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Tipo: PATENTE DE INVENCION E/S 379 FASE NACIONAL II  
Act. 441 RESPUESTA REG. LL Folios: 10

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISIÓN DE NUEVAS CREACIONES

E. \_\_\_\_\_ S. \_\_\_\_\_ D. \_\_\_\_\_

Ref.: Expediente N°. 07-089.738

Solicitud de Patente de Invención titulada: "COMPUESTOS AROMATICOS  
CONDENSADOS CON ACTIVIDAD ANDIABETICA".

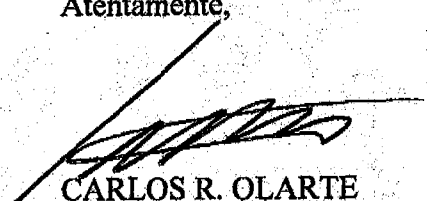
Solicitante: MERCK & CO. INC.

**RESPUESTA AL OFICIO N°. 13784 NOTIFICADO**  
**POR FIJACION EN LISTA No. 402, DE FECHA 2 DE NOVIEMBRE DE 2007,**  
**(EXAMEN DE FORMA)**

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

1. En respuesta a la única observación del Examinador, me permito aclarar al despacho que la presente ~~solicitud entra en Fase Nacional Capítulo I y no Capítulo II~~ como inicialmente se presentó. Para tal efecto, adjunto copia del Reporte Preliminar Internacional de Patentabilidad, el cual, valga la pena aclarar, no contiene anexos.

Atentamente,

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

Anexos: Copia del Reporte de Examen Preliminar Internacional

From the INTERNATIONAL BUREAU

**PCT****NOTIFICATION CONCERNING  
TRANSMITTAL OF COPY OF INTERNATIONAL  
PRELIMINARY REPORT ON PATENTABILITY  
(CHAPTER I OF THE PATENT COOPERATION  
TREATY)**

(PCT Rule 44bis.1(c))

To:

MERCK & CO., INC.  
MERCK & CO., INC.  
126 East Lincoln Avenue  
Rahway, New Jersey 07065-0907  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

20 September 2007 (20.09.2007)

Applicant's or agent's file reference

PCT 21869Y

**IMPORTANT NOTICE**

International application No.

PCT/US2006/007740

International filing date (day/month/year)

03 March 2006 (03.03.2006)

Priority date (day/month/year)

04 March 2005 (04.03.2005)

Applicant

MERCK &amp; CO., INC. et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

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MERCK & CO., INC.  
2007 OCT -2 AM 9:05  
PATENT DOCKET

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Nora Lindner

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

|                                                                                                                                  |                                                                          |                                                              |
|----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------|
| Applicant's or agent's file reference<br>PCT 21869Y                                                                              | FOR FURTHER ACTION                                                       | See item 4 below                                             |
| International application No.<br>PCT/US2006/007740                                                                               | International filing date (day/month/year)<br>03 March 2006 (03.03.2006) | Priority date (day/month/year)<br>04 March 2005 (04.03.2005) |
| International Patent Classification (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 |                                                                          |                                                              |
| Applicant<br>MERCK & CO., INC.                                                                                                   |                                                                          |                                                              |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                                 |                                                                                                                                                                 |
|-------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> Box No. I   | Basis of the report                                                                                                                                             |
| <input type="checkbox"/> Box No. II             | Priority                                                                                                                                                        |
| <input checked="" type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability                                                                |
| <input type="checkbox"/> Box No. IV             | Lack of unity of invention                                                                                                                                      |
| <input checked="" type="checkbox"/> Box No. V   | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI             | Certain documents cited                                                                                                                                         |
| <input type="checkbox"/> Box No. VII            | Certain defects in the international application                                                                                                                |
| <input type="checkbox"/> Box No. VIII           | Certain observations on the international application                                                                                                           |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

|                                                                                                                                     |                                                                         |
|-------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No. +41 22 338 82 70 | Date of issuance of this report<br>12 September 2007 (12.09.2007)       |
|                                                                                                                                     | Authorized officer<br><br>Nora Lindner<br><br>e-mail: pt02.pct@wipo.int |

# PATENT COOPERATION TREATY

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From the  
INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

|                                                                                                                                                                                                           |                                                          |                                                    |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------|--|
| Applicant's or agent's file reference<br>see form PCT/ISA/220                                                                                                                                             |                                                          | <b>FOR FURTHER ACTION</b><br>See paragraph 2 below |  |
| International application No.<br>PCT/US2006/007740                                                                                                                                                        | International filing date (day/month/year)<br>03.03.2006 | Priority date (day/month/year)<br>04.03.2005       |  |
| International Patent Classification (IPC) or both national classification and IPC<br>INV. C07D261/20 C07D307/80 C07D413/04 C07D403/04 C07D239/34 A61K31/416 A61K31/423 A61K31/4439<br>A61K31/513 A61P3/10 |                                                          |                                                    |  |
| Applicant<br>MERCK & CO., INC.                                                                                                                                                                            |                                                          |                                                    |  |

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1 (a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

|                                                                                                                                                                                                                                                                                        |                                                                |                                                                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|-------------------------------------------------------------------------------|
| Name and mailing address of the ISA:<br><br> European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Date of completion of this opinion<br><br>see form PCT/ISA/210 | Authorized Officer<br><br>Von Daacke, A<br><br>Telephone No. +49 89 2399-8286 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|-------------------------------------------------------------------------------|



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
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**Box No. I Basis of the opinion**

1. With regard to the language, this opinion has been established 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)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No. **PCT/US2006/007740**

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 16,17 (IA)

because:

☒ the said international application, or the said claims Nos. 16,17 (IA) relate to the following subject matter which does not require an international search (*specify*):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for the whole application or for said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

|                               |             |         |
|-------------------------------|-------------|---------|
| Novelty (N)                   | Yes: Claims | 1-18    |
|                               | No: Claims  |         |
| Inventive step (IS)           | Yes: Claims |         |
|                               | No: Claims  | 1-18    |
| Industrial applicability (IA) | Yes: Claims | 1-15,18 |
|                               | No: Claims  |         |

**2. Citations and explanations**

**see separate sheet**

**III NON-ESTABLISHMENT**

Claims 16 and 17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**V REASONED STATEMENT**

**1. PRIOR ART**

The documents cited in the International Search Report

- D1: WO 02/10137 A (SIGNAL PHARMACEUTICALS, INC; BHAGWAT, SHRIPAD, S; SATOH, YOSHITAKA; SA) 7 February 2002 (2002-02-07)
- D2: WO 2004/019869 A (MERCK & CO., INC; ACTON, JOHN, J., III; MEINKE, PETER, T; WOOD, HAROLD) 11 March 2004 (2004-03-11)
- D3: WO 01/60807 A (MERCK & CO. INC; LIU, KUN; XU, LIBO; JONES, A., BRIAN) 23 August 2001 (2001-08-23)
- D4: WO 01/79197 A (NIPPON CHEMIPHAR CO., LTD; SAKUMA, SHOGO; ENDO, TSUYOSHI; TENDO, ATSUSHI) 25 October 2001 (2001-10-25)
- D5: WO 2004/014860 A (TAKEDA CHEMICAL INDUSTRIES, LTD; OI, SATORU; MAEZAKI, HIRONOBU; IKEDOU) 19 February 2004 (2004-02-19)
- D6: WO 02/064094 A (MERCK & CO., INC; ADAMS, ALAN, D; JONES, A., BRIAN; BERGER, JOEL, P; D) 22 August 2002 (2002-08-22)

have been considered for the examination procedure.

**2. NOVELTY**

The claimed subject-matter is considered to be a novel selection of those of D1 (indazole compounds) (Article 33(2) PCT). The essential structural difference

between the other claimed compounds and those of D2-D6 relates in the presence of the substituent Ar1-B-Ar2, combined with the substituent WZ at the central fused phenyl ring.

## 2. INVENTIVE STEP

The claimed subject-matter does not fulfil the requirements of Article 33(3) PCT for the following reasons.

All cited documents relate at least to antidiabetic compounds, if not to PPAR mediating agents and are thus equally relevant in the assessment of inventive step. The closest state of the art for the presently claimed indazole derivatives is represented by D1. Claim 1 of D1 covers the present Ar1-B-Ar2 structure (A-R1 in D1) as well as the WZ structure (R2 in D1). Both types are exemplified in D1. See examples 141 and 142 (WZ) and e.g. examples 209, 270 and 351 (Ar1-B-Ar2). Even though the latter **examples** do not match with the presently claimed definition for B, the **definition** of the related part in D1 is overlapping with the present definitions. A skilled person would thus have arrived at the claimed indazole derivatives in view of D1 without any further inventive activity.

The other hetero-fused compounds of Claim 1, at least the benzisoxazole, benzisothiazole and quinoline derivatives are also obvious. D2 discloses benzisoxazole derivatives wherein the substituent WZ (present nomenclature) is positioned at Ar2 and wherein Ar1 denotes indolyl. See the single compounds in Table 1. D3 and D6 disclose already benzisoxazole derivatives with the "right" position of WZ, i.e. at the said fused heteroaromatic ring and the "right" Ar1. Ar2 is, however, absent. See examples 23-25 and 9,10, respectively. D4 discloses also benzisoxazole derivatives with the "right" position of WZ, but with the sequence B-Ar1-Ar2 of the other substituent rather than Ar1-B-Ar2. Lastly, D5 relates to quinoline derivatives which include the WZ substituent (e.g. example 117). Thus, each of the claimed essential structural features are already known or foreshadowed from D2, D3, D4, D5 and D6. A skilled person, in view of the problem underlying the present application, i.e. the provision of further antidiabetic compounds would thus have come to the claimed variants by combining two or more of the teachings above without further inventive activity.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No. 2007  
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An inventive step may, however, be recognized if it can be demonstrated in a representative way that the claimed compounds are expected to show surprising or unexpected properties over those of the cited prior art. In the absence of comparative test results or other appropriate information it is not possible to decide whether such a problem has been solved. In the case where comparative tests are envisaged in order to support an inventive step, these must be carried out between the compounds of the present application having the maximum structural similarity with the compounds of the closest prior art, such that the effect is shown to have its origins in the distinguishing feature of the claimed invention. It should be noted that the same problem should be demonstrated as having been solved for unity reasons (R.13 PCT).

**4. INDUSTRIAL APPLICABILITY**

No objection for Claims 16 and 17. For the assessment of the other claims on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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**REPUBLICA DE COLOMBIA**  
**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO**

Folio 200

2020  
Bogotá D.C.,

Doctor(a)  
OLARTE GARCIA CARLOS REINALDO  
Apoderado(a) y/o Representante de  
MERCK & CO., INC .

|            |                            |                   |
|------------|----------------------------|-------------------|
| REFERENCIA | Radicación No.             | 07 89738          |
|            | Solicitud internacional    | PCT/US2006/007740 |
|            | Fecha inicio fase nacional | 04/10/2007        |
|            | Trámite                    | 11                |
|            | Evento                     | 379               |
|            | Actuación                  | 416               |
|            | Oficio No.                 | 6547              |
|            | Folios                     | 1                 |

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 la Decisión 486 de la Comisión de la Comunidad Andina, el Tratado de Cooperación en Materia de Patentes (PCT), el Reglamento y la Circular Única de la Superintendencia de Industria y Comercio, se envía el extracto de la solicitud a la Oficina de Comunicaciones para efecto de su publicación en la Gaceta de Propiedad Industrial.

Cúmplase  
Dado en Bogotá DC,

06 AGO. 2008

ALIX CARMENZA CESPEDES DE VERGEL  
Jefe de la división de Nuevas Creaciones

adpa10