

HUMBERTO RUBIO & CIA.

ABOGADOS

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Bogota, D.C. - Colombia

53

Doctora

Alix Carmenza CESPEDES DE VERGEL

**Jefe de la División de Nuevas Creaciones
Superintendencia de Industria y Comercio**

E. S. D.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-063336-00002-0000

REGISTRO DE MARCAS Y DISEÑOS INDUSTRIALES
MINISTERIO DE RELACIONES EXTERIORES
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Expediente No.

07-063.336

Patente de Invención:

**"METODOS PARA LA PRODUCCION
DE ANSAMITOCINAS"**

Titular:

IMMUNOGEN, INC.

DESTINO: 444

HUMBERTO RUBIO CAMACHO, mayor de edad, domiciliado en Bogotá, D.C., identificado con la cédula de ciudadanía número 17.192.062 de Bogotá, abogado en ejercicio, portador de la Tarjeta Profesional No. 50.007 expedida por el Consejo Superior de la Judicatura, actuando en carácter de **APODERADO** de la Sociedad **IMMUNOGEN, INC.**, domiciliada en 128 Sidney Street, Cambridge, Massachussets 02139-4239, Estados Unidos de América; encontrándome dentro del término legal para dar contestación al auto proferido por su Despacho mediante Oficio No. 10380 notificado por fijación en lista el 31 de Agosto de 2007, me permito anexar:

- 1.- Copia expedida y autenticada del **documento de cesión** que reposa en la Oficina de Patentes y Marcas de los Estados Unidos debidamente legalizado por el sistema de Apostille; traducido oficialmente del idioma Inglés al Español y reconocido por el Ministerio de Relaciones Exteriores en Colombia; por medio del cual se cede todos los derechos poseídos sobre la presente invención a favor de mi representada la Sociedad **IMMUNOGEN, INC.**
- 2.- Con el ánimo de complementar la solicitud de registro de la patente de invención mencionada en la referencia, anexo Copia del Reporte Preliminar Internacional de Patentabilidad (Capítulo I).

Teniendo en cuenta lo anterior solicito se continúe con el trámite correspondiente.

Atentamente,

HUMBERTO RUBIO CAMACHO

C.C. 17.192.062 de Bogotá

**T.P. 50.007 Consejo Superior
de la Judicatura.**

COD. 4134

07/1884/P000655
/Bap

54

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: *United States of America*

This public document

2. has been signed by *T. Wallace*

3. acting in the capacity of *Certifying Officer*

4. bears the seal/stamp of *Patent and Trademark Office*

Certified

5. at Washington, D.C.

6. the *thirteenth* of September, 2007

7. by ~~Assistant~~ *Authentication Officer, United States Department of State*

8. No. *07036334-1*

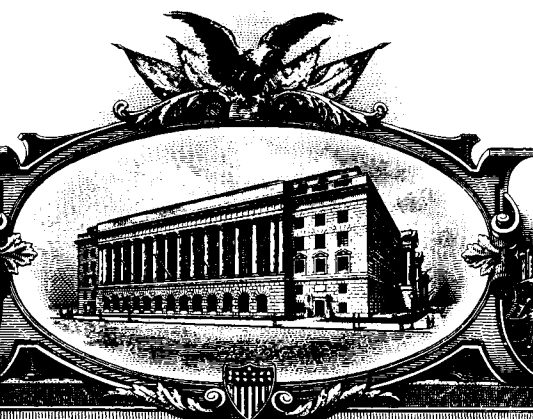
9. Seal/Stamp:

10. Signature:



Denitra T. Hawkins

A 1621607



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

June 13, 2007

**THIS IS TO CERTIFY THAT ANNEXED IS A TRUE COPY FROM THE
RECORDS OF THIS OFFICE OF A DOCUMENT RECORDED ON
April 08, 2005.**

By Authority of the

**Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office**



T. Wallace
T. WALLACE

Certifying Officer

04-14-2005

A8868

MODIFIED Form PTO-1595
(Rev. 10/02)

RECO

102980246
PATENTS UNITU.S. DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office

To the Director of the U.S. Patent and Trademark Office: Please record the attached original documents or copy thereof.

1. Name of conveying party(ies):

Cynthia KUO
Graham S. BYNG
Wayne C. WIDDISON

2. Name and address of receiving party(ies):

IMMUNOGEN, INC.
128 Sidney Street,
Cambridge, MA 02139-4239Additional name(s) of conveying party(ies) attached? ☐ Yes ☒ No

3. Nature of conveyance:

- ☒ Assignment ☐ Merger
☐ Security Agreement ☐ Change of Name
☐ Other

Execution Date: January 20, 2005 for inventors 1 and 2;
January 19, 2005 for inventor 3Additional name(s) & address(es) attached? ☐ Yes ☒ No

4. Application number(s) or patent number(s):

If this document is being filed together with a new application, the execution date of the application is:

A. Patent Application No.(s)
11/037,104

B. Patent No.(s)

Additional numbers attached? ☐ Yes ☒ No

5. Name and address of party to whom correspondence concerning document should be mailed:

SUGHRUE MION, PLLC

WASHINGTON OFFICE

23373

CUSTOMER NUMBER

6. Total number of applications and patents involved:

1

7. Total fee (37 CFR 3.41): \$40.00

☒ Enclosed.☐ Authorized to be charged to Deposit Account No. 19-4880.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

8. Deposit Account Number:

19-4880

(Attach duplicate copy of this page if paying by deposit account)

DO NOT USE THIS SPACE

9. Statement and signature.

To the best of my knowledge and belief, the foregoing information is true and correct and any attached copy is a true copy of the original document.

Susan J. Mack

Reg. No. 30,951

APR 8 2005

Date

Total number of pages including cover sheet, attachments, and documents: 3

Mail documents to be recorded with required cover sheet information to:

MAIL STOP ASSIGNMENT RECORDATION SERVICES

Director of the U.S. Patent and Trademark Office

P.O. Box 1450

Alexandria, VA 22313-1450

4/13/2005 BYRNE 00000231 11037104

1 FC:0021

(40.00 OP)

PATENT
REEL: 016447 FRAME: 0844

58

Assignment

Whereas, I/We, Cynthia KUO, Graham S. BYNG, and Wayne C. WIDDISON of Taipei, Taiwan, Snohomish, WA and Somerville, MA, respectively, hereinafter called assignor(s), have invented certain improvements in METHODS FOR THE PRODUCTION OF ANSAMITOCINS and filed a United States Patent Application therefor on January 19, 2005; and

Whereas, IMMUNOGEN, Inc. 128 Sidney Street, Cambridge, MA 02139-4239, (assignee), desires to acquire the entire right, title, and interest in the application and invention, and to any United States patents to be obtained therefor;

Now therefore, for valuable consideration, receipt whereof is hereby acknowledged,

I/We, the above named assignor(s), hereby sell, assign and transfer to the above named assignee, its successors and assigns, the entire right, title and interest in the application and the invention disclosed therein for the United States of America and all countries foreign thereto, including rights of priority under the International Convention of Paris (1883) as amended, and I/we request the Director of the U.S. Patent and Trademark Office to issue any Letters Patent granted upon the invention set forth in the application to the assignee, its successors and assigns; and I/we hereby agree that the assignee may apply for foreign Letters Patent on the invention and I/we will execute without further consideration all papers deemed necessary by the assignee in connection with the United States and foreign applications when called upon to do so by the assignee.

I/We hereby authorize and request our attorneys SUGHRUE MION, PLLC of 2100 Pennsylvania Avenue, NW, Washington, DC 20037-3213 to insert here in parentheses (Application number 11/637,104 and Confirmation number 7455), filed January 19, 2005, the application number and filing date of said application when known.

Date: Cynthia Kuo January 20, 2005
s/Cynthia KUO
Date: Graham S. BYNG January 20, 2005
s/Graham S. BYNG
Date: _____
s/Wayne C. WIDDISON

(Legalization not required for recording but is prima facie evidence of execution under 35 U.S.C. §261)

PATENT
REEL: 016447 FRAME: 0845

Assignment

Whereas, I/We, Cynthia KUO, Graham S. BYNG, and Wayne C. WIDDISON of Taipei, Taiwan, Snohomish, WA and Somerville, MA, respectively, hereinafter called assignor(s), have invented certain improvements in METHODS FOR THE PRODUCTION OF ANSAMITOCINS and filed a United States Patent Application therefor on January 19, 2005; and

Whereas, IMMUNOGEN, Inc. 128 Sidney Street, Cambridge, MA 02139-4239, (assignee), desires to acquire the entire right, title, and interest in the application and invention, and to any United States patents to be obtained therefor;

Now therefore, for valuable consideration, receipt whereof is hereby acknowledged,

I/We, the above named assignor(s), hereby sell, assign and transfer to the above named assignee, its successors and assigns, the entire right, title and interest in the application and the invention disclosed therein for the United States of America and all countries foreign thereto, including rights of priority under the International Convention of Paris (1883) as amended, and I/we request the Director of the U.S. Patent and Trademark Office to issue any Letters Patent granted upon the invention set forth in the application to the assignee, its successors and assigns; and I/we hereby agree that the assignee may apply for foreign Letters Patent on the invention and I/we will execute without further consideration all papers deemed necessary by the assignee in connection with the United States and foreign applications when called upon to do so by the assignee.

I/We hereby authorize and request our attorneys SUGHRUE MION, PLLC of 2100 Pennsylvania Avenue, NW, Washington, DC 20037-3213 to insert here in parentheses (Application number 10/037,104 and Confirmation number 7455, filed January 19, 2005, the application number and filing date of said application when known.

Date:

s/Cynthia KUO

Date:

s/Graham S. BYNG

Date:

1/19/2005

Wayne C. Widdison
s/Wayne C. WIDDISON

(Legalization not required for recording but is prima facie evidence of execution under 35 U.S.C. §261)

RECORDED: 04/08/2005

PATENT
REEL: 016447 FRAME: 0846

LUIS ENRIQUE GOMEZ V. - Traductor Oficial

Resolución 283 / 88 Ministerio de Justicia

C.C. 438.449 Usaquén D.C. Colombia S.A

Traducción oficial de un documento escrito en Inglés. Septiembre 24, 2007

APOSTILLA

(Convención de La Haya, Octubre 5, 1961)

1. País. Estados Unidos de América

Este documento público

2. Ha sido firmado por T. Wallace
3. En su condición de Oficial Certificador
- 4 Lleva la estampilla/sello de la Oficina de Patentes y Marcas Registradas

Certificado

5. En Washington D.C.
6. En Septiembre 13, 2007
7. Por: Oficial de Autenticaciones. Departamento de Estado de los Estados Unidos
8. Número **07036334-1**
9. Sello/Estampilla: Departamento de Estado. Estados Unidos de América
10. Firma:

Ilegible
Denitra T. Hawkins

Es fiel traducción del documento que he tenido a la vista
E-mail: legomez2@tutopia.com

LUIS ENRIQUE GOMEZ V. - Traductor Oficial

Resolución 283 / 88 Ministerio de Justicia

C.C. 438.449 Usaquén D.C. Colombia S.A.

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Departamento de Comercio
Oficina de Patentes y Marcas Registradas de los Estados Unidos
Referencia 04-14-2005 - 102980246

Al Director de la Oficina de Patentes y Marcas Registradas de los Estados Unidos;
Favor registrar los documentos adjuntos o las siguientes direcciones:

1. Nombre de las partes Cedentes y Fechas de Ejecución:

1. Cynthia KUO
2. Graham S. BYNG
3. Wayne C. WIDDISON

2. Nombre y Dirección de Beneficiario

IMMUNOGEN, Inc.
128 Sidney Street,
Cambridge, MA 02139-4239

3. Naturaleza del Traspaso

Cesión de Derechos

Fecha de Ejecución: Enero 20 de 2005 para los inventores 1 y 2;
Enero 19 de 2005 para el inventor 3

4. Aplicación o Número de Patente

11/037,104

5. Nombre y Dirección a quien debe dirigirse la correspondencia

SUGHRUE MION, PLLC

Oficina en Washington. Número de Cliente: 23373

6. Número Total de Aplicaciones: 1

7. Tarifa \$40.00

Adjunta

8. Información sobre el Pago

Número de Cuenta para el Depósito

19-4880

9. Declaración y Firma

De acuerdo con mi saber y entender, la anterior información es cierta y correcta y la copia adjunta tomada del documento original es verdadera. Nombre de la persona que firma: Susan J. Mack. Firma: Ilegible. Registro N° 30,951 Fecha: Abril 8, 2005.

Número total de páginas incluyendo los documentos adjuntos: 3

Es fiel traducción del documento que he tenido a la vista

E-mail: legomez2@tutopia.com.

62

Traducción oficial de un documento escrito en Inglés. Septiembre 24, 2007

Archivo Legal A8868
Para clientes en los Estados Unidos

Cesión

Considerando que, nosotros Cynthia KUO, Graham S. BYNG, y Wayne C. WIDDISON de las ciudades de Taipei, Taiwan, Snohomish, WA y Somerville, MA, respectivamente, denominados, de ahora en adelante, los cedentes, hemos inventado un mejoramiento en el "METODOS PARA LA PRODUCCION DE ANSAMITOCINAS", y para ello hemos registrado una Aplicación para Patente en los Estados Unidos en Enero 19 de 2005; y,

Considerando que; IMMUNOGEN, Inc., localizada en 128 Sidney Street, Cambridge, MA 02139-4239 (beneficiaria), tiene la intención de adquirir el pleno derecho, título e interés en la aplicación e invención y de cualquier patente a ser obtenida en el futuro en los Estados Unidos.

Ahora y por consiguiente, por las consideraciones económicas de valor, de lo cual y por la presente se certifica,

Nosotros, los anteriormente mencionados cedentes, por la presente vendemos, cedemos y transferimos el pleno derecho, título e interés en la aplicación divulgada sobre la misma para los Estados Unidos de América y todos los países del exterior, incluyendo los derechos de prioridad bajo la Convención Internacional de Paris (1883), tal como se ha modificado y, le solicitamos al Director de la Oficina de Patentes y Marcas Registradas de los Estados Unidos de América para expedir cualquiera y todas las cartas de patente otorgadas sobre la invención establecida en la aplicación a la beneficiaria, sus sucesores y beneficioarios y, por la presente, aceptamos que la beneficiaria puede aplicar para Cartas de Patente en el exterior sobre la invención y, ejecutaremos sin consideración económica todos los documentos que se estimen necesarios por parte de la beneficiaria en relación con las aplicaciones en los Estados Unidos y en los países del exterior, cuando ello sea solicitado por la beneficiaria.

Nosotros, por la presente autorizamos y le solicitamos a nuestros abogados SUGHRUE MION, PLLC localizados en 2100 Pennsylvania Avenue, NW, Washington, DC 20037-3213 a colocar en los paréntesis la información (Número de Aplicación 11/037,104 y Número de Confirmación 7455, registrada en Enero 19 de 2005, el número de Aplicación y la fecha de registro cuando sean conocidos.

Firmado por: Cynthia KUO

Fecha: Enero 20, 2005

Firmado por: Graham S, BYNG

Fecha: Enero 20, 2005.

Patente
Rollo: 016447 Referencia:0845

Es fiel traducción del documento que he tenido a la vista
E-mail: legomez2@tutopia.com.

LUIS ENRIQUE GOMEZ V. : Traductor Oficial
Resolución 283 / 88 Ministerio de Justicia
C.C. 438.449 Usaquéen D.C. Colombia S.A.

Traducción oficial de un documento escrito en Inglés. Septiembre 24, 2007

Archivo Legal A8868
Para clientes en los Estados Unidos

Cesión

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Considerando que; IMMUNOGEN, Inc., localizada en 128 Sidney Street, Cambridge, MA 02139-4239 (beneficiaria), tiene la intención de adquirir el pleno derecho, título e interés en la aplicación e invención y de cualquier patente a ser obtenida en el futuro en los Estados Unidos.

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Nosotros, por la presente autorizamos y le solicitamos a nuestros abogados SUGHRUE MION, PLLC localizados en 2100 Pennsylvania Avenue, NW, Washington, DC 20037-3213 a colocar en los paréntesis la información (Número de Aplicación 11/037,104 y Número de Confirmación 7455, registrada en Enero 19 de 2005, el número de Aplicación y la fecha de registro cuando sean conocidos.

Firmado por: Wayne C, WIDDISON

Fecha: Enero 19, 2005

Patente
Rollo: 016447 Referencia: 0846

Registrado en: 04/08/2005

Es fiel traducción del documento que he tenido a la vista
E-mail: legomez2@tutopia.com.

46 64

PATENT COOPERATION TREATY

PCT/US2005/044783

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:

MACK, Susan, J.
SUGHRUE MION, PLLC
2100 Pennsylvania Ave., Nw
Suite 800
Washington, District Of Columbia 20037-3213
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)
02 August 2007 (02.08.2007)

Applicant's or agent's file reference
F198922

IMPORTANT NOTICE

International application No.
PCT/US2005/044783

International filing date (day/month/year)
12 December 2005 (12.12.2005)

Priority date (day/month/year)
19 January 2005 (19.01.2005)

Applicant

IMMUNOGEN, INC. 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

Simin Baharlou

Facsimile No. +41 22 338 82 70

e-mail: pct@wipo.int

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 F198922	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2005/044783	International filing date (day/month/year) 12 December 2005 (12.12.2005)	Priority date (day/month/year) 19 January 2005 (19.01.2005)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant IMMUNOGEN, 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 5 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 Facsimile No. +41 22 338 82 70	Date of issuance of this report 24 July 2007 (24.07.2007)
	Authorized officer Simin Baharlou e-mail: pt09.pct@wipo.int

PATENT COOPERATION TREATY

REC'D 23 JUN 2006

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WIPO

PCT

To:
SUSAN J. MACK
SUGHRUB MION, PLLC
2100 PENNSYLVANIA AVE., N.W.
SUITE 800
WASHINGTON, DC 20037-3213

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) 21 JUN 2006

Applicant's or agent's file reference

FOR FURTHER ACTION

See paragraph 2 below

F198922

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US05/44783

12 December 2005 (12.12.2005)

19 January 2005 (19.01.2005)

International Patent Classification (IPC) or both national classification and IPC

IPC: Please See Continuation Sheet

USPC: 435/118,119,120;424/179.1,181.1

Applicant

IMMUNOGEN, 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 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/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this
opinion

13 April 2006 (13.04.2006)

Authorized officer

HERBERT J. ILLING

J. Roberts for
Telephone No. (571) 272-1600

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/44783

Box No. I Basis of this 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(s) 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/US05/44783

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

1. Statement

Novelty (N)	Claims <u>6-16, 37-39, 43-44</u>	YES
	Claims <u>1-5, 17-36, 40-42, 45-73</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-73</u>	NO
Industrial applicability (IA)	Claims <u>1-73</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-5, 17-36, 40-42, 45-52 and 55-73 lack novelty under PCT Article 33(2) as being anticipated by Asai (U.S. 4,294,757), Asai et al. (U.S. 4,322,348) or Asai et al. (U.S. 4,361,650). Each of the references teaches the processing or purification of ansamitocins which includes the extraction with acetate, aldehydes or halogenated compounds within the scope of the claimed inventions. In addition, the references teach the purification by crystallization and the use of silica gel. The references teach the same pH which includes pH 7.2 as well as the temperature for carrying the fermentation.

Claims 53-54 lack novelty under PCT Article 33(2) as being anticipated by Chari et al. I. U.S. 5,208,050; II. U.S. 5,416,064 or III. U.S. 6,441,163. Each of the references teaches a product which is a combination (complex or binding agent complex) of ansamitocins with a linking antibody that is considered to be within the scope of the claimed inventions.

Claims 6-16, 37-39 and 43-44 lack an inventive step under PCT Article 33(3) as being obvious over Asai (U.S. 4,361,650) alone or further in view of Hatano et al. (U.S. 4,356,265) references that teach the synthesis of various 3 substituted compounds with a "culture medium including a member selected from the group consisting of isobutyl aldehyde, isobutyl alcohol and a fatty acid ester of isobutyl alcohol" which disclosure renders obvious the claimed inventions.

Claims 1-73 meet the criteria set out in PCT Article 33(4), and thus the claimed inventions have industrial applicability because the subject matter claimed can be made or used in industry.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

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70

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