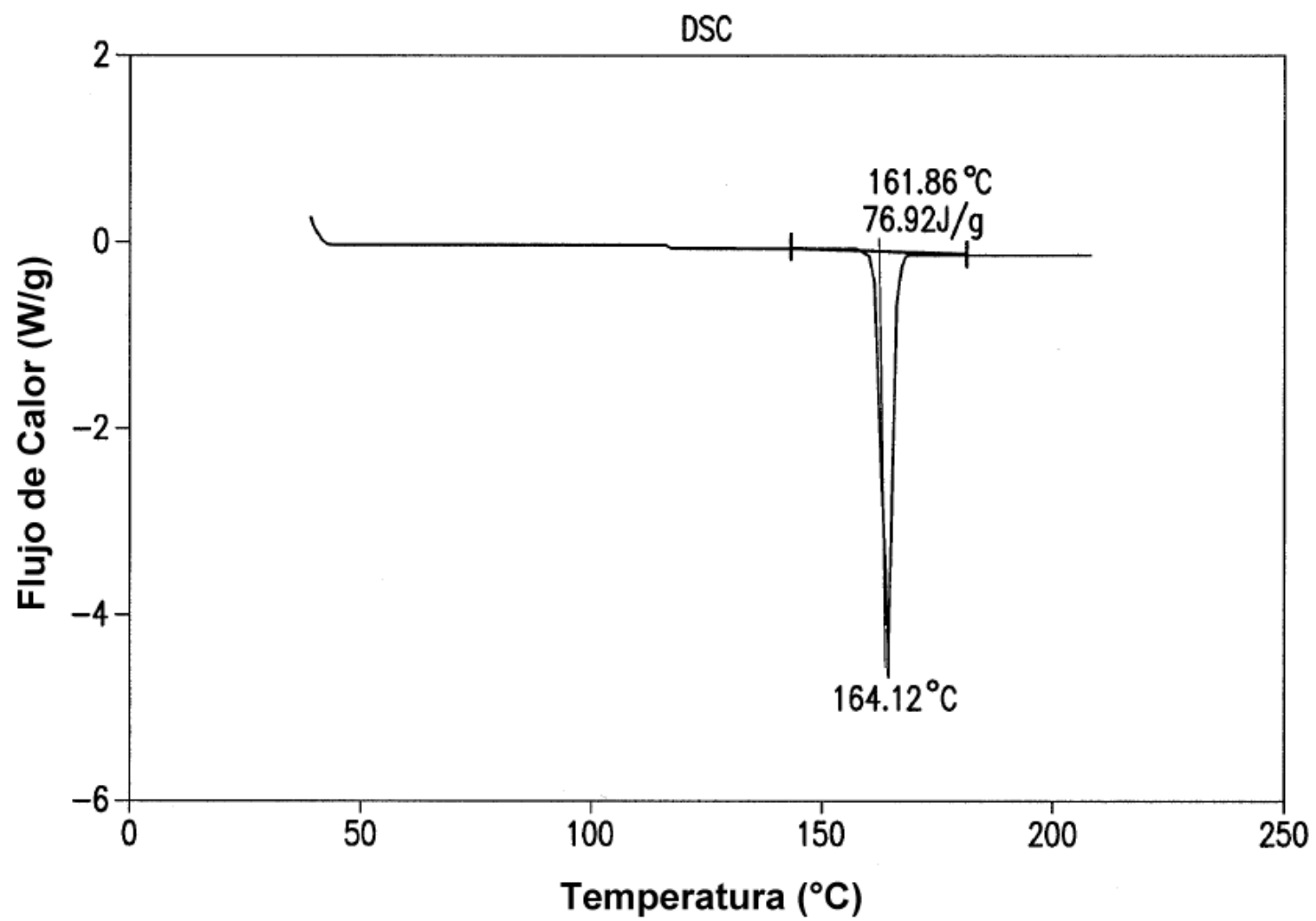


FIG. 5

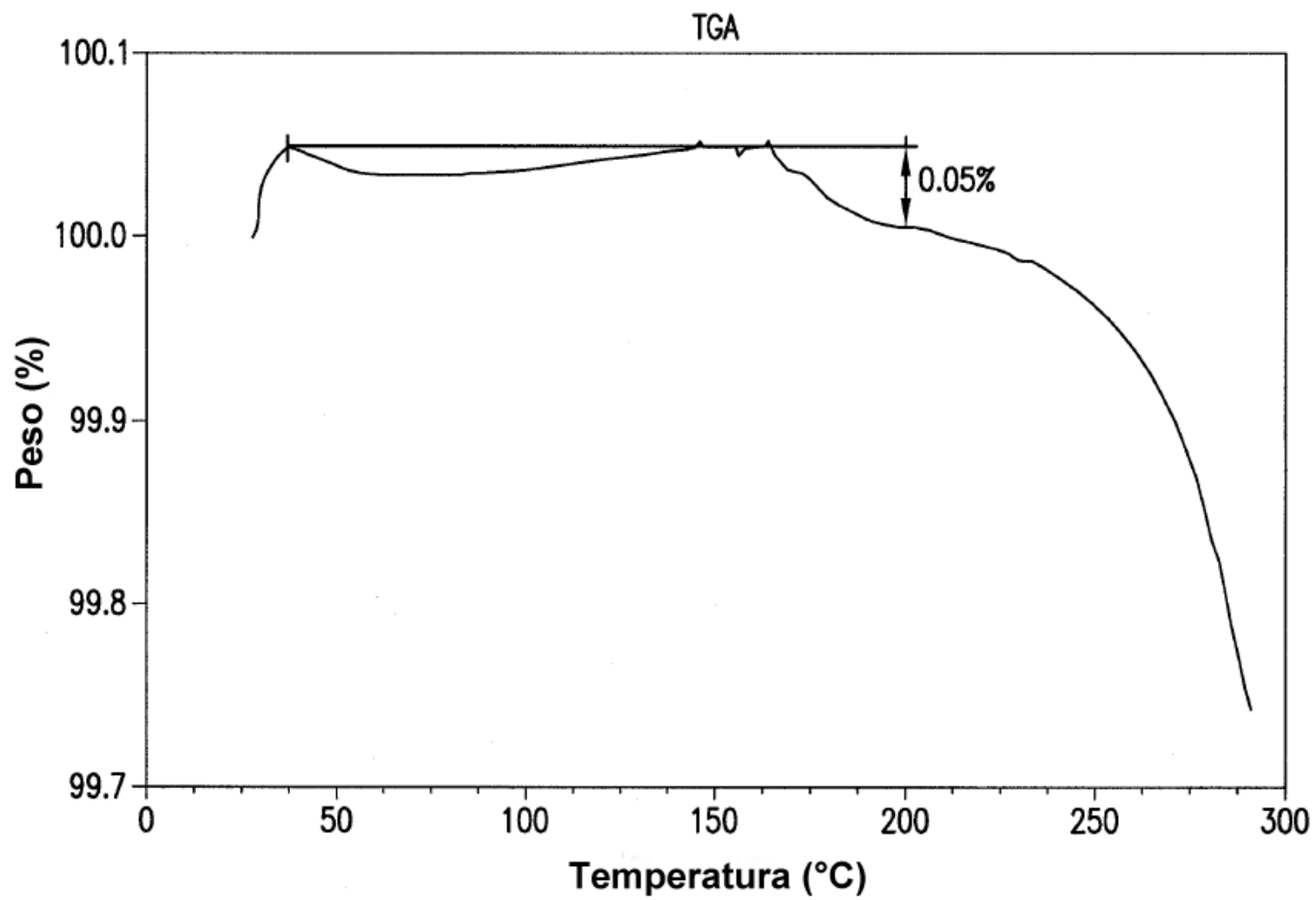


FIG. 6

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 54479 - WO - PCT	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2011/065030	International filing date (day/month/year) 15/12/2011	(Earliest) Priority Date (day/month/year) 17/12/2010
Applicant NOVARTIS AG		

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 4 sheets.

☒ 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:

- ☒ 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. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **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**,

- ☒ 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**,

- ☐ 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. _____
- ☐ as suggested by the applicant
- ☐ as selected by this Authority, because the applicant failed to suggest a figure
- ☐ as selected by this Authority, because this figure better characterizes the invention
- b. ☒ none of the figures is to be published with the abstract

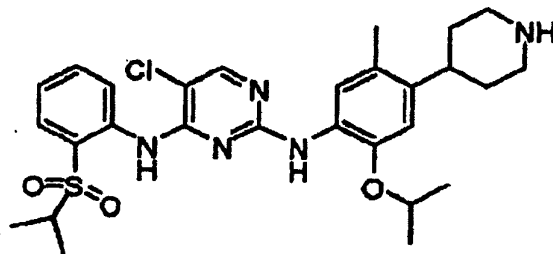
INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2011/065030

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present invention describes specific crystalline forms of 5-chloro-N-(2-isopropoxy-5-methyl-4-(piperidin-4-ylphenyl)-N-2-(isopropylsulfonyl)phenyl)-2,4-diamine. The present invention further relates to methods for preparing said crystalline forms, pharmaceutical compositions comprising said crystalline forms, and methods of using said crystalline forms and pharmaceutical compositions to treat disease.



INTERNATIONAL SEARCH REPORT

International application No

PCT/US2011/065030

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D401/12 A61K31/506 A61P35/00
ADD.

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)

C07D A61K A61P

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, 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	WO 2008/073687 A2 (IRM LLC; MICHELLYS PIERRE-YVES [US]; PEI WEI [US]; MARSILJE THOMAS H []) 19 June 2008 (2008-06-19) page 45; example 7 -----	1-29



Further documents are listed in the continuation of Box C.



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

15 March 2012

Date of mailing of the international search report

30/03/2012

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
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Fax: (+31-70) 340-3016

Authorized officer

Fazzi, Raffaella

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2011/065030

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008073687 A2	19-06-2008	AU 2007333394 A1	19-06-2008
		AU 2010210018 A1	02-09-2010
		AU 2010210019 A1	02-09-2010
		BR PI0720264 A2	10-05-2011
		CA 2671744 A1	19-06-2008
		CO 6231028 A2	20-12-2010
		CR 10832 A	14-07-2009
		EA 200970557 A1	30-12-2009
		EC SP099500 A	28-08-2009
		EP 2091918 A2	26-08-2009
		JP 2010512329 A	22-04-2010
		KR 20090087127 A	14-08-2009
		MA 30923 B1	02-11-2009
		SM AP200900058 A	19-01-2010
		SV 2009003290 A	17-08-2010
		WO 2008073687 A2	19-06-2008

CAPÍTULO REIVINDICATORIO MODIFICADO
(Solicitud de Divisional A)

1. Un proceso para preparar una composición farmacéutica, en donde 5-cloro-N2-(2-isopropoxi-5-metil-4-piperidin-4-il-fenil)-N4-[2-(propan-2-sulfonil)-fenil]-pirimidin-2,4-diamina que exhibe uno o más picos de difracción en polvo de rayos-X que tienen la máxima en los ángulos de difracción seleccionados a partir de 7.2°, 8.1°, 10.8°, 12.0°, 12.4°, 13.4°, 14.4°, 14.8°, 15.7°, 16.9°, 17.7°, 18.5°, 19.0°, 19.5°, 20.0°, 20.3°, 21.1°, 21.6°, 22.4°, 22.6°, 23.0°, 24.1°, 24.5°, 25.5°, 26.0°, 26.2°, 27.0°, 27.3°, 28.3°, 29.0°, 29.1°, 30.6°, 31.3°, 32.8°, 33.5°, 34.2° y 36.4° (grados 2θ) es mezclado con por lo menos un vehículo farmacéuticamente aceptable.

2. Un proceso para preparar una composición farmacéutica, en donde 5-cloro-N2-(2-isopropoxi-5-metil-4-piperidin-4-il-fenil)-N4-[2-(propan-2-sulfonil)-fenil]-pirimidin-2,4-diamina que exhibe uno o más picos de difracción en polvo de rayos-X que tienen la máxima en los ángulos de difracción seleccionados a partir de 5.1°, 5.5°, 5.6°, 9.5°, 9.6°, 10.1°, 11.0°, 11.8°, 12.1°, 12.6°, 13.7°, 14.5°, 14.9°, 15.2°, 16.1°, 16.6°, 16.7°, 17.0°, 17.1°, 17.5°, 17.7°, 18.0°, 18.8°, 19.0°, 19.3°, 19.5°, 20.5°, 20.9°, 21.5°, 21.9°, 22.1°, 22.4°, 22.8°, 23.2°, 23.7°, 23.9°, 24.3°, 24.5°, 24.8°, 25.1°, 25.4°, 25.9°, 26.4°, 26.8°, 27.8°, 28.1°, 28.6°, 29.1°, 29.6°, 29.8°, 30.6°, 31.6°, 32.7°, 33.5°, 34.2°, 35.4°, 35.6° y 36.8° (grados 2θ) es mezclado con por lo menos un vehículo farmacéuticamente aceptable..
