34

Señor Jefe

DIVISION DE NUEVAS CREACIONES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Santa Fe de Bogotá, D.C.

02-01-09

Re.: Expediente No. 00 - 28.932

Solicitud de Patente

SMITHKLINE BEECHAM plc

SUPERINDUSTRIA Y COMERCIO
Radicacion : 00028932 00000001 Folios: 17
Fecha (AMD): 2000-05-09 10:11:17
Tramite : 002 PATENTES D 1 REGISTRO/ 329 COMPLEMEN
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Debidamente traducida adjunto acompaño la solicitude de patente básica Inglesa No. 9909472.4 la cual le solicito agregar a este expediente para los efectos legales respectivos.

De Usted atentamente,

GERMAN CASTILLO GRAU

T.P.#2.978 del C.S.J.

The Patent Office

INVESTOR IN PEOPLE

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed

Dated 23 March 2000

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26APR99 E442524-1 D02029
P01/7700 0.00 - 9909472.4

Patent Form 1/77

Patents Act 1977
(Rule 16)

The Patent Office

1/77

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office
Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference — KR/JW/P32284

2. Patent application number
(The Patent Office will fill in his part) — **9909472.4**

3. Full name, address and postcode of the or of each applicant *(underline all surnames)* — SmithKline Beecham plc
New Horizons Court, Brentford, Middx TW8 9EP,
Great Britain

Patents ADP number *(if you know it)* — 7605058001

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention — Novel Compounds

5. Name of your agent *(if you have one)* — CORPORATE INTELLECTUAL PROPERTY

"Address for service" in the United Kingdom to which all correspondence should be sent
(including the postcode)

SMITHKLINE BEECHAM PLC
TWO NEW HORIZONS COURT
BRENTFORD
MIDDLESEX TW8 9EP

Patents ADP number *(if you know it)* — 58009740004

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer yes if:*
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is named as an applicant, or
c) any named applicant is a corporate body
See note (d)

Patents Form 1/77

9. Enter number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	8
Claim(s)	
Abstract	
Drawings	4

10. If you are also filing any of the following, state how many against each item.

Priority Documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 1/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. We request the grant of a patent on the basis of this application

Signature K Rutter Date 23-Apr-99

K Rutter

12. Name and daytime telephone number of person to contact in the United Kingdom: K Rutter 01279 644396

Warning

After an application for a Patent has beeen filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission unless an application has been filed at least six weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505

b) Write your answers in capital letters using black ink or you may type them.

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d) If you have answered 'Yes' Patents Form 7/77 will need to be filed.

f) For details of the fee and ways to pay please contact the Patent Office.

NOVEL PHARMACEUTICAL

This invention relates to a novel pharmaceutical, to a process for the preparation of the pharmaceutical and to the use of the pharmaceutical in medicine.

International Patent Application, Publication Number WO94/05659 discloses certain thiazolidinedione derivatives having hypoglycaemic and hypolipidaemic activity including 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (hereinafter also referred to as "Compound (I)").

It has now been discovered that Compound (I) exists in a novel polymorphic form which is particularly suitable for bulk preparation and handling. The novel form can be prepared by an efficient, economic and reproducible process particularly suited to large scale preparation.

The novel polymorphic form ('the Polymorph') also has useful pharmaceutical properties and in particular it is indicated to be useful for the treatment and/or prophylaxis of diabetes mellitus, conditions associated with diabetes mellitus and certain complications thereof.

Accordingly, the present invention provides a polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt characterised in that it:

(i) provides an infra red spectrum containing peaks at 1360, 1326, 1241, 714 and 669 cm^{-1}; and/or

(ii) provides a Raman spectrum containing peaks at 1581, 768, 670, 271 and 226 cm^{-1}; and/or

(iii) provides a solid-state nuclear magnetic resonance spectrum containing peaks at chemical shifts substantially as set out in Table I; and/or

(iv) provides an X-ray powder diffraction (XRPD) pattern containing peaks substantially as set out in Table II.

In one favoured aspect, the Polymorph provides an infrared spectrum substantially in accordance with Figure I.

In one favoured aspect, the Polymorph provides a Raman spectrum substantially in accordance with Figure II.

In one favoured aspect, the Polymorph provides a solid-state nuclear magnetic resonance spectrum substantially in accordance with Figure III.

In one favoured aspect, the Polymorph provides an X-ray powder diffraction (XRPD) pattern substantially in accordance with Figure IV.

The present invention encompasses the Polymorph isolated in pure form or when admixed with other materials, for example the known forms of Compound I or any other material.

Thus in one aspect there is provided the Polymorph in isolated form.

In a further aspect there is provided the Polymorph in pure form.

In yet a further aspect there is provided the Polymorph in crystalline form.

The invention also provides a process for preparing the Polymorph , characterised in that a slurry of Compound (I) and denatured ethanol containing 0.8 to 2.5% w/v water, is heated at 45°C for an extended period of time, for example 65 hours, after which time the Polymorph is recovered from the denatured ethanol.

In an alternative process a solution of Compound (I) in denatured ethanol containing 0.8 to 2.5% w/v water at 55°C is seeded with the Polymorph then cooled to 20-25°C to provide the Polymorph. The Polymorph is then recovered from the denatured ethanol.

The solution of Compound (I) in the denatured ethanol is conveniently prepared by dissolving Compound (I) in the required amount of denatured ethanol at an elevated temperature, for example 60°C.

Conveniently the Polymorph is recovered from the denatured ethanol by filtration and subsequent drying, preferably at an elevated temperature, for example 45°C.

Compound (I) is prepared according to known procedures, such as those disclosed in WO94/05659. The disclosures of WO94/05659 are incorporated herein by reference.

When used herein "denatured ethanol" means ethanol containing small amounts of methanol for example ethanol containing 4%v/v of methanol.

When used herein the term 'prophylaxis of conditions associated with diabetes mellitus' includes the treatment of conditions such as insulin resistance, impaired glucose tolerance, hyperinsulinaemia and gestational diabetes.

Diabetes mellitus preferably means Type II diabetes mellitus.

Conditions associated with diabetes include hyperglycaemia and insulin resistance and obesity. Further conditions associated with diabetes include hypertension, cardiovascular disease, especially atherosclerosis, certain eating disorders, in particular the regulation of appetite and food intake in subjects suffering from disorders associated with under-eating ,such as anorexia nervosa, and disorders associated with over-eating, such as obesity and anorexia bulimia. Additional conditions associated with diabetes include polycystic ovarian syndrome and steroid induced insulin resistance.

The complications of conditions associated with diabetes mellitus encompassed herein includes renal disease, especially renal disease associated with the development of Type II diabetes including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis and end stage renal disease.

As mentioned above the compound of the invention has useful therapeutic properties: The present invention accordingly the Polymorph for use as an active therapeutic substance.

More particularly, the present invention provides the Polymorph for use in the treatment and/or prophylaxis of diabetes mellitus, conditions associated with diabetes mellitus and certain complications thereof.

The Polymorph may be administered per se or, preferably, as a pharmaceutical composition also comprising a pharmaceutically acceptable carrier. The formulation of the Polymorph and dosages thereof are generally as disclosed for Compound (I) in International Patent Application, Publication Number WO94/05659.

Accordingly, the present invention also provides a pharmaceutical composition comprising the Polymorph and a pharmaceutically acceptable carrier therefor.

The Polymorph is normally administered in unit dosage form.

The active compound may be administered by any suitable route but usually by the oral or parenteral routes. For such use, the compound will normally be employed in the form of a pharmaceutical composition in association with a pharmaceutical carrier, diluent and/or excipient, although the exact form of the composition will naturally depend on the mode of administration.

Compositions are prepared by admixture and are suitably adapted for oral, parenteral or topical administration, and as such may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, pastilles, reconstitutable powders, injectable and infusable solutions or suspensions, suppositories and transdermal devices. Orally administrable compositions are preferred, in particular shaped oral compositions, since they are more convenient for general use.

Tablets and capsules for oral administration are usually presented in a unit dose, and contain conventional excipients such as binding agents, fillers, diluents, tabletting agents, lubricants, disintegrants, colourants, flavourings, and wetting agents. The tablets may be coated according to well known methods in the art.

Suitable fillers for use include cellulose, mannitol, lactose and other similar agents. Suitable disintegrants include starch, polyvinylpyrrolidone and starch derivatives such as sodium starch glycollate. Suitable lubricants include, for example,

magnesium stearate. Suitable pharmaceutically acceptable wetting agents include sodium lauryl sulphate.

Solid oral compositions may be prepared by conventional methods of blending, filling, tabletting or the like. Repeated blending operations may be used to distribute the active agent throughout those compositions employing large quantities of fillers. Such operations are, of course, conventional in the art.

Oral liquid preparations may be in the form of, for example, aqueous or oily suspensions, solutions, emulsions, syrups, or elixirs, or may be presented as a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, for example sorbitol, syrup, methyl cellulose, gelatin, hydroxyethylcellulose, carboxymethyl cellulose, aluminium stearate gel or hydrogenated edible fats, emulsifying agents, for example lecithin, sorbitan monooleate, or acacia; non-aqueous vehicles (which may include edible oils), for example, almond oil, fractionated coconut oil, oily esters such as esters of glycerine, propylene glycol, or ethyl alcohol; preservatives, for example methyl or propyl p-hydroxybenzoate or sorbic acid, and if desired conventional flavouring or colouring agents.

For parenteral administration, fluid unit dose forms are prepared containing a compound of the present invention and a sterile vehicle. The compound, depending on the vehicle and the concentration, can be either suspended or dissolved. Parenteral solutions are normally prepared by dissolving the active compound in a vehicle and filter sterilising before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are also dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum.

Parenteral suspensions are prepared in substantially the same manner except that the active compound is suspended in the vehicle instead of being dissolved and sterilised by exposure to ethylene oxide before suspending in the sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the active compound.

In addition such compositions may contain further active agents such as anti-hypertensive agents and diuretics.

As is common practice, the compositions will usually be accompanied by written or printed directions for use in the medical treatment concerned.

As used herein the term 'pharmaceutically acceptable' embraces compounds, compositions and ingredients for both human and veterinary use: for example the term 'pharmaceutically acceptable salt' embraces a veterinarily acceptable salt.

The present invention further provides a method for the treatment and/or prophylaxis of diabetes mellitus, conditions associated with diabetes mellitus and certain complications thereof, in a human or non-human mammal which comprises administering an effective, non-toxic, amount of the Polymorph to a human or non-human mammal in need thereof.

Conveniently, the active ingredient may be administered as a pharmaceutical composition hereinbefore defined, and this forms a particular aspect of the present invention.

In the treatment and/or prophylaxis of diabetes mellitus, conditions associated with diabetes mellitus and certain complications thereof the Polymorph may be taken in doses, such as those described above.

Similar dosage regimens are suitable for the treatment and/or prophylaxis of non-human mammals.

In a further aspect the present invention provides the use of the Polymorph for the manufacture of a medicament for the treatment and/or prophylaxis of diabetes mellitus, conditions associated with diabetes mellitus and certain complications thereof.

No adverse toxicological effects are indicated in the above mentioned treatments for the compounds of the invention.

The following examples illustrate the invention but do not limit it in any way.

Examples:

Example 1: A slurry of Compound (I) (3.0 g, prepared as per WO94/05659 in denatured ethanol (30.5 ml, water content 2.5% w/v)) was heated at 45°C for 65 hours. The product was filtered at 45°C and dried at 50°C *in vacuo* to give the Polymorph (1.55 g).

Example 2: Compound (I) (6.0 g) was heated at 60°C in denatured ethanol (60 ml, water content 0.8% w/v) until complete dissolution was obtained. The resultant solution was cooled to 55°C, seeded with the title compound (0.06 g), then cooled to 20-25°C. The product was filtered, washed with denatured ethanol (10 ml) and dried at 50°C *in vacuo* to give the Polymorph (4.8 g, 80%).

CHARACTERISING DATA: The following characterising data were generated for The polymorph:

A Water content

This was determined as 0.08% w/w using a Karl Fischer apparatus.

B Infrared

The infrared absorption spectrum of a mineral oil dispersion of the Polymorph was obtained using a Nicolet 710 FT-IR spectrometer at 2 cm^{-1} resolution. Data were digitised at 1 cm^{-1} intervals. The spectrum obtained is shown in Figure I. Peak positions are as follows: 2720, 1750, 1703, 1640, 1618, 1610, 1573, 1541, 1529, 1513, 1412, 1400, 1360, 1326, 1309, 1300, 1265, 1241, 1213, 1183, 1162, 1112, 1096, 1080, 1068, 1033, 1014, 989, 972, 933, 902, 866, 843, 832, 812, 774, 741, 734, 729, 669, 660, 636, 613, 605, 577, 558, 540, 527, 515, 508 and 473 cm^{-1}.

C Raman

The Raman spectrum of the Polymorph was recorded through a glass vial using a Perkin Elmer 2000R spectrometer at 4 cm^{-1} resolution and is shown in Figure II (X-axis shows Intensity, Y-axis shows Raman shift cm^{-1}, 1800 - 200 cm^{-1}). Excitation was achieved using a Nd:YAG laser (1064 nm) with a power output of 400 mW. Peak positions are as follows: 1749, 1706, 1683, 1611, 1581, 1546, 1511, 1468, 1445, 1435, 1388, 1361, 1327, 1301, 1269, 1250, 1229, 1210, 1179, 1149, 1103, 1056, 1036, 1024, 1005, 989, 920, 843, 827, 800, 782, 768, 744, 722, 670, 637, 605, 560, 541, 512, 473, 429, 408, 397, 347, 322, 298, 271 and 226 cm^{-1}.

D NMR

The 90.56 MHz ^{13}C CP-MAS NMR spectrum for the Polymorph is shown in Figure III. Chemical shifts are tabulated in Table 1. Data were recorded at ambient temperature and 10 kHz spinning frequency on a Bruker AMX360 spectrometer, with 1.6 ms cross polarization, and a repetition time of 15 s. Chemical shifts were

externally referenced to the carboxylate signal of a glycine test sample at 176.4 ppm relative to tetramethylsilane, and are regarded as accurate to within +/- 0.5 ppm. Peaks were not assigned.

Table I.

^{13}C Chemical Shifts of the Polymorph.

Chemical Shift (ppm)				
42.2	112.3	131.5	146.5	172.4
50.7	113.9	134.1	151.4	177.4
55.9	118.8	138.7	158.7	
62.7	129.8	140.5	170.3	

E X-Ray Powder Diffraction (XRPD)

The XRPD pattern of the Polymorph is shown below in Figure IV and a summary of the XRPD angles and calculated lattice spacings characteristic of the Polymorph is given in Table II.

A PW1710 X-ray powder diffractometer (Cu X-ray source) was used to generate the powder pattern using the following acquisition conditions:

Tube anode:	Cu
Generator tension:	40 kV
Generator current:	30 mA
Start angle:	3.5 °2θ
End angle:	35.0 °2θ
Step size:	0.020 °2θ
Time per step:	2.3 s

Table II.

X-Ray Powder Diffraction Angles and Calculated Lattice Spacings Characteristic of the Polymorph.

Diffraction Angle (°2θ)	Lattice Spacing (Angstroms)
8.9	9.90
12.0	7.35
14.0	6.32
15.4	5.73
15.9	5.55
16.8	5.26
17.4	5.08
18.1	4.89
19.2	4.60
19.6	4.52
20.0	4.44
20.3	4.37
20.8	4.27
21.2	4.18
22.3	3.97
23.7	3.80
24.3	3.75
25.1	3.54
25.8	3.44
26.7	3.33
27.2	3.27
28.7	3.10
29.6	3.01
30.6	2.92
31.6	2.83
32.2	2.78
33.3	2.69

%Transmittance
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
4000
3500
3000
2500
2000

Figure I. Infrared Spectrum of the Polymorph

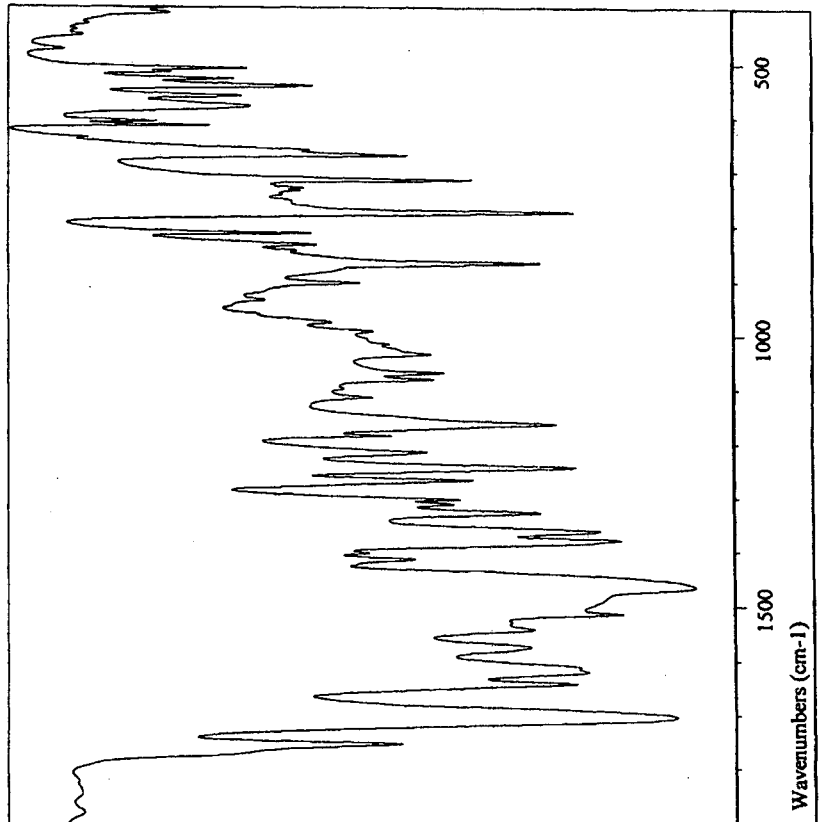


Figure II. Raman Spectrum of the Polymorph

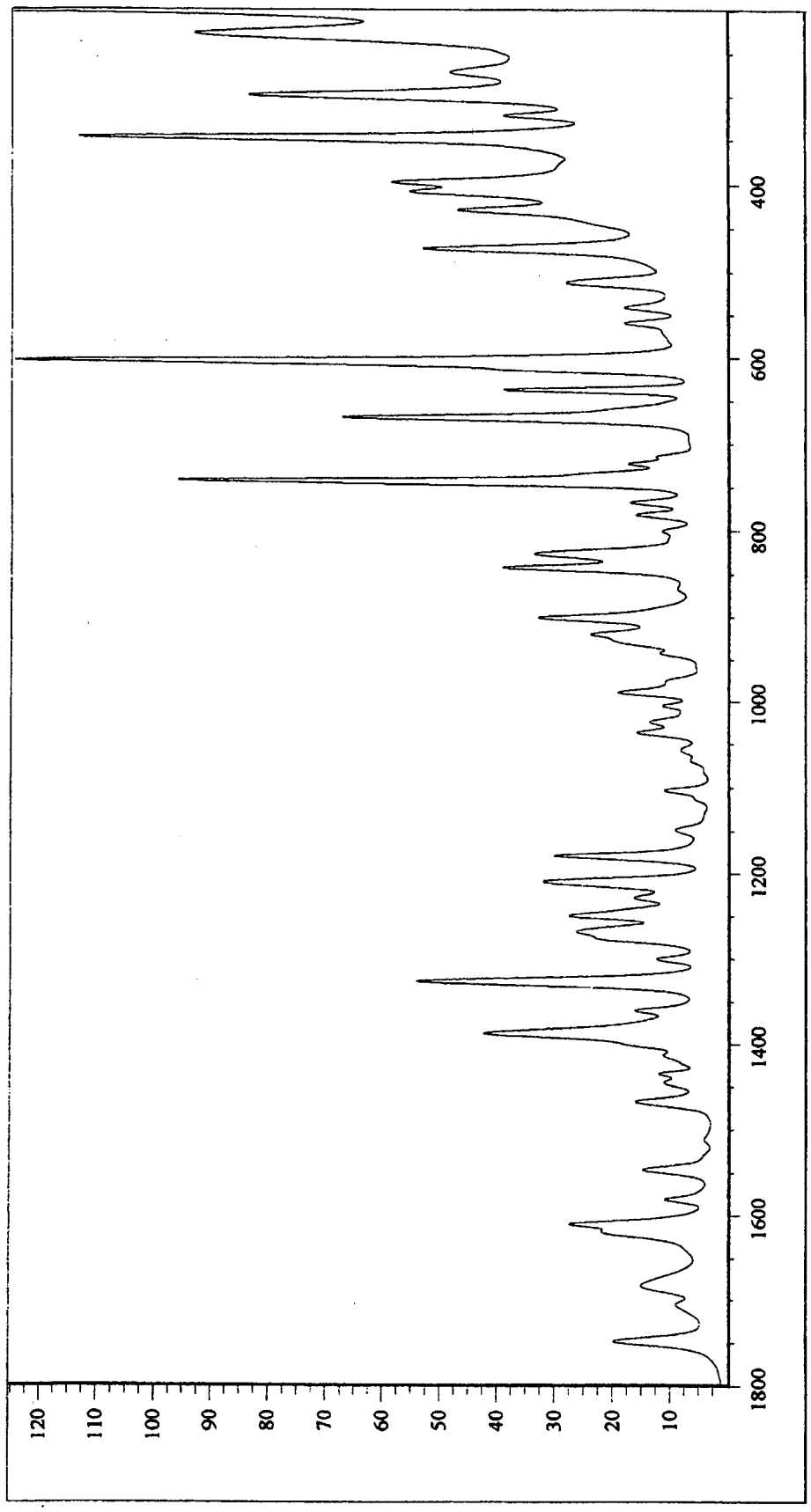


Figure III. Solid-State NMR Spectrum of the Polymorph

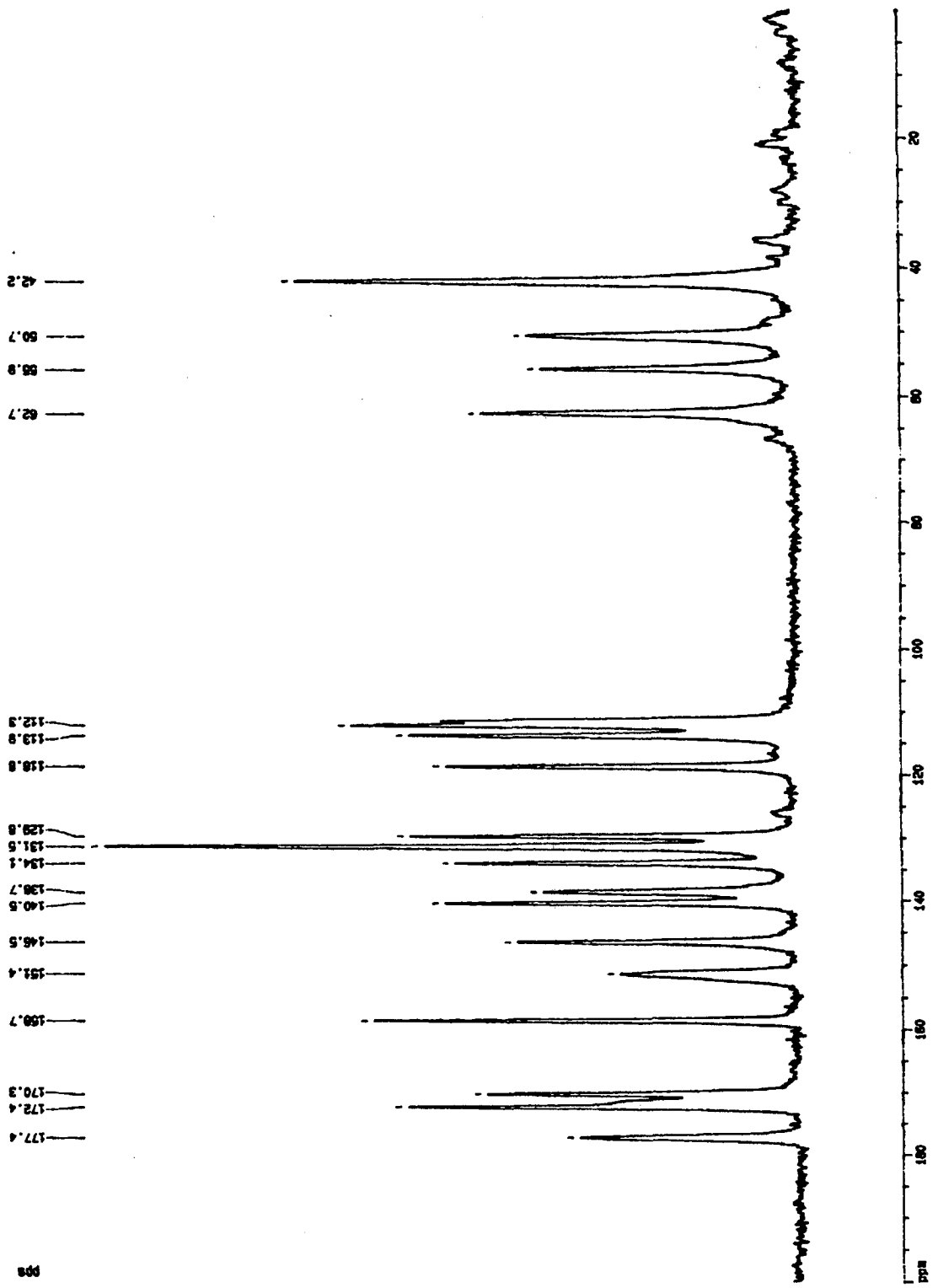
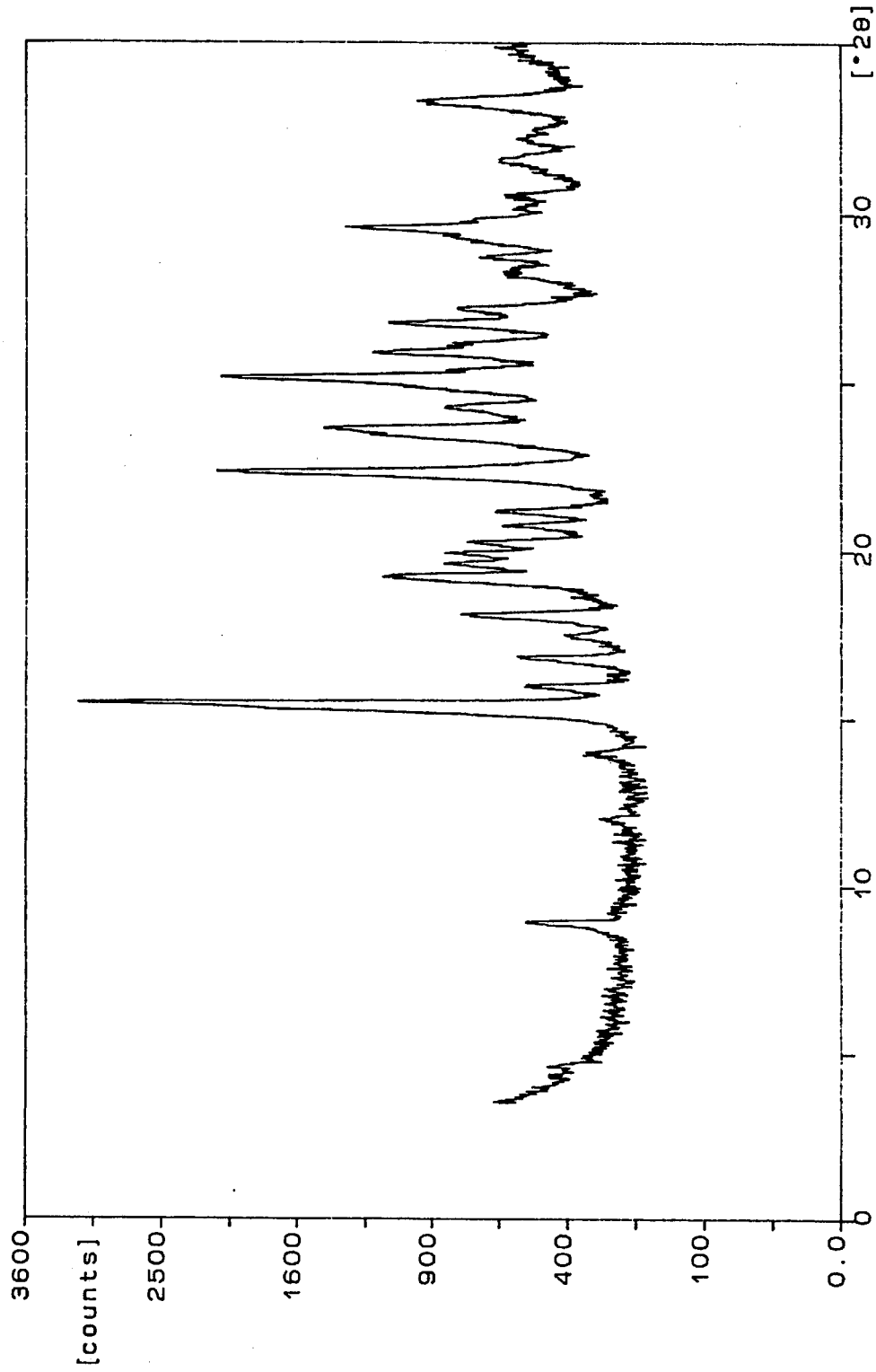


Figure IV. X-Ray Powder Diffraction Pattern
of the Polymorph



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LEGALIZACIONES

OFICINA DE PATENTES
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

El suscrito, un funcionario debidamente autorizado conforme a los Artículos 74(1) y (4) de la Ley de Desreglamentación y Contratación de 1994 para firmar y expedir certificados en nombre del Contralor General, certifico que la copia adjunta es una copia correcta de los documentos archivados originalmente con respecto a la solicitud de patente que allí se identifica.

De acuerdo con las Reglamentaciones de Patentes de 1982 (Re-registro de Compañías), si una compañía nombrada en este certificado y en los documentos adjuntos se ha vuelto a registrar según la Ley de Compañías de 1980 con el mismo nombre con el que fue registrada inmediatamente antes del re-registro, salvo la sustitución o inclusión como la última parte del nombre de las palabras "sociedad anónima" o su equivalente en galés, las referencias al nombre de la compañía y sus documentos adjuntos serán tratadas como referencias al nombre con el cual fue re-registrada.

De acuerdo con las reglas, las palabras "sociedad anónima" (o en inglés *public limited company)* pueden ser reemplazadas por las letras p.l.c, plc. P.L.C ó PLC.

El re-registro bajo la Ley de Compañías no constituye una nueva entidad legal sino simplemente somete a la compañía a ciertas normas de ley adicionales.

(FIRMA) ANDREW BREWER FECHA: 23 de marzo de 2000

(SELLO DE LACRE)

70-46

OFICINA DE PATENTES

SOLICITUD DE PATENTE

1. Su referencia: **KR/JW/P32284**

2. Solicitud No. **9909472.4** 23 de abril de 1999

3. Nombre completo y código postal de cada solicitante:

Dirección: (1) SMITHKLINE BEECHAM BIOLOGICAS S.A.
New Horizons Court,
Brentford, Mddlesex TW8 9EP

No. APD 7605050001

Si el solicitante es una entidad, indique el pais/estado de constitución:

REINO UNIDO

4. TITULO DEL INVENTO:

COMPUESTOS NOVEDOSOS

5. NOMBRE DE SU AGENTE:

Nombre del Agente: CORPORATE INTELLECTUAL PROPERTY

Dirección para notificaciones: SMITHKLINE BEECHAM PLC
TWO NEW HORIZONS COURT
BRENTFORD
MIDDLESEX TW8 9EP

NO. ADP Patentes 5800974004

6. N/A

7. N/A

8. SI

9. Número de hojas radicadas (En inglés). Descripción: 8 Reivindicaciones:

Resumen : - Dibujos: - 4

10. Solicitud de examen preliminar y búsqueda:

11. Solicitamos se nos adjudique una patente con base en esta solicitud.

K RUTTER 23 de abril de 1999

12. Nombre y teléfono del contacto en el Reino Unido Nombre y teléfono del contacto en el Reino Unido (FIRMA) K RUTTER 01279 644396

COMPUESTOS NOVEDOSOS

La invención se refiere a un producto farmacéutico novedoso, a un proceso para la preparación del fármaco y al uso del fármaco en medicina.

La Solicitud de Patente Internacional, No. de Públicación WO94/05659 revela ciertos derivados de tiazolidinediona que tienen actividad hipoglicémica e hipolipidémica incluyendo 5-[4-[2-(N-metil-N-(2-piridil)amino)etoxi]bencitia zolidine-2,4-diona, sal de ácido maléico (Compuesto (I).

Se ha descubierto que el Compuesto (I) existe en una forma polimórfica novedosa que es particularmente adecuada para preparación y manejo de volúmenes. La forma novedosa puede ser preparada mediante un proceso eficiente, económico y reproducible indicado para preparación a grande escala.

La forma polimórfica (el "Polimorfo") también tiene propiedades farmacéuticas útiles y en particular está indicada para el tratamiento y/o profilaxis de diabetes mellitus, condiciones asociadas con diabetes mellitus y ciertas complicaciones de la misma.

Por lo tanto, la presente invención provee una forma polimórfica de 5-[4-[2-(N-metil-N-(2-piridil)amino)etoxi]bencitiazolidine-2,4-diona, sal de ácido maléico, caracterizada en que:

i) provee un espectro infrarrojo que contiene picos a 1360, 1326, 1241, 714 y 669 cm^{-1}; y/o

ii) provee un especto Raman que contiene picos a 1581, 768, 670, 271 y 226 cm^{-1}; y/o

iii) provee un espectro de resonancia magnética nuclear de estado sólido que contiene picos a desplazamientos químicos sustancialmente como los que se indica en la Tabla I ; y/o

iv) provee un patrón de diracción de polvo de rayos X (XRPD) que contiene picos sustancialmente como los que se indica en la Tabla II.

La presente invención abarca el Polimorfo aislado en forma pura o cuando es mezclado con otros materiales, por ejemplo, las formas conocidas del Compuesto I o cualquier otro material.

Así es como en un aspecto, se provee el Polimorfo en forma aislada.

En otro aspecto, se provee el Plimorfo en forma ura.

Aún en otro aspecto, se provee el Polimorfo en forma cristalina.

La invención también provee un proceso para preparar el Polimorfo, caracterizado en que una suspensión del Compuesto (I) y etanol desnaturalizado conteniendo 0,8 a 2,5% peso por volumen de agua, es calentado a 45°C por un periodo de tiempo prolongado, por ejemplo 65 horas, luego del cual el Polimorfo es recuperado del etanol desnaturalizado.

En un proceso alternativo, una solución del Compuesto (I) en etanol desnaturalizado conteniendo 0,8 a 2,5% peso por volumen de agua a 55°C es germinado con el Polimorfo y luego enfriado a 20-25°C para proveer el Polimorfo. El Polimorfo es luego recuperado del etanol desnaturalizado.

El Compuesto (I) es preparado de acuerdo con procedimientos conocidos, tales como los que revela la Patente WO94/05659 cuyo contenido se incorpora en esta Patente por referencia.

Diabetes mellitus, significa preferiblemente diabetes mellitus Tipo II

En otro aspecto, la presente invención provee el uso del Polimorfo para la fabricación de un medicamento para el tratamiento y/o profilaxis de diabetes mellitus, condiciones asociadas con diabetes mellitus y ciertas complicaciones de la misma.

Para los compuestos de esta invención no se indican efectos toxicológicos adversos en los tratamientos mencionados.

S1

Industria y Comercio
SUPERINTENDENCIA

2do. EXAMEN DE FORMA PATENTE DE INVENCION

Folio ~~75~~

Radicación no 00-28932

Concepto Técnico no 506 Clasificación Internacional de Patentes A61K 31/12 // 31/425 // 31/44

Practicado el examen de acuerdo a lo establecido en el Art. 38 de la Decisión 486 se determinó que esta solicitud de **Patente de Invención:**

SI [X]	NO [ ]	Contiene un resumen de la invención (Art.26-e).
SI [X]	NO [ ]	Contiene el título o nombre de la invención (Art.27-d).
SI [X]	NO [ ]	Contiene la descripción de la invención (Art.26-b).
SI [X]	NO [ ]	NO ES APLICABLE [ ] Contiene los dibujos necesarios para comprender la invención (Art.26-d)
SI [X]	NO [ ]	Contiene una o más reivindicaciones. (Art.26-c).
SI [ ]	NO [ ]	NO ES APLICABLE [X] Han sido desarrollados los productos y/o procedimientos a partir de recursos genéticos o de sus productos derivados de los que cualquiera de los Países Miembros es país de origen. (Art. 26- h).
SI [ ]	NO [ ]	NO ES APLICABLE [X]Los productos y/o procedimientos han sido obtenidos o desarrollados a partir de los conocimientos tradicionales de las comunidades indígenas, afroamericanas, o locales de los países miembros, de acuerdo a lo establecido en la Decisión 391 y sus modificaciones y reglamentaciones vigentes.(Art.26-i).
SI [ ]	NO [X]	La invención se refiere a un producto relativo a un material biológico. (Art.26-J).
SI [X]	NO [ ]	La prioridad coincide con la materia reivindicada.
SI [X]	**NO [ ]**	**CUMPLE LOS REQUISITOS TÉCNICOS**

OBSERVACIONES Y OTROS: SI [X] NO [ ] ver hoja(s) anexa(s)

El título ha sido modificado folio 34
El solicitante no hizo las conecciones sugeridas folio 32. numerales 2 y 3, para lo cual da las ratones en el folio 34 y 35.
Se anexa nuevo Extracto para publicación folio 38, Nuevas Tarjetas de Propietarios y de Archivo temático folios 39 y 40.

EXAMINADOR TÉCNICO
202038

Bogotá D. C., Marzo 19/02

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Industria y Comercio
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Folio 76 2002-06-27 416

2020
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GERMÁN CASTILLO GRAU
Apoderado(a)

REFERENCIA:	Radicación No.	**00-28932**
	Trámite	002
	Evento	001
	Actuación	416
	Oficio No.	**655**
	Folios	001

Teniendo en cuenta que la solicitud de privilegio de patente que se tramita bajo el expediente indicado en la referencia, reúne los requisitos de forma establecidos en los artículos 26 y 27 de la Decisión 486 de la Comisión de la comunidad andina, y en las demás disposiciones vigentes sobre la materia, se envía el extracto de la solicitud a la Oficina de comunicaciones para efecto de su publicación en la Gaceta de Propiedad Industrial, conforme lo establece el artículo 40 de la misma Decisión.

Cúmplase
Dado en Bogotá, D.C., a los 17 ABR 2002

ALIX CÉSPEDES DE VERGEL
Jefe de la División de Nuevas Creaciones

Bogotá, D.C., 09-03-2005 El extracto de esta solicitud fue publicado en el número 517 de la Gaceta de Propiedad Industrial, de fecha 27-06-2002 . El término hábil señalado por la ley expiró el 24-09-02 y SI__ NO X se presentaron oposiciones por parte de terceros.

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