

Señora

Alix Carmenza Céspedes de Vergel

Jefe de División de Nuevas Creaciones

SUPERINTENDENCIA DE INDUSTRIA Y

E. S.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-089192-00001-0000

Fecha: 20/05-01-17 13:06:12 Dep. 2020 NUECREACION
Tra. 11 PATENTLIYI Lve: 378 FASENACIONALI
Act. 329 OTG INFORMACION Folios: 9

Referencia: Expediente No. 07.089.192

Solicitud de Patente de Invención titulada: "Purificación de rapamicina"

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 30 de agosto de 2007, bajo el número de radicación 07.089.192, 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.

Atentamente,

ÁLVARO CORREA ORDÓÑEZ

C.C.No.79.143.366 de Usaquén

T.P.20281

Anexo: Informe preliminar internacional sobre patentabilidad, capítulo I

BOGLMS/BOGDMS-100591-V1-.DOC

PATENT COOPERATION TREATY

PCT/US2006/006212

From the INTERNATIONAL BUREAU

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

(PCT Rule 44bis.1(c))

To:

DODROFF, Cathy
HOWSON AND HOWSON
SUITE 210
501 Office Center Drive
Fort Washington, Pennsylvania 19034
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

20 September 2007 (20.09.2007)

Applicant's or agent's file reference

AM-100922PCT

IMPORTANT NOTICE

International application No.

PCT/US2006/006212

International filing date (day/month/year)

22 February 2006 (22.02.2006)

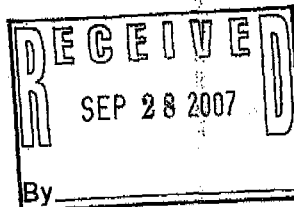
Priority date (day/month/year)

02 March 2005 (02.03.2005)

Applicant

WYETH et al

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

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

Authorized officer

Athina Nickitas-Etienne

Facsimile No. +41 22 338 82 70

e-mail: pt04.pct@wipo.int

Form PCT/IB/326 (January 2004)

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 AM-100922PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2006/006212	International filing date (day/month/year) 22 February 2006 (22.02.2006)	Priority date (day/month/year) 02 March 2005 (02.03.2005)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant 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 7 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:

☒ Box No. I	Basis of the report
☐ 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 Article 35(2) 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

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 34, chemin des Colombettes 1211 Geneva 20, Switzerland		Date of issuance of this report 11 September 2007 (11.09.2007)
Facsimile No. +41 22 338 82 70		Authorized officer Athina Nickitas-Etienne
Form PCT/IB/373 (January 2004)		e-mail: pt04.pct@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

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
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2006/006212

International filing date (day/month/year)
22.02.2006

Priority date (day/month/year)
02.03.2005

International Patent Classification (IPC) or both national classification and IPC
INV. C07D498/18 A61K31/435 A61K31/55 A61P31/00 A61P35/00 A61P37/06

Applicant
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") 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:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Bourghida, E.M.

Telephone No. +31 70 340-9517



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2006/006212

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/US2006/006212

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	7-20
	No: Claims	1-6
Inventive step (IS)	Yes: Claims	
	No: Claims	1-20
Industrial applicability (IA)	Yes: Claims	1-20
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

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

International application No.

PCT/US2006/006212

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1.0 Reference is made to the following documents:

- D1: US 2001/039338 A1 (SHAW CHIA-CHENG ET AL) 8 November 2001 (2001-11-08)
D2: US-A-3 993 749 (SEHGAL ET AL) 23 November 1976 (1976-11-23)
D3: WO 2005/016935 A (WYETH; CHEW, WARREN; SHAW, CHIA-CHENG) 24 February 2005 (2005-02-24)

Novelty:

- 2.0 Rapamycin is an already known compound from the prior art (see D1: page 1 paragraph [0003]). Its degree of purity does not render this compound novel, and therefore the subject-matter of claims 1-6 is not new in the sense of Article 33(2) PCT (see also T990/96).
- 2.1 D1 discloses the reaction of rapamycin with chloromethylsilane, in ethyl acetate, in the presence of imidazole to synthesize 31,42-O-trimethylsiyl rapamycin, and the further cleavage of the trimethylsiyl groups with sulfuric acid to get rapamycin (see D1: example 1 page 4). However, D1 does not disclose the washing of a solution of rapamycin with charcoal and the further pH adjustment with a buffer of a solution of rapamycin in acetone. Thus, the subject-matter of claims 7-20 is new in the sense of Article 33(2) PCT.

Inventive Step:

- 3.0 D1 is regarded as the closest prior art to the inventive step assessment of the subject-matter of claims 7-20, and discloses the reaction of rapamycin with chloromethylsilane, in ethyl acetate, in the presence of imidazole to synthesize 31,42-O-trimethylsiyl rapamycin, and the further cleavage of the trimethylsiyl groups with sulfuric acid to get rapamycin (see D1: example 1 page 4).

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

International application No.

PCT/US2006/006212

- 91 89
- 3.1 The subject-matter of claims 7-20 differs from D1 in that the compound 31,42-O-trimethylsilyl rapamycin once synthesized, is not washed with charcoal prior the cleavage of the trimethylsilyl groups, and the rapamycin, after the deprotection step, is not further treated with a buffer to adjust the pH of its solution in acetone.
- 3.2 The problem to be solved can be regarded as the provision of a further process for the purification of rapamycin.
- 3.3 D2 discloses a purification of rapamycin by using charcoal (see D2: column 5 lines 29-41), and D3 discloses the shifting of the equilibrium between a rapamycin derivative B and a rapamycin derivative C towards the desired form B, through the pH adjustment of about 5-6 by treating the solution of rapamycin in acetone with sodium acetate as a buffer (see D3: page 8 lines 11-35).
- 3.4 The solution proposed in the subject-matter of claims 7-20 is not regarded as involving an inventive step in the sense of Article 33(3) PCT, because the skilled person, working in the field of purification of natural products, would use the knowledge of D2 and D3 to increase the purity of rapamycin by washing with charcoal the 31,42-O-protected rapamycin intermediate in a non-polar solvent, and shifting the equilibrium between rapamycin B and C towards the desired form B, through the pH adjustment of about 5-6 by treating the solution of rapamycin in acetone with sodium acetate as a buffer.
- Hence, no inventive step can be acknowledged for the subject-matter of claims 7-20.

Re Item VII

Certain defects in the international application

- 4.0 The statement "herein incorporated by reference" page 9 lines 15-16 in the description, implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby rendering in lack of clarity (Article 6

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

International application No.

PCT/US2006/006212

PCT).

- 4.1 The expression "yellow color index" used in claim 1 has no well recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).
- 4.2 The expression "isomeric B:C ratio" used in claims 2-3, 5-6, 12-13 has no well recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).
- 4.3 The embodiments of the invention about packaging and kits containing purified rapamycin described on page 8 lines 5-11 do not fall within the scope of the claims. This inconsistency between the claims and the description leads to doubt concerning the matter for which protection is sought, thereby rendering the claims unclear, Article 6 PCT.