

Señor
SUPERINTENDENTE DE INDUSTRIA Y COMERCIO
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
Bogotá, D.C.

SUPERINDUSTRIA Y COMERCIO

Radicación : 00028927 00000009

Folios: 12

Fecha (AMD): 2005-10-05 15:59:20

Trámite : 002 PATENTES D 1 REGISTRO/ 412 REPOSIC -

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Re: Actuación: 412
Radicación: 00028927
Patente de Invención:
NUEVO COMPUESTO ANTIDIABETICO
CON BASE E SALES DEL ÁCIDO MALÉICO
RECURSO DE REPOSICIÓN

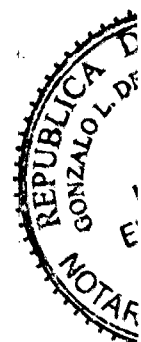
En relación con el expediente de la referencia y actuando como apoderado de la sociedad SMITHKLINE BEECHAM P.L.C., legalmente constituida y domiciliada en Brentford, Middlesex, Inglaterra, manifiesto que de conformidad con lo dispuesto en los artículos 50 y 51 del Código Contencioso Administrativo, interpongo recurso de **REPOSICIÓN** contra la resolución N° 24079 dictada por el Superintendente de Industria y Comercio el 23 de Septiembre de 2005, notificada mediante memorial el día 23 de Septiembre de 2005, mediante la cual se negó el privilegio de patente de invención para la solicitud correspondiente a **NUEVO COMPUESTO ANTIDIABETICO CON BASE EN SALES DEL ÁCIDO MALÉICO**.

I. OBJETO DEL RECURSO

Este recurso tiene como objeto que el Superintendente de Industria y Comercio revoque en su totalidad la resolución N° 24079 del 23 de Septiembre de 2005 y en su lugar dicte otra en la conceda el privilegio de patente de invención para la solicitud correspondiente a **NUEVO COMPUESTO ANTIDIABETICO CON BASE EN SALES DEL ÁCIDO MALÉICO** por cumplir con los requisitos de novedad, altura inventiva y aplicación Industrial, exigidos por la normatividad Andina.

II. FUNDAMENTOS DE HECHO DEL RECURSO

1. El día 19 de Abril de 2000 actuando como representante legal y apoderado de la sociedad SMITHKLINE BEECHAM P.L.C. solicité el



misma estructura química cuando se escriben en el papel, y por ende el mismo nombre, pero que tengan diferentes puntos de fusión, espectros y patrones de difracción de rayos X. Estas características diferentes definen al novedoso polimorfo de la presente invención y se declaran en la reivindicación 1.

2. El rechazo de la presente solicitud se basa en varias suposiciones hechas por el examinador que en realidad están equivocadas. Por ejemplo, en la página 5, párrafo 3, afirma lo siguiente:

"Se aclara además, que el ser un polimorfo es una característica inherente al compuesto".

deliza espontánea

Esto es incorrecto. Si ser un polimorfo fuese inherente, cualquier compuesto podría únicamente tener existencia en un único estado polimórfico. Esto es incorrecto en sí mismo y es una contradicción de los términos. En el caso de la sal del ácido maleico de la 5-[4-[2-(N-metil-N-(2-piridil)amino)etoxi]benzil]tiazolidine-2,4-diona existen varias formas polimórficas. El polimorfismo no es predecible ni inherente.

3. Afirma también el examinador en el último párrafo de la página 10, que:

"De manera que lo obtenido es otro compuesto, el cual tiene otra estructura química y otro nombre"

Esta afirmación es incorrecta y sugiere que el examinador no entiende el polimorfismo o su análisis. Solicito a su Despacho tener en cuenta el artículo de Pharmaceutical Technology publicado en agosto de 2004 y disponible en la siguiente dirección de Internet: http://www.findarticles.com/particles/mi_m0EEH/is_8_28/ai_n6361510 #continue en donde se observa con claridad que los diferentes polimorfos del mismo compuesto tendrán diferentes perfiles espectrales y de XRPD. Es decir que, aunque los polimorfos tengan la

El anterior memorial fue presentado personalmente por

German de Jesus Castillo Grau

quien se identificó con C. de C. No. 17.017.671

de Bogotá

Tarjeta Profesional No. _____

Bogotá, D. E.

-5 OCT 2005



Thomas J. Offerdahl

in which N is the number of nuclei present, $[\Delta E] = \frac{\gamma \hbar B_0}{2\pi}$, k is the Boltzmann constant, and T is the temperature in Kelvin. The NMR signal is proportional to the population difference. With increasing magnetic field, a larger $[\Delta E]$ produces a bigger population difference and a larger NMR signal. In Fourier transform NMR spectroscopy, the nuclei are perturbed from equilibrium and the precessing spins produce an alternating current in a coil. The resulting signal, or free induction decay (FID), is processed to produce the NMR spectrum.

152 8

Solution-state NMR spectroscopy. Solution-state NMR spectroscopy elucidates the structure of many organic molecules because researchers can consistently predict or interpret the NMR spectrum for small organic molecules. The rapid motion of the molecules in solution creates high-resolution NMR spectra with linewidths less than 1 Hz, with an average acquisition time of a ^1H NMR spectrum less than 1 min. Because of the high resolution that is possible in a solution NMR spectrum, the structure of the molecule often can be determined (4, 5). This technique can be easily automated and can be used in conjunction with other solution techniques such as liquid chromatography. More advanced NMR pulse sequences such as DEPT, INEPT, NOESY, and REDOR are two-dimensional NMR pulse sequences that allow researchers to observe the molecular dynamics and give insight into its structure. Higher magnetic field strengths, currently at 21.1 T (^1H = 900 MHz), and better magnet designs allow scientists to apply solution-state NMR spectroscopy to study the structure and associated dynamics of large, complex molecules such as proteins.

Solid-state NMR spectroscopy. Solid-state NMR spectroscopy is an emerging technique for analyzing various API forms. In contrast to solution-state NMR spectroscopy, in which a high degree of molecular mobility exists and rotational averaging is conducted, solid-state NMR methods involve little or no molecular mobility. NMR spectra of a solid sample, therefore, generate very broad peaks as a result of two prominent interactions: dipolar coupling and chemical shift anisotropy (CSA).

Dipolar couplings are through-space interactions between the magnetic moments of two or more nuclei. Because nuclei have magnetic moments, the "magnet" of one nucleus influences the neighboring field of another nucleus. The magnitude of the dipolar coupling has a $1/r^3$ dependence and is proportional to the magnetogyric ratios of the coupled nuclei. This coupling is either homonuclear or heteronuclear. Most often, only ^1H - ^{13}C heteronuclear dipolar interactions are significant in solid-state ^{13}C NMR spectroscopy because the low natural abundance of ^{13}C (1.1%) means that the probability that two ^{13}C nuclei are in close proximity is very small.

CSA is the other main broadening factor in solid-state NMR spectra. When a sample is placed in a magnetic field, the individual crystallites exhibit various orientations with respect to the magnetic field, thereby creating a range of chemical shifts for the sample, often called a powder pattern. Powder patterns may be ~200 ppm broad for sp^2 hybridized carbons (e.g., carbonyl, aromatic). If multiple sites are present, as is typical for APIs, the result is a broad, featureless NMR spectrum. High-power decoupling and/or magic-angle spinning (MAS) can almost eliminate the effects of these two interactions.

High-power ^1H decoupling can greatly reduce or eliminate the ^1H - ^{13}C dipolar interactions. During the acquisition of FID, a continuous radio frequency (RF) pulse at the ^1H Larmor frequency is applied to the sample. The ^1H spins rapidly "flip" between the α and β states such that the ^{13}C nucleus sees only the average dipolar interaction, which is zero.

Magic-angle spinning averages the chemical-shift anisotropy. Andrew (6) and Lowe (7) independently discovered this technique. When a sample spins rapidly at 54.74[degrees] (the magic angle) relative to a static magnetic field, the anisotropic component of the chemical shift is either partially or completely averaged to the isotropic chemical shift, thereby yielding high-resolution solid-state NMR spectra. This angle dependence also reduces the dipolar interaction. When the spinning speed is less than the width of the powder pattern, spinning sidebands appear at multiples of the spinning speed. This magic-angle, calculated using average Hamiltonian theory, can be rationalized by simpler means. The body diagonal of a cube is 54.74[degrees], so if a sample is spinning about that axis of rotation, then the individual vectors from each nuclei will spend an equal amount of time in all three axes, thereby averaging out the CSA.

Cross-polarization (CP) provides a four-fold signal enhancement for ^{13}C experiments. It also shortens acquisition delay times because the recycle delay is determined by the ^1H relaxation rate, which often is much slower than that of a ^{13}C nuclei (8). Stejskal and Schaefer described the combination of these three techniques (CP, MAS, and high-power decoupling) in 1977 (9). Figure 1 shows the solid-state NMR spectrum of hexamethylbenzene, a common solid-state NMR standard, obtained using multiple pulse sequences. The use of CP reduced the acquisition time by a factor of nine and greatly improved the sensitivity.

[FIGURE 1 OMITTED]

Probe designs and pulse-sequence designs for solid-state NMR spectroscopy have advanced significantly since the development of the CPMAS NMR experiment. Initial MAS speeds were slow, but improved technologies and materials have increased spinning speeds to 50 kHz (3,000,000 rpm). Other improvements include the design of new pulse sequences. For example, the use of the total sideband suppression (TOSS) experiment removes the spinning sidebands present in a MAS NMR spectrum (see Figure 1) (10). The interrupted-decoupling experiment can differentiate methyl and quaternary carbons from methines and methylenes (11). Recently, two-dimensional pulse sequences that normally are used in solution have been applied to solid samples. One example is the heteronuclear correlation (HETCOR) experiment, in which assignments are made on the basis of the connectivities between two

153 9

different nuclei (12).

Advantages and disadvantages of solid-state NMR spectroscopy

Solid-state NMR spectroscopy offers several advantages over other analytical techniques. NMR spectroscopy is a selective technique that allows researchers to focus on a specific nucleus of interest (i.e., [¹³C], [¹⁹F], [¹⁵N]). Moreover, if the molecule has specific reactive sites, the use of isotopic labeling can increase the sensitivity of those particular sites by two orders of magnitude. Solid-state NMR spectroscopy is not greatly affected by particle size; in fact, intact tablets of the correct diameter can be analyzed directly. Formulations also can be analyzed directly, without the need to extract the API from the matrix. Typically excipient peaks lie in a region of the NMR spectrum that does not overlap with many of the peaks from the API. Techniques such as spectral subtraction can even remove the excipient peaks from the spectrum.

Solid-state NMR spectroscopy makes it possible to directly observe API-excipient interaction occurring in a tablet, which is critical to the investigation of stability and bioavailability issues. Solid-state NMR spectroscopy is highly sensitive to changes in the local environment such that it can detect small changes that are sometimes not seen in PXRD patterns. In addition, polymorphs are readily identified because of the change in the chemical shift of a specific peak and, in contrast to XRD, even amorphous material can be observed easily.

NMR spectroscopy is inherently quantitative: the intensity of the peaks is directly proportional to the number of magnetically equivalent nuclei. When the technique is conducted properly, quantitation can be performed without the need for a standard curve. This capability is extremely useful when a specific polymorph cannot be isolated at a high enough purity for use in generating a standard curve, which is a necessary step in other analytical techniques.

Solid-state NMR spectroscopy also has some disadvantages. The technique is nonroutine and requires a highly trained operator. The instrumentation is generally more expensive than that used for the other analytical techniques discussed. Solid-state NMR spectroscopy is difficult to automate, meaning that individual samples must be switched manually, which limits sample throughput. For the analysis of pharmaceutical materials, solution NMR spectroscopy generally involves [¹H] NMR spectroscopy because of its high natural abundance and Larmor frequency. This is not possible in the solid state because of high dipolar interactions. Solid-state [¹H] NMR spectroscopy generates broad peaks, usually spanning 20-30 ppm. Analysis of pharmaceuticals in the solid-state requires [¹³C] NMR spectroscopy. However, because the natural abundance of [¹³C] is 1.1% and the Larmor frequency is approximately one-fourth that of [¹H], [¹³C] NMR spectroscopy is ~6000 times less sensitive than [¹H] NMR spectroscopy. This, of course, leads to longer acquisitions because of the increased number of transients required for adequate signal-to-noise. Moreover, for some samples the relaxation time between transients can be as short as a second to as long as an hour or even longer. So acquiring a simple one-dimensional solid-state NMR spectrum could take from a couple of minutes to several days. Isotopic enrichment of certain sites in the molecule shortens the acquisition time by increasing the sensitivity; however, it also increases the expense of the analysis.

Applications of solid-state NMR spectroscopy to pharmaceutical solids

This section discusses some of the current literature describing the use of solid-state NMR spectroscopy to characterize pharmaceuticals and shows some spectra of several over-the-counter medications with different API loading levels. These spectra show the ability of solid-state NMR spectroscopy to characterize formulations, to quantify polymorphic mixtures, to differentiate polymorphic forms, and to complement the information provided by other analytical techniques.

Solid-state NMR spectroscopy of pharmaceutical dosage forms. Solid-state NMR spectroscopy is uniquely suited to studying intact formulations. The selectivity of the technique and its nondestructive nature allow direct analysis of intact formulations. For this article, the author tested several over-the-counter medications using solid-state NMR spectroscopy. Analysis was conducted on site using an NMR spectrometer (Unityplus, Varian Inc., Palo Alto, CA) and an Oxford 9.4 T ([¹H] = 399.870 MHz, [¹³C] = 100.557 MHz) narrow-bore magnet. Samples were obtained from a local pharmacy store and gently broken apart with a mortar and pestle. These fragments were packed in a [³Si][⁴N] 7-mm rotor, placed in a double resonance CPMAS probe, and spun from 3500 to 4000 Hz.

Ibuprofen is a very simple molecule with a relatively fast relaxation rate. A fast relaxation rate and moderate loading of the API (approximately 40%) lead to a very fast acquisition time. Figure 2 shows the resulting spectrum in which the API peaks are readily identified among those peaks owing to the excipients (marked with an asterisk).

Ibuprofen represents a relatively ideal case: a fast relaxation rate and moderate API loading. Therefore, to better demonstrate the ability of solid-state NMR spectroscopy to deal with a range of APIs and drug loadings, the author tested a set of similar heartburn

154 10

relieving medications, each having different API loads: cimetidine 200 mg (70.9% w/w), ranitidine 75 mg (50.9% w/w), nizatidine 75 mg (21.3% w/w), and famotidine 10 mg (4.9% w/w). Figure 3 shows the resultant spectra. The excipient peaks are easily identifiable as well as the peaks owing to the specific API, all of which appear crystalline because of the sharp peaks seen in the NMR spectra. The individual peaks from the API all have different chemical shifts, thereby making it relatively simple to determine which API is present in the formulation or whether there is a mixture of APIs present in the formulation. At the lowest loading level, only the methyl peak appears because time constraints limited full optimization of the NMR parameters for acquisition.

[FIGURES 2-3 OMITTED]

Pharmaceutical analysts also use solid-state NMR spectroscopy to study products with low API loading. Figure 4 shows that one can obtain a usable spectrum of loperamide hydrochloride in 2 mg (1.2% w/w) API loading. The most intense peaks in the NMR spectrum are attributed to the excipients, but a few low-intensity peaks owing to the API also are visible. When the NMR conditions are fully optimized, significantly better spectra are obtainable. Isotopic enrichment would have lowered the loading level, perhaps down to 0.01% w/w in an ideal case.

[FIGURE 4 OMITTED]

Quantitation of drug forms. Under ideal circumstances, an NMR spectrum in the solid state should be quantitative. Solid-state NMR spectra, however, are often not quantitative because they are usually acquired with a CP experiment. In this type of experiment, the peak areas in the NMR spectrum are a result of the amount of the specific molecular form in the sample and the dynamics involved with the magnetization transfer from the abundant spin (normally [sup.1]H) to the dilute (normally [sup.13]C) spin. These dynamics must be taken into account to achieve accurate results. Gao used this approach to determine the composition of polymorphic mixtures of delavirdine mesylate (13).

Binary mixtures of a minor polymorphic or pseudopolymorphic form were mixed with a major form and quantitation was performed. Taking the CP dynamics into account, the author used multiple contact times to measure the change in magnetization transfer with respect to time. The initial buildup of magnetization was attributed to the rate of transfer of magnetization from [sup.1]H to [sup.13]C, characterized by the heteronuclear cross-polarization rate constant [T.sub.CH]. The decrease of the intensity over time is a result of one of the proton relaxation rates, [T.sub.1[rho]]. Calculations revealed that the isopropyl methyl carbon peaks--the peaks that were used for the quantitation--had the same [T.sub.1[rho]] rates for all of the forms.

Quantitation, therefore, could be carried out directly on the basis of the peak area to provide a relative measure of the one form with respect to the other. The areas of the peak corresponding to each of the polymorphic forms were taken and the experimental weight percent was determined for each polymorphic form. Experimental results agreed to within 1% (absolute error) of the actual amount present (see Table I). Moreover, a plot of the actual weight percent versus the NMR determined weight percent confirmed the overall accuracy of the method. The data fit the expected straight line with a slope near one and an intercept near zero.

Assigning the NMR spectrum of aspartame forms

Numerous articles discuss using solid-state NMR spectroscopy for identifying and characterizing polymorphic systems. Solid-state NMR spectroscopy can identify the number of crystallographically inequivalent molecules in the unit cell on the basis of the number of peaks for each carbon. However, this can make it even more difficult to assign the peaks in the NMR spectrum to a specific carbon in the molecule, because chemical shift values in the solid state can be as much as 10 ppm different from their values in solution (14). Aspartame exists in several different forms. Forms I and II are hemihydrate, and Form III is dihemihydrate. The [sup.13]C CPMAS NMR spectra of these three forms are easily distinguishable (see Figure 5). Form I has only one peak per carbon, which indicates that only one crystallographically inequivalent molecule in the unit cell, which agrees with the crystal structure. The other two forms show up to three resonances for several of the carbons, indicating multiple crystallographically inequivalent molecules in the unit cell. To assign the spectra, the authors synthesized aspartame in which all of the carbons were [sup.13]C. By combining high speed MAS with very strong [sup.1]H decoupling powers, the authors were able to obtain high-resolution NMR spectra of uniformly [sup.13]C-labeled aspartame. Two-dimensional exchange experiments were then used to assign the individual resonances for the resolved peaks.

[FIGURE 5 OMITTED]

Comparison to other analytical techniques

Pharmaceutical scientists use several analytical techniques to fully characterize a sample. Sometimes these techniques provide contradictory information. A recent article by Padden et al. highlights the use of PXRD and solid-state NMR spectroscopy for

155 //

identifying different forms of a new artificial sweetener Neotame, a derivative of aspartame (15). Neotame exists in multiple polymorphic forms (16). Several of these forms were generated via dehydration and were successfully analyzed by PXRD and solid-state [sup.13]C CPMAS NMR spectroscopy. In the study, a sample containing a mixture of two anhydrous polymorphic forms was allowed to rehydrate for several days. Solid-state NMR spectroscopy showed that a transformation was occurring, and at one stage of the rehydration, as many as five different polymorphic forms were present (see Figure 6). Interestingly, the PXRD patterns did not change during the rehydration experiment. The researchers concluded that the NMR experiment was observing changes in the local conformation of the molecules, which the PXRD method did not identify because the long-range order was not affected.

[FIGURE 6 OMITTED]

Conclusion

Solid-state nuclear magnetic resonance spectroscopy is a valuable technique for analyzing pharmaceuticals. Using this technique, researchers can evaluate formulations in a nondestructive manner and gain far more information than by using other methods. NMR spectroscopy can readily identify the contributions of excipients, and in some cases, eliminate them. Polymorphs, polymorphic transitions, and amorphous forms can be easily identified, and quantitation can be performed without the need of a standard curve.

Table I: Comparison of actual versus NMR-determined weight percents for a physical mixture of delavirdine mesylate polymorphs (13).

Actual weight percent	NMR-determined weight percent
2.00	2.7
3.00	2.8
5.00	5.4
10.00	9.4
15.00	14.5
19.90	20.2
25.00	24.0
50.00	48.7

Acknowledgment

I would like to thank Drs. Gary Silvey, Marty Power, and Jeff Botts for their contributions to this work.

References

- (1.) D.E. Bugay, "Solid-State Nuclear Magnetic Resonance Spectroscopy: Theory and Pharmaceutical Applications," Pharm. Res. 10 (3), 317-327 (1993).
- (2.) H.G. Brittain, Physical Characterization of Pharmaceutical Solids (Marcel Dekker, New York, NY, 1995).
- (3.) S. Byrn et al., "Pharmaceutical Solids: A Strategic Approach to Regulatory Considerations," Pharm. Res. 12, 945-954 (1995).
- (4.) T.D.W. Claridge, High-Resolution NMR Techniques in Organic Chemistry (Permagon, New York, NY, 1999).
- (5.) R.K. Harris, Nuclear Magnetic Resonance Spectroscopy (John Wiley & Sons, New York, NY, 1989).
- (6.) A.R. Andrew, A. Bradbury, and R.G. Eades, "Removal of Dipolar Broadening of Nuclear Magnetic Rsonance Spectra of Solids by Specimen Rotation," Nature 182, 1659 (1958).
- (7.) I.J. Lowe, "Free Induction Decays of Rotating Solids," Phys. Rev. Lett. 2, 285 (1959).
- (8.) A. Pines, M.G. Gibby, and J.S. Waugh, "Proton-Enhanced NMR of Dilute Spins," J. Chem. Phys. 59, 569-590 (1973).
- (9.) E.O. Stejskal and J. Schaefer, "Magic-Angle Spinning and Polarization Transfer in Proton-Enhanced NMR," J. Magn. Reson. 28,

156

105-112 (1977).

(10.) W.T. Dixon et al., "Total Suppression of Sidebands in CP/MAS C-13 NMR," J. Magn. Reson. 49, 341-345 (1982).

(11.) S.J. Opella and M.H. Frey, "Selection of Nonprotonated Carbon Resonances in Solid-State Nuclear Magnetic Resonance," J. Am. Chem. Soc. 101, 5854 (1979).

(12.) A. Lesage, "Carbon-Proton Chemical Shift Correlation in Solid-State NMR by Through-Bond Multiple-Quantum Spectroscopy," J. Am. Chem. Soc. 120, 13194-13201 (1998).

(13.) P. Gao, "Determination of the Composition of Delavirdine Mesylate Polymorph and Pseudopolymorph Mixtures Using [sup.13] C CP/MAS NMR," Pharm. Res. 13 (7), 1095-1104 (1996).

(14.) M.T. Zell et al., "Two-Dimensional High-Speed CP/MAS NMR Spectroscopy of Polymorphs I: Uniformly [sup.13]C-Labeled Aspartame," J. Am. Chem. Soc. 121, 1372-1378 (1999).

(15.) B.E. Padden et al., "Comparison of Solid-State [sup.13]C NMR Spectroscopy and Powder X-ray Diffraction for Analyzing Mixtures of Polymorphs of Neotame," Anal. Chem. 71, 3325-3331 (1999).

(16.) Z. Dong et al., "Neotame Anhydrate Polymorphs I: Preparation and Characterization," Pharm. Res. 19 (3), 330-336 (2002).

Thomas J. Offerdahl, PhD, is the manager of the solid-state NMR facility at Quintiles, Inc., 10245 Hickman Mills Drive, Kansas City, MO 64137, tel. 816.767.4798, fax 816.767.7301, Thomas.Offerdahl@Quintiles.com.

COPYRIGHT 2004 Advanstar Communications, Inc.

COPYRIGHT 2004 Gale Group

Las reivindicaciones 1 - 8 y 11 - 13 se refieren al uso del polimorfo I del ácido maléico de la 5-[4-[2-(N-metil-N-(2-piridil)amino)etoxi]bencil]-1,2,4-diona.

Las reivindicaciones 9 y 14 - 19 mencionan un proceso para preparar un polimorfo que se caracteriza porque una disolución del compuesto en etanol ó acetona a elevada temperatura se enfría de manera que se produce la cristalización del polimorfo, después de lo cual se recupera.

La reivindicación 10 se refiere a una composición que contiene un polimorfo de la reivindicación 1 y un vehículo.

La reivindicación 13 se refiere al uso del polimorfo.

El problema planteado en esta solicitud es la necesidad de proporcionar un nuevo producto farmacéutico para tratamiento y/o profilaxis de diabetes

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

180

RADICACIÓN: 0-28927

EDICTO No. 5813

LA SECRETARÍA GENERAL AD-HOC
HACE SABER:

Que esta Superintendencia profirió Resolución No. 7010 de 27-MAR-2006. Que el contenido de la parte resolutive es como sigue: El Superintendente de Industria y Comercio.

RESUELVE

ARTICULO PRIMERO: Confirmar la decisión contenida en la Resolución 24079 de 23 de septiembre de 2005 por medio de la cual se negó una patente de invención.

ARTICULO SEGUNDO: Notificar personalmente el contenido de la presente resolución al doctor Germán Castillo Grau, en su calidad de apoderado de la sociedad SMITHKLINE BEECHAM P.L.C., o a quien haga sus veces, entregándole copia de la misma, advirtiéndole que contra ella no procede recurso alguno por encontrarse agotada la vía gubernativa.

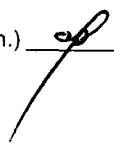
NOTIFIQUESE Y CUMPLASE

Dada en Bogotá, D. C., a los 27 MAR. 2006

EL SUPERINTENDENTE DE INDUSTRIA Y COMERCIO (E),


GIANCARLO MARCENARO JIMENEZ

Para notificar a los interesados, se fija el presente EDICTO en lugar visible al público en la SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO, por el término de (10) diez días hábiles contados a partir de las 8:30 a.m. de hoy.

Secretaría General Ad-Hoc 12-ABR-2006  Este edicto se desfija hoy 27-ABR-2006 a las cinco (5:00 p.m.) 
Secretaría General Ad-Hoc
EDICTO No. 5813