

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 06-127030-00001-0000

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Act. 329 CTOINFORMACION Folios: 19

Señora

Alix Carmenza Céspedes de Vergel

Jefe de División de Nuevas Creaciones

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

E. S. D.

Referencia: Expediente No. 06.127.030

Solicitud de Patente de Invención titulada: "Metabolitos de indolilalquilamina como ligandos 5-hidroxitriptamina-6."

Solicitante: Wyeth

### MEMORIAL DE ALCANCE

ÁLVARO CORREA ORDÓÑEZ, mayor de edad y vecino de Bogotá D.C., identificado según aparece al pie de mi firma, en mi condición de apoderado de la sociedad en referencia, manifiesto lo siguiente:

El día 19 de Diciembre de 2006, bajo el número de radicación 06.127.030, presenté la solicitud de patente de invención de la referencia, para la cual adjunto informe preliminar internacional sobre patentabilidad, capítulo I del tratado de cooperación en materia de patentes con su respectiva traducción.

Atentamente,

ÁLVARO CORREA ORDÓÑEZ

C.C.No.79.143.366 de Usaquén

T.P.20.281

Anexo: Informe preliminar internacional sobre patentabilidad, capítulo I

BOGLMSBOGDMS-7634-V1-.DOC

## PATENT COOPERATION TREATY

PCT

00042

102

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

|                                                                                                                                  |                                                                         |                                                             |
|----------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------------|
| Applicant's or agent's file reference<br>AM101726                                                                                | FOR FURTHER ACTION                                                      | See item 4 below                                            |
| International application No.<br>PCT/US2005/021852                                                                               | International filing date (day/month/year)<br>21 June 2005 (21.06.2005) | Priority date (day/month/year)<br>23 June 2004 (23.06.2004) |
| International Patent Classification (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 |                                                                         |                                                             |
| Applicant<br>WYETH                                                                                                               |                                                                         |                                                             |

|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                 |                                     |           |                     |                          |            |          |                          |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                                     |            |                         |                          |             |                                                  |                          |              |                                                       |
|-------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|-----------|---------------------|--------------------------|------------|----------|--------------------------|-------------|--------------------------------------------------------------------------------------------------|--------------------------|------------|----------------------------|-------------------------------------|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|------------|-------------------------|--------------------------|-------------|--------------------------------------------------|--------------------------|--------------|-------------------------------------------------------|
| 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 6 sheets, including this cover sheet.<br><br>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:<br><br><table><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table> |                                                                                                                                                                 | <input checked="" type="checkbox"/> | Box No. I | Basis of the report | <input type="checkbox"/> | Box No. II | Priority | <input 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 checked="" 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 |
| <input checked="" type="checkbox"/> | Box No. I                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Basis of the report                                                                                                                                             |                                     |           |                     |                          |            |          |                          |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                                     |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input type="checkbox"/>            | Box No. II                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Priority                                                                                                                                                        |                                     |           |                     |                          |            |          |                          |             |                                                                                                  |                          |            |                            |                                     |           |                                                                                                                                                                 |                                     |            |                         |                          |             |                                                  |                          |              |                                                       |
| <input 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 checked="" 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>Facsimile No. +41 22 338 82 70<br>Form PCT/IB/373 (January 2004) | Date of issuance of this report<br>28 December 2006 (28.12.2006)<br>Authorized officer<br>Masashi Honda<br>e-mail: pt08@wipo.int |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|

# PATENT COOPERATION TREATY

103  
5/12/2003

From the  
INTERNATIONAL SEARCHING AUTHORITY

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                                                                       |                                                          | FOR FURTHER ACTION<br>See paragraph 2 below  |
| International application No.<br>PCT/US2005/021852                                                                                  | International filing date (day/month/year)<br>21.06.2005 | Priority date (day/month/year)<br>23.06.2004 |
| International Patent Classification (IPC) or both national classification and IPC<br>C07D417/12, C07D417/14, A61K31/4045, A61P25/28 |                                                          |                                              |
| Applicant<br>WYETH                                                                                                                  |                                                          |                                              |

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"). However, 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 68.1bis(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 three 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:                                                                                                                                                                        | Authorized Officer                                                                                                                          |
|  <p>European Patent Office<br/>D-80298 Munich<br/>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br/>Fax: +49 89 2399 - 4465</p> | <p>Lauro, P</p> <p>Telephone No. +49 89 2399-8288</p>  |

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/021852

**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, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 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:  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing:  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable 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:

105  
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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/021852

**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 |           |
|                               | No: Claims  | 1-13      |
| Inventive step (IS)           | Yes: Claims |           |
|                               | No: Claims  | 1-13      |
| Industrial applicability (IA) | Yes: Claims | 1-7,11-13 |
|                               | No: Claims  | 8-10      |

**2. Citations and explanations**

see separate sheet

**Box No. VI Certain documents cited**

**1. Certain published documents (Rules 43bis.1 and 70.10)**

and /or

**2. Non-written disclosures (Rules 43bis.1 and 70.9)**

see form 210

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

106  
00003  
International application No.

PCT/US2005/021852

**Re Item V.**

1 Reference is made to the following documents:

- D1 : WO 03/053433 A (WYETH) 3 July 2003 (2003-07-03)  
D2 : US 6 187 805 B1 (PINEIRO JOSE LUIS CASTRO ET AL) 13 February 2001  
(2001-02-13)  
D3 : A. SLASSI ET AL.: "Recent progress in the 5-HT<sub>6</sub> receptor antagonists for the  
treatment of CNS diseases" EXPERT OPIN. THER. PATENTS, vol. 12,  
no. 4, 2002, pages 513-527, XP002350180  
D4 : DE 16 18 865 A1 (SUMITOMO CHEMICAL COMPANY LTD; SUMITOMO  
CHEMICAL CO. LTD., OSAKA) 30 April 1970 (1970-04-30)  
D5 : DATABASE WPI Derwent Publications Ltd., London, GB; AN  
1966-34623 &; JP 43 024418 B (SUMITOMO CHEMICAL INDUSTRIES) 1968  
D6 : V. LECLERC ET AL.: "Synthesis of nitroindole derivatives with high affinity and  
selectivity for melatoninergic binding sites MT<sub>3</sub>" J. MED. CHEM.,  
vol. 45, no. 9, 2002, pages 1853-59, XP002350181  
D7 : SAKAMOTO T ET AL.: "Synthesis of ethoxyethynylarenes by the palladium-  
catalyzed reaction of aryl iodides with ethoxy(trialkylstannyl)acetylenes"  
CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL  
SOCIETY OF JAPAN, TOKYO, JP, vol. 42, no. 10, 1994, pages 2032-2035,  
XP002269345 ISSN: 0009-2363  
D8: WO 2005/009958 A (PLEXIKON, INC; ARNOLD, JAMES; ARTIS, DEAN, R;  
HURT, CLARENCE; IBRAHIM) 3 February 2005 (2005-02-03)  
D9: WO 2005/040112 A (OXAGEN LIMITED; MIDDLEMISS, DAVID; ASHTON,  
MARK, RICHARD; BOYD, EDWARD) 6 May 2005 (2005-05-06)  
D10: WO 2004/078719 A (ONC PHARMACEUTICAL CO., LTD; IWAHASHI, MAKI;  
NAGANAWA, ATSUSHI; NISHIY) 16 September 2004 (2004-09-16)

2. Documents D8 to D10 have been published after the priority date of the current  
application and are therefore not taken into account for the purpose of the present  
report.

3. **Novelty**

The compounds of formula (I) and their pharmaceutical formulations are anticipated

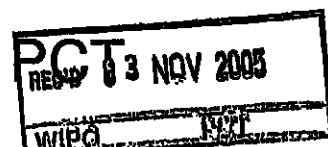
# PATENT COOPERATION TREATY

107  
5/7  
11/03

From the  
INTERNATIONAL SEARCHING AUTHORITY

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/US2005/021852                                                                                  | International filing date (day/month/year)<br>21.06.2005 | Priority date (day/month/year)<br>23.06.2004       |  |
| International Patent Classification (IPC) or both national classification and IPC<br>C07D417/12, C07D417/14, A61K31/4045, A61P25/28 |                                                          |                                                    |  |
| Applicant<br>WYETH                                                                                                                  |                                                          |                                                    |  |

### 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"). However, 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 three 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.

|                                                                                                                                                                                                                                                         |                                                                                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Name and mailing address of the ISA:</p>  <p>European Patent Office<br/>D-80298 Munich<br/>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br/>Fax: +49 89 2399 - 4465</p> | <p>Authorized Officer</p> <p>Lauro, P</p> <p>Telephone No. +49 89 2399-8288</p>  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/021852

108 not a g

**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, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 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:  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing:  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable 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/US2005/021852

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

1. Statement

|                               |             |           |
|-------------------------------|-------------|-----------|
| Novelty (N)                   | Yes: Claims |           |
|                               | No: Claims  | 1-13      |
| Inventive step (IS)           | Yes: Claims |           |
|                               | No: Claims  | 1-13      |
| Industrial applicability (IA) | Yes: Claims | 1-7,11-13 |
|                               | No: Claims  | 8-10      |

2. Citations and explanations

see separate sheet

**Box No. VI Certain documents cited**

1. Certain published documents (Rules 43*b*/s.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*b*/s.1 and 70.9)

see form 210

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

International application No.

PCT/US2005/021852

**Re Item V.**

1 Reference is made to the following documents:

- D1 : WO 03/053433 A (WYETH) 3 July 2003 (2003-07-03)  
D2 : US 6 187 805 B1 (PINEIRO JOSE LUIS CASTRO ET AL) 13 February 2001  
(2001-02-13)  
D3 : A. SLASSI ET AL.: "Recent progress in the 5-HT<sub>6</sub> receptor antagonists for the  
treatment of CNS diseases" EXPERT OPIN. THER. PATENTS, vol. 12,  
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CHEMICAL CO. LTD., OSAKA) 30 April 1970 (1970-04-30)  
D5 : DATABASE WPI Derwent Publications Ltd., London, GB; AN  
1966-34623 &; JP 43 024418 B (SUMITOMO CHEMICAL INDUSTRIES) 1968  
D6 : V. LECLERC ET AL.: "Synthesis of nitroindole derivatives with high affinity and  
selectivity for melatoninergic binding sites MT<sub>3</sub>" J. MED. CHEM.,  
vol. 45, no. 9, 2002, pages 1853-59, XP002350181  
D7 : SAKAMOTO T ET AL: "Synthesis of ethoxyethynylarenes by the palladium-  
catalyzed reaction of aryl iodides with ethoxy(trialkylstannyl)acetylenes"  
CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL  
SOCIETY OF JAPAN, TOKYO, JP, vol. 42, no. 10, 1994, pages 2032-2035,  
XP002269345 ISSN: 0009-2363  
D8: WO 2005/009958 A (PLEXXIKON, INC; ARNOLD, JAMES; ARTIS, DEAN, R;  
HURT, CLARENCE; IBRAHIM) 3 February 2005 (2005-02-03)  
D9: WO 2005/040112 A (OXAGEN LIMITED; MIDDLEMISS, DAVID; ASHTON,  
MARK, RICHARD; BOYD, EDWARD) 6 May 2005 (2005-05-06)  
D10: WO 2004/078719 A (ONO PHARMACEUTICAL CO., LTD; IWAHASHI, MAKI;  
NAGANAWA, ATSUSHI; NISHIY) 16 September 2004 (2004-09-16)

2. Documents D8 to D10 have been published after the priority date of the current application and are therefore not taken into account for the purpose of the present report.

**3. Novelty**

The compounds of formula (I) and their pharmaceutical formulations are anticipated

by D3 to D7. Novelty is not acknowledged for claim 1 and claim 11.

**4. Inventive step**

The problem underlying the current application appears to reside in the provision of indolakylamine metabolite derivatives useful in the treatment of 5-HT<sub>6</sub> related diseases. D1 to D3 disclose indolylakylamine derivatives of which the compounds of the current application are metabolites. Since the metabolites are active species produced upon introduction of a pharmaceutically active compound into a biological system, their activity would have been expected and their provision is considered to be the result of a mere discovery. An inventive step could therefore be acknowledged, only if it were shown that upon administration of the metabolites in the place of the parent indolakylamine derivatives an unexpected effect is obtained. On the basis of the comparative test contained in the description, no unexpected effect can be observed in comparison with compounds known to have an affinity for the 5-HT<sub>6</sub>, since the activity of compound 1 is worse than that of 4 of the 6 comparative compounds and compound 2 with a binding K<sub>i</sub> of 248 can be said to be almost inactive. It is also to be noted that in the present case, the assessment of inventive step can only be based on a comparison carried out with compounds of which the present compounds are the metabolites, i.e. the compounds disclosed in D1 or D2 or D3. In the absence of such data no inventive step can be acknowledged.

**5. Industrial applicability**

Claims 8-10 are directed to a method for treatment of the human or animal body by therapy.

6. Claim 12 lacks all technical features necessary to carry out the method. It is noted also that no support is found in the description for the subject-matter of claim 12.

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# TRATADO DE COOPERACION EN MATERIA DE PATENTES

## PCT

### INFORME PRELIMINAR INTERNACIONAL SOBRE PATENTABILIDAD (Capítulo I del Tratado de Cooperación en Materia de Patentes)

(Regla 44bis del PCT)

|                                                                                                                                                         |                                                                                 |                                                                |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|----------------------------------------------------------------|
| Referencia del expediente del solicitante o del agente<br>AM101726                                                                                      | <b>PARA ACCION ADICIONAL</b> Ver punto 4 adelante                               |                                                                |
| Solicitud Internacional No.<br>PCT/US2005/021852                                                                                                        | Fecha de presentación Internacional (Día/Mes/Año)<br>21 Junio 2005 (21.06.2005) | Fecha de Prioridad (Día/Mes/Año)<br>23 Junio 2004 (23.06.2004) |
| Clasificación internacional de Patentes (8va. Edición a menos que se indique una edición anterior)<br>Ver información relevante en la Forma PCT/ISA/237 |                                                                                 |                                                                |
| Solicitante<br>WYETH                                                                                                                                    |                                                                                 |                                                                |

1. Este informe preliminar Internacional sobre patentabilidad (Capítulo I) es emitido por la Oficina Internacional a nombre de la Autoridad de Búsqueda Internacional bajo la regla 44 bis.1(a).

2. Este **INFORME** consiste de un total de 6 hojas, incluyendo esta carátula.

En las hojas adjuntas, cualquier referencia a la opinión escrita de la Autoridad de Búsqueda Internacional debe leerse, en su lugar, como una referencia al informe preliminar internacional sobre patentabilidad (Capítulo I)

3. Este informe contiene indicaciones relacionadas con los siguientes puntos:

|                                     |               |                                                                                                                                                              |
|-------------------------------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Caja No. I    | Base del informe                                                                                                                                             |
| <input type="checkbox"/>            | Caja No. II   | Prioridad                                                                                                                                                    |
| <input type="checkbox"/>            | Caja No. III  | Opinión no establecida con respecto a Novedad, Nivel Inventivo y Aplicación Industrial.                                                                      |
| <input type="checkbox"/>            | Caja No. IV   | Carece de unidad de invención                                                                                                                                |
| <input checked="" type="checkbox"/> | Caja No. V    | Afirmación razonada bajo el Artículo 35(2) con respecto a novedad Nivel inventivo o aplicación industrial; citas y explicaciones que soportan tal afirmación |
| <input checked="" type="checkbox"/> | Caja No. VI   | Algunos documentos citados                                                                                                                                   |
| <input type="checkbox"/>            | Caja No. VII  | Algunos defectos en la solicitud internacional                                                                                                               |
| <input type="checkbox"/>            | Caja No. VIII | Algunas observaciones sobre la solicitud internacional                                                                                                       |

4. La Oficina Internacional comunicará este informe a las Oficinas designadas de acuerdo con las reglas 44bis.3(c) y 93bis.1 pero no, excepto cuando el solicitante haga una solicitud expresa bajo el Artículo 23(2), antes de la expiración de los 30 meses desde la fecha de prioridad (Regla 44bis.2).

|                                                                                                                                                                   |                                                                                                                |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| La Oficina internacional de la OMPI<br>34, chemin des Colombettes<br>1211 Ginebra 20, Suiza<br><br>Facsimil No. +41 22 338 82 70<br>Forma PCT/IB/373 (Enero 2004) | Fecha de emisión de este informe<br>28 Diciembre 2006 (28.12.2006)                                             |
|                                                                                                                                                                   | Oficial autorizado<br><br><b>Masashi Honda</b><br><br>e-mail: <a href="mailto:pt08@wipo.int">pt08@wipo.int</a> |

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TRATADO DE COOPERACION EN PATENTES

De la

AUTORIDAD DE BÚSQUEDA INTERNACIONAL

PCT

OPINIÓN ESCRITA DE LA  
AUTORIDAD INTERNACIONAL  
DE BÚSQUEDA  
(Regla PCT 43bis.1)

Ver forma PCT/ISA/220

Fecha de despacho  
(día/mes/año) ver la forma PCT/ISA/210 (segunda  
hoja)

Referencia del expediente del solicitante o del agente  
Ver forma PCT/ISA/220

PARA ACCION ADICIONAL  
Ver parágrafo 2 abajo

Solicitud Internacional No.  
PCT/US2005/021852

Fecha de presentación Internacional  
(Día/Mes/Año)  
21.06.2005

Fecha de  
Prioridad  
(Día/Mes/Año)  
23.06.2004

Clasificación internacional de Patentes (IPC) o tanto la clasificación nacional como la IPC  
C07D417/12, C07D417/14, A61K31/4045, A61P251/28

Solicitante  
WYETH

1. Este informe contiene indicaciones relacionadas con los siguientes puntos:

- |                                     |               |                                                                                                                                                              |
|-------------------------------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <input checked="" type="checkbox"/> | Caja No. I    | Base del informe                                                                                                                                             |
| <input type="checkbox"/>            | Caja No. II   | Prioridad                                                                                                                                                    |
| <input type="checkbox"/>            | Caja No. III  | Opinión no establecida con respecto a Novedad, Nivel Inventivo y Aplicación Industrial.                                                                      |
| <input type="checkbox"/>            | Caja No. IV   | Carece de unidad de invención                                                                                                                                |
| <input checked="" type="checkbox"/> | Caja No. V    | Afirmación razonada bajo el Artículo 35(2) con respecto a novedad Nivel inventivo o aplicación industrial; citas y explicaciones que soportan tal afirmación |
| <input checked="" type="checkbox"/> | Caja No. VI   | Algunos documentos citados                                                                                                                                   |
| <input type="checkbox"/>            | Caja No. VII  | Algunos defectos en la solicitud internacional                                                                                                               |
| <input type="checkbox"/>            | Caja No. VIII | Algunas observaciones sobre la solicitud internacional                                                                                                       |

2. ACCIÓN ADICIONAL

Si una solicitud de examen preliminar internacional se hace, esta opinión será considerada usualmente una opinión escrita de la Autoridad de Examen Preliminar Internacional ("IPEA"). Sin embargo, esto no aplica en el caso en que el solicitante escoja una Autoridad diferente a esta para ser la IPEA y la IPEA halla notificado a la Oficina Internacional bajo la regla 66.1bis(b) que las opiniones escritas de esta Autoridad de Búsqueda Internacional no serán tenidas en cuenta.

Si esta opinión, como ha sido emitida, es tomada en cuenta como la opinión escrita de la IPEA, se invita al solicitante a presentar ante la IPEA una respuesta escrita junto con, cuando sea apropiado, las modificaciones, antes de la expiración del término de tres meses desde la fecha de despacho de la forma PCT/ISA/220 o antes de la expiración de 22 meses desde la fecha de prioridad, lo que suceda más tarde.

Para opciones adicionales, ver la Forma PCT/ISA/220.

3. Para detalles adicionales, ver las notas de la Forma PCT/ISA/220.

| Nombre y dirección de correo de la ISA:                                                                                 | Oficial que autoriza                                |
|-------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| <p>European Patent Office<br/>D-80298 Munich<br/>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br/>Fax: +49 89 2399 - 4465</p> | <p>Lauro, P<br/>Teléfono No. +49 89 2399 - 8288</p> |

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**OPINIÓN ESCRITA DE LA  
AUTORIDAD DE BÚSQUEDA INTERNACIONAL**

**Solicitud Internacional No.  
PCT/US2005/021852**

Caja No. 1 Base de la opinión

1. Con respecto al **lenguaje**, esta opinión ha sido establecida sobre la base de la solicitud internacional en el lenguaje en que fue presentada, a menos que se indique otra cosa en este punto.
  - ☐ Esta opinión ha sido establecida sobre la base de una traducción del idioma original al siguiente lenguaje , que es el lenguaje de una traducción suministrada para los propósitos de la búsqueda internacional (bajo las reglas 12.3 y 23.1(b)).
2. Con respecto a cualquier **secuencia de nucleótido y/o aminoácido** descrita en la solicitud internacional y necesaria para la invención reivindicada, esta opinión ha sido establecida con base en:
  - a. tipo de material
    - ☐ un listado de la secuencia
    - ☐ tabla(s) relacionada(s) con el listado de la secuencia
  - b. formato del material:
    - ☐ en formato escrito
    - ☐ en forma legible por computadora
  - c. momento de la presentación/suministrando:
    - ☐ contenida en la solicitud internacional según se presentó.
    - ☐ presentado junto con la solicitud internacional en forma legible por computadora.
    - ☐ suministrado después a esta Autoridad para los propósitos de la búsqueda.
3. ☐ Adicionalmente, en el caso de que más de una versión o copia de un listado de secuencia y/o tabla relacionada con esta halla sido presentada o suministrada, las afirmaciones requeridas de que la información en las copias adicionales o subsiguientes es idéntica a aquella en la solicitud como se presentó o que no va más allá de la solicitud como se presentó, según sea lo apropiado, fueron presentadas.
4. Comentarios adicionales:

**OPINIÓN ESCRITA DE LA  
AUTORIDAD DE BÚSQUEDA INTERNACIONAL**

**Solicitud Internacional No.  
PCT/US2005/021852**

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**Caja No.V      Afirmación razonada bajo la regla 43bis.1(a)(i) con respecto a la novedad, nivel inventivo o aplicación industrial; citas y explicaciones que soportan tal afirmación**

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**1. Afirmación**

**Novedad (N)**                      Si: reivindicaciones  
                                            No: reivindicaciones 1 - 13

**Nivel Inventivo (IS)**           Si: reivindicaciones  
                                            No: reivindicaciones 1 - 13

**Aplicación industrial (IA)**   Si: reivindicaciones 1-7, 11-13  
                                            No: reivindicaciones 8 - 10

**2. Citas y explicaciones**

**Ver hoja separada**

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**Caja No.VI      Ciertos documentos citados**

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**1. Ciertos documentos publicados (Reglas 43bis.1 y 70.10)**

**y/o**

**2. Divulgaciones no escritas (Reglas 43bis.1 y 70.9)**

**Ver Forma 210**

**Ref. al Punto V**

1. Se hace referencia a los siguientes documentos:

- D1: WO 03/053433 A (WYETH) Julio 3 de 2003 (2003-07-03)
- D2: US 6 187 805 B1 (PINEIRO JOSE LUIS CASTRO ET AL) Febrero 13 de 2001 (2001-02-13)
- D3: A. SLASSI ET AL.: "Progreso reciente en los antagonistas del receptor 5-HT6 para el tratamiento de enfermedades CNS" EXPERT OPIN. THER. PATENTS, Vol. 12, no. 4, 2002, páginas 513-527, XP002350180
- D4: DE 16 18 865 A1 (SUMITOMO CHEMICAL COMPANY LTD; SUMITOMO CHEMICAL CO. LTD., OSAKA) Abril 30 de 1970 (1970-04-30)
- D5 DATABASE WPI Derwent Publications Ltd., Londres, GB; AN 1966-34623 &; JP 43 024418 B (SUMITOMO CHEMICAL INDUSTRIES) 1968
- D6 V. LECLERC ET AL.: "Síntesis de derivados de nitroindol con alta afinidad y selectividad para sitios de ligado melatoninergicos MT3" J. MED. CHEM., vol 45, no. 9, 2002, páginas 1853-59, XP002350181
- D7 SAKAMOTO T ET AL.: "Síntesis de etoxietinilarenos mediante la reacción catalizada por paladio de yoduros de arilo con etoxy(trialquilestanil)acetilenos" CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, JP, vol 42, no. 10, 1994, páginas 2032-2035, XP002269345 ISSN: 0009-2363
- D8 WO 2005/009958 A (PLEXXIKON, INC; ARNOLD, JAMES; ARTIS DEAN, R; HURT, CLARENCE; IBRAHIM) Febrero 3 de 2005 (2005-02-03)
- D9 WO 2005/040112 A (OXAGEN LIMITED; MIDDLEMISS, DAVID; ASHTON, MARK, RICHARD; BOYD, EDWARD) Mayo 6 de 2005 (2005-05-06)
- D10 WO 2004/078719 A (ONO PHARMACEUTICAL CO., LTD; IWAHASHI, MAKI; NAGANAWA, ATSUSHI; NISHIY) Septiembre 16 de 2004 (2004-09-16)

2. Los documentos D8 a D10 fueron publicados después de la fecha de prioridad de la presente solicitud y por lo tanto no se tomaron en cuenta para el propósito del presente informe.

3. **Novedad**

Los Compuestos de fórmula (I) y sus formulaciones farmacéuticas son anticipados por D3 a D7. No se reconoce la novedad para la reivindicación 1 ni para la reivindicación 11.

4. **Nivel inventivo**

El problema subyacente en la presente solicitud parece residir en la provisión de derivados de metabolito de indolalquilamina útiles en el tratamiento de enfermedades relacionadas con 5-HT6.

Forma (PCT/ISA237) (hoja separada) (hoja 1) (EPO-Enero 2004)

D1 a D3 describen derivados de indolilalquilamina de los cuales los compuestos de la presente solicitud son metabolitos. Ya que los metabolitos son especies activas producidas luego de la introducción de un compuesto farmacéuticamente activo dentro de un sistema biológico, su actividad se habría esperado y su provisión es considerada como el resultado de un mero descubrimiento. Solo pudiera reconocerse la existencia de nivel inventivo si se hubiera mostrado que luego de la administración de los metabolitos en lugar de los derivados de indolalquilamina parientes un efecto inesperado se hubiera obtenido. Sobre la base del ensayo comparativo contenido en la descripción, no se puede observar ningún efecto inesperado en comparación a los compuestos conocidos con respecto a tener afinidad por el 5-HT<sub>6</sub>, ya que la actividad del compuesto 1 es peor que la de 4 de los 6 compuestos comparativos y el compuesto 2 con un enlace K<sub>i</sub> de 248 puede decirse que es prácticamente inactivo. También se notó que en el presente caso, la determinación del nivel inventivo solo puede basarse en una comparación llevada a cabo con compuestos de los cuales los presentes compuestos son los metabolitos, es decir, los compuestos en D1 o D2 o D3. Debido a la ausencia de tales datos no se puede reconocer nivel inventivo.

**5. Aplicación industrial**

Las reivindicaciones 8 a 10 están dirigidas a un método para el tratamiento del cuerpo humano o animal mediante terapia.

6. La reivindicación 12 carece de todos los rasgos técnicos necesarios para llevar a cabo el método. Se ha encontrado también que no existe soporte en la descripción para la materia objeto de la reivindicación 12.