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263

Señora
Alix Carmenza Céspedes de Vergel
Jefe de División de Nuevas Creaciones
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
E. S. D.

00001

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 07-092447- -00003-0000
Fecha: 2007-12-10 16:31:44 Dep: 2020 NUECREACIONI
Tra: 11 PATENTEIYII Eve: 378 FASENACIONALI
Act: 444 RESPUESTAREQUE Folios: 68

Referencia: Expediente No. 07.092.447
Solicitud de Patente de Invención titulada: "Un método de cromatografía de partición débil"

Solicitante: Wyeth

RESPUESTA AL AUTO NOTIFICADO POR FIJACIÓN EN LISTA NO. 378 DEL 12 DE OCTUBRE DE 2007, OFICIO NO. 13116 (EXAMEN DE FORMA)

ÁLVARO CORREA ORDÓÑEZ, mayor de edad y vecino de Bogotá D.C., identificado tal como aparece al pie de mi firma, en mi carácter de apoderado de la sociedad en referencia, doy respuesta al auto emanado por ese Despacho dentro del término legal:

1. Presento copia debidamente legalizada del documento de cesión presentado en la solicitud estadounidense USSN 11/372,054 y en la solicitud USSN 60/660,437 en los cuales consta la cesión del derecho a la patente de los inventores a la entidad solicitante.

De igual manera, presento copia de la publicación de la solicitud de patente USSN 11/372,054 en donde se muestra que la solicitud provisional correspondiente es USSN 60/660,437, sobre la cual se reclama prioridad en la presente solicitud de patente.

2. Presento copia debidamente legalizada del poder de abogado así como copia del documento que acredita la existencia y representación legal de la entidad solicitante.

3. Aprovecho esta oportunidad para presentar el Reporte de Búsqueda Internacional y el Reporte Preliminar Internacional sobre Patentabilidad para esta solicitud elaborados por la Oficina Internacional de Búsqueda.

Atentamente,

ALVARO CORREA ORDÓNEZ
C.C.No.79.143.366 de Usaquén
T.P.20.281

Anexos: Documentos de Cesión de Inventores
Copia de la publicación para USSN 11/372,054
Poder de Abogado
Reporte de Búsqueda Internacional y Reporte Preliminar Internacional en Patentabilidad

BOGLMS/BOGDMS-96069-V1-.DOC

TRADUCCIÓN OFICIAL No. 526/07 de un documento escrito en inglés, el cual para su identificación se sella con el sello del Traductor. Esta es una Traducción Oficial efectuada el día 29 de noviembre de 2007 por la Sra. María Teresa Lara, c.c. 41.568.055 de Bogotá, Traductora Oficial según Resolución No. 01016 del 2 de octubre de 1998, expedida por el Ministerio de Justicia.

= =

Cesión a WYETH del invento titulado "MÉTODO DE CROMATOGRAFÍA DE PARTICIÓN DÉBIL". Certificación notarial suscrita por Barbara A. Kiely, Notario Público del estado de Nueva Jersey, y legalizaciones subsiguientes.

AM101950

DECLARACIÓN JURAMENTADA

MARIA TERESA LARA R. TRADUCTORA OFICIAL RESOLUCION No. 01016 DE MINJUSTICIA

Yo, Michelle L. McGowan, Asociada para Legalizaciones, Wyeth, certifico por la presente que la copia adjunta ha sido comparada con la Cesión original (para la U.S.S.N. 11/372,054 y cualquier equivalente legal de la misma en un país extranjero, para el invento titulado: "MÉTODO DE CROMATOGRAFÍA DE PARTICIÓN DÉBIL"), fechada el 24 de abril de 2006 de Brian D. Kelley, James Edward Booth, Paul Brown, Jon Coffman, Ranganathan Godavarti, Tim Iskra, Shujun Sun, Mary B. Switzer y Tianning Yu; y fechada el 25 de abril de 2006 de Suresh Vunnum a Wyeth y que la citada copia es fiel copia del original.

Dado el día 1 de noviembre de 2007, en Madison, Nueva Jersey, Estados Unidos de América.

Wyeth

(Fdo.) Michelle L. McGowan

Michelle L. McGowan
Asociada para Legalizaciones

PARA USO EN COLOMBIA

RECONOCIMIENTO

Estado de Nueva Jersey)
)
Condado de Morris)

El día 1 de noviembre de 2007 ante mi personalmente compareció Michelle L. McGowan, Asociada para Legalizaciones de Wyeth, a quien conozco y de quien me consta que es la persona descrita en el instrumento anterior y quien lo suscribió, y reconoció ante mi haber suscrito el mismo.

(Fdo.) Barbara A. Kiely
Notario Público

(Sello notarial en relieve)

[Sello] Barbara A. Kiely ID. 33893
Notario Público de Nueva Jersey
Mi comisión expira el 20 de junio de 2009

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 0107
DE MINJUSTICIA

Expediente No: 36119.179US2 (AM101950)
Patente

Cesión de Invento

En virtud del pago por la CESIONARIA al CEDENTE de contraprestación válida y valiosa, el recibo de la cual se reconoce por la presente, el CEDENTE:

(1) Nombre Completo del Inventor: Brian D. KELLEY
Residencia: 108 Blakely Road, Medford, MA 02155
Ciudadanía: Estados Unidos de América

---

(2) Nombre Completo del Inventor: James Edward BOOTH
Residencia: 29 Flint Circle, Andover, MA 01810
Ciudadanía: Estados Unidos de América

---

(3) Nombre Completo del Inventor: Paul BROWN
Residencia: 94 Meadowood Road, Andover, MA 01845
Ciudadanía: Estados Unidos de América

---

(4) Nombre Completo del Inventor: Jon COFFMAN
Residencia: 20 Sawmill Lane, Hampstead, NH 03841
Ciudadanía: Estados Unidos de América

---

(5) Nombre Completo del Inventor: Ranganathan GODAVARTI
Residencia: 27 Dolores Drive, Burlington, MA 01803
Ciudadanía: India

---

(6) Nombre Completo del Inventor: Tim ISKRA
Residencia: 7 James Street, Derry, NH 03038
Ciudadanía: Estados Unidos de América

---

(7) Nombre Completo del Inventor: Shujun SUN
Residencia: 43 Peabody Drive, Brentwood, NH 03833
Ciudadanía: Estados Unidos de América

---

(8) Nombre Completo del Inventor: Mary Beth SWITZER
Residencia: 235 Farnum Street, North Andover, MA 01845
Ciudadanía: Estados Unidos de América

---

(9) Nombre Completo del Inventor: Suresh VUNNUM
Residencia: 6 Oak Street, Burlington, MA 01803
Ciudadanía: India

---

(10) Nombre Completo del Inventor: Tianning YU
Residencia: 4 Amherst Street, Arlington, MA 02474
Ciudadanía: República Popular China

---

por la presente vende y cede a:

Wyeth
Five Giralda Farms
Madison, Nueva Jersey 07940

y a los sucesores, cesionarios y representantes legales de la CESIONARIA, todo derecho, título e interés para los Estados Unidos y sus posesiones

territoriales y en todos los países extranjeros, incluidos todos los derechos a reclamar prioridad, en y sobre el invento titulado:

MÉTODO DE CROMATOGRAFÍA DE PARTICIÓN DÉBIL

e inventado por el CEDENTE y los siguientes inventores adicionales, en caso de haberlos:

y el cual se encuentra en la Solicitud Provisional de los E.U. No. 11/372,054 presentada el 10 de marzo de 2006

[marcar también si se están cediendo solicitud(es) extranjera(s)]

[X] y cualquier equivalente legal de las mismas en un país extranjero,

debiendo insertarse anteriormente la fecha de presentación y número de solicitud de dicha solicitud de los E.U., una vez se conozcan, incluyendo el derecho a reclamar prioridad, incluidas todas y cada una de las mejoras allí divulgadas, y en y sobre todas las Patentes que hayan de obtenerse para dicho invento en virtud de la solicitud anterior o cualquier solicitud provisional, no provisional, de continuación, divisional, de renovación o sustituta de la misma posteriormente presentada, y respecto de Patentes, cualquier reemisión o reexamen de las mismas.

El CEDENTE pacta por el presente que no se ha hecho ni se hará ni se realizará ninguna cesión, venta, acuerdo o gravamen que pudiese entrar en conflicto con esta cesión.

El CEDENTE autoriza a la CESIONARIA a presentar solicitudes y recibir Patentes para dicho invento en cualquiera de dichos países en su propio nombre, o en nombre del CEDENTE, a su elección.

El CEDENTE pacta y acuerda suscribir u obtener cualquier garantía

adicional necesaria del título sobre dicho invento y cualquier Patente que pueda expedirse para el mismo y, en cualquier momento, a solicitud y por cuenta de la CESIONARIA, entregar cualquier testimonio en cualquier interferencia, litigio o proceso relacionado con el mismo y otorgar todos los documentos que puedan ser necesarios o convenientes para perfeccionar el título sobre dicho invento o cualquier Patente que pueda otorgarse para el mismo a la CESIONARIA, sus sucesores, cesionarios u otros representantes legales y, en cualquier momento, a solicitud y por cuenta de la CESIONARIA suscribir cualquier continuación, continuación en parte, solicitud divisional, de renovación o sustituta de la misma, y en cuanto a Patentes y reemisión o reexamen de las mismas, o cualquier otra solicitud adicional de Patente para dicho invento o cualquier parte del mismo, todas las cuales solicitudes y cualesquiera Patentes que se expidan sobre las mismas son por la presente cedidas a la CESIONARIA, y hará todos los juramentos o declaraciones lícitos, y realizará todo los actos lícitos requeridos para adquirir las mismas, sin otra compensación, pero por cuenta de la CESIONARIA, sus sucesores, cesionarios u otros representantes legales.

El CEDENTE autoriza y solicita al Comisionado de Patentes expedir todas y cada una de las Patentes de los Estados Unidos para dicho invento, resultantes de cualquiera de las anteriores solicitudes a su CESIONARIA.

(Fdo.) Brian D. Kelley — 24 abril 2006
Brian D. KELLEY — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Brian D. KELLEY, quien me demostró mediante prueba de identidad

satisfactoria en la forma de Licencia de Conducción de Massachusetts, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) James Edward Booth — 24 abril 2006
James Edward BOOTH — Fecha

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 01016
DE MINJUSTICIA

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí James Edward BOOTH, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de Massachusetts, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Paul Brown — 24 abril 2006
Paul BROWN — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Paul BROWN, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de Massachusetts, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello]

DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Jon Coffman
Jon COFFMAN

24 abril 2006
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Jon COFFMAN, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de New Hampshire, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello]

DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Ranganathan Godavarti
Ranganathan GODAVARTI

24 abril 2006
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Ranganathan GODAVARTI, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de Massachusetts, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello]

DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Tim Iskra
Tim ISKRA

24 abril 2006
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Tim ISKRA, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de New Hampshire, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Shujun Sun — 24 abril 2006
Shujun SUN — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Shujun SUN, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de New Hampshire, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Mary B. Switzer — 24 abril 2006
Mary B. SWITZER — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Mary B. SWITZER, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de Massachusetts, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció

haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Suresh Vunnum — 25 abril 2006
Suresh VUNNUM — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 25 días del mes de abril de 2006, compareció personalmente ante mí Suresh VUNNUM, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de Massachusetts, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Tianning Yu — 24 abril 2006
Tianning YU — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 24 días del mes de abril de 2006, compareció personalmente ante mí Tianning YU, quien me demostró mediante prueba de identidad satisfactoria en la forma de Licencia de Conducción de Massachusetts, ser la persona cuyo nombre suscribe el documento anterior o adjunto, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello]

DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 01016
DE MINJUSTICIA

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. País: Estados Unidos de América
2. Este documento público ha sido firmado por: Barbara A. Kiely
3. actuando en calidad de: Notario Público de Nueva Jersey
4. lleva el sello/timbre de: Barbara A. Kiely, Notario

CERTIFICADO

5. en Trenton, Nueva Jersey
6. el día 7 de noviembre de 2007
7. por Michellene Davis, TESORERO DE NUEVA JERSEY
8. No. A308260
9. Sello/Timbre:

(Sello del Estado de Nueva Jersey)

10. Firma

(Fdo.) Michellene Davis

= =

La anterior es traducción fiel y completa del documento en referencia, de la cual se deja copia en este archivo para su confrontación.

María Teresa Lara R.
c.c. 41.568.055 de Bogotá
Traductora Oficial según
Resolución No. 01016 del
2 de octubre de 1998, del
Ministerio de Justicia

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 01016
DE MINJUSTICIA

APOSTILLE

(CONVENTION DE LA HAYE DU 5 OCTOBRE 1961)

1. COUNTRY: UNITED STATES OF AMERICA

2. THIS PUBLIC DOCUMENT HAS BEEN SIGNED BY:
BARBARA A KIELY

3. ACTING IN THE CAPACITY OF:
NOTARY PUBLIC OF NEW JERSEY

4. BEARS THE SEAL/STAMP OF:
BARBARA A KIELY, NOTARY

CERTIFIED

5. AT TRENTON, NEW JERSEY

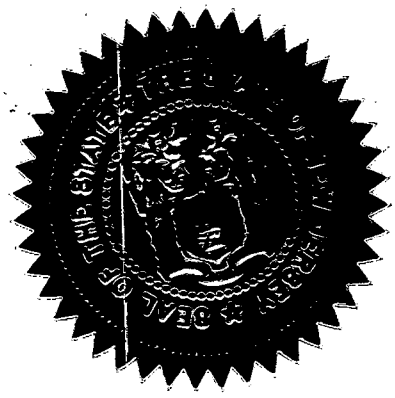
6. THE 7TH DAY OF NOVEMBER 2007

7. BY: Michellene Davis, NEW JERSEY TREASURER

8. NO. A308260

9. SEAL/STAMP:

10. SIGNATURE



AM101950

AFFIDAVIT

I, Michelle L. McGowan, Legalization Associate, Wyeth, do hereby certify that the attached copy has been compared with the original Assignment (for U.S.S.N. 11/372,054, and any legal equivalent thereof in a foreign country, for the invention entitled: "METHOD OF WEAK PARTITIONING CHROMATOGRAPHY") dated April 24, 2006 from Brian D. Kelley, James Edward Booth, Paul Brown, Jon Coffman, Ranganathan Godavarti, Tim Iskra, Shujun Sun, Mary B. Switzer, and Tianning Yu; and dated April 25, 2006 from Suresh Vunnum to Wyeth and that the said copy is a true copy of the original.

Dated this 1st day of November, 2007, at Madison, New Jersey, United States of America.

Wyeth

Michelle L. McGowan
Legalization Associate

TO BE USED IN COLOMBIA

ACKNOWLEDGMENT

State of New Jersey)
)
County of Morris)

On this 1st day of November, 2007, before me personally appeared Michelle L. McGowan, Legalization Associate of Wyeth, to me known and known to me to be the individual described in and who executed the foregoing instrument, and she acknowledged to me that she executed the same.

Notary Public

Barbara A. Kiely ID. 33893
Notary Public of New Jersey
My Commission Expires June 20, 2009

Assignment of Invention

In consideration of the payment by ASSIGNEE to ASSIGNOR of good and valuable consideration, the receipt of which is hereby acknowledged,
ASSIGNORS:

(1) Full Name of Inventor: Brian D. KELLEY
Residence: 108 Blakely Road, Medford, MA 02155
Citizenship: US

---

(2) Full Name of Inventor: James Edward BOOTH
Residence: 29 Flint Circle, Andover, MA 01810
Citizenship: US

---

(3) Full Name of Inventor: Paul BROWN
Residence: 94 Meadowood Road, Andover, MA 01845
Citizenship: US

---

(4) Full Name of Inventor: Jon COFFMAN
Residence: 20 Sawmill Lane, Hampstead, NH 03841
Citizenship: US

---

(5) Full Name of Inventor: Ranganathan GODAVARTI
Residence: 27 Dolores Drive, Burlington, MA 01803
Citizenship: India

---

(6) Full Name of Inventor: Tim ISKRA
Residence: ~~40 Kinge Way, Unit 601C, Waltham, MA 02451~~ ~~IL~~
Citizenship: US 7 James Street, Derry, NH 03038 25 Apr 06

---

(7) Full Name of Inventor: Shujun SUN
Residence: 43 Peabody Drive, Brentwood, NH 03833
Citizenship: US

---

(8) Full Name of Inventor: Mary Beth SWITZER
Residence: 235 Farnum Street, North Andover, MA 01845
Citizenship: US

---

(9) Full Name of Inventor: Suresh VUNNUM
Residence: 6 Oak Street, Burlington, MA 01803
Citizenship: India

---

(10) Full Name of Inventor: Tianning YU
Residence: 4 Amherst Street, Arlington, MA 02474
Citizenship: People's Republic of China

hereby sells and assigns to:

Wyeth
Five Giralda Farms
Madison, New Jersey 07940

and the successors, assigns and legal representatives of the ASSIGNEE the entire right, title and interest for the United States and its territorial possessions and in all foreign countries, including all rights to claim priority, in and to the invention entitled:

METHOD OF WEAK PARTITIONING CHROMATOGRAPHY

and invented by ASSIGNOR and the following additional inventors, if any:

and which is found in U.S. Application No. 11/372,054 filed on March 10, 2006

[also check if foreign application(s) is(are) also being assigned]

☒ and any legal equivalent thereof in a foreign country,

the date of filing and application number of said U.S. application when known, to be inserted above, including the right to claim priority, including any and all improvements disclosed therein, and in and to all Letters Patent to be obtained for said invention by the above application or any subsequently filed provisional, nonprovisional, continuation, divisional, renewal, or substitute thereof, and as to Letters Patent any reissue or re-examination thereof.

ASSIGNOR hereby covenants that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this assignment.

ASSIGNOR authorizes ASSIGNEE to make applications for and to receive Letters patent for said invention in any of said countries in its own name, or in ASSIGNOR's name, at its election.

ASSIGNOR covenants and agrees to execute or procure any further necessary assurance of the title to said invention and any Letters Patent which may issue therefore and to, at any time, upon the request and at the expense of ASSIGNEE deliver any testimony in any interference, litigation or proceeding related thereto and execute all papers that may be necessary or desirable to perfect the title to said invention or any Letters Patent which may be granted therefore in ASSIGNEE, its successors, assigns or other legal representatives, and that to, at any time, upon the request and at the expense of ASSIGNEE execute any continuation, continuation-in-part, divisional, renewal or substitute thereof, and as to Letters Patent and reissue or re-examination thereof, or any other additional applications of Letters Patent for said invention or any part thereof, all of which applications and any Letters Patent issuing thereon are hereby assigned to ASSIGNEE, and will make all rightful oaths or declarations, and do all lawful acts requisite for procuring the same therein, without further compensation, but at the expense of ASSIGNEE, its successors, assigns or other legal representatives.

ASSIGNOR authorizes and requests the Commissioner of Patents to issue any and all Letters Patent of the United States for said invention, resulting from any of the aforesaid applications to its ASSIGNEE.

~~119~~ 121

Brian D. KELLEY

24 April 2006
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Brian D. KELLEY, proved to me through satisfactory evidence of identity which was MA driver's license to be the person whose name is signed on the preceding or attached document, and acknowledged that he/~~she~~ executed the same, of his/~~her~~ own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

James Edward BOOTH

24-April-2006
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared James Edward BOOTH, proved to me through satisfactory evidence of identity which was MA driver's license to be the person whose name is signed on the preceding or attached document, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

Paul BROWN

24 Apr 2006
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Paul BROWN, proved to me through satisfactory evidence of identity which was MA driver's license to be the person whose name is signed on the preceding or attached document, and acknowledged that he/~~she~~ executed the same, of his/~~her~~ own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

Jon COFFMAN

24 APRIL 2006
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Jon COFFMAN, proved to me through satisfactory evidence of identity which was MA drivers license to be the person whose name is signed on the preceding or attached document, and acknowledged that he/~~she~~ executed the same, of his/~~her~~ own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

Ranganathan GODAVARTI — 24 Apr, 2006
Ranganathan GODAVARTI — Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Ranganathan GODAVARTI, proved to me through satisfactory evidence of identity which was MA driver's license to be the person whose name is signed on the preceding or attached document, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

Tim ISKRA — 24 Apr 06
Tim ISKRA — Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Tim ISKRA, proved to me through satisfactory evidence of identity which was MA driver's License to be the person whose name is signed on the preceding or attached document, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

Shujun SUN

Apr-24-2006
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Shujun SUN, proved to me through satisfactory evidence of identity which was MA drivers License to be the person whose name is signed on the preceding or attached document, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Notary Public

Mary B. SWITZER

Apr-24-2006
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Mary B. SWITZER, proved to me through satisfactory evidence of identity which was MA drivers license to be the person whose name is signed on the preceding or attached document, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Notary Public

Suresh VUNNUM

April 25, 2006
Date

ACKNOWLEDGMENT

State of ~~Essex~~ Massachusetts
ss:
County of Essex }

On the 25th day of April 2006, before me, personally appeared Suresh VUNNUM, proved to me through satisfactory evidence of identity which was MA drivers license to be the person whose name is signed on the preceding or attached document, and acknowledged that he/~~she~~ executed the same, of his/~~her~~ own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

Tianning YU

Apr 24, 2006
Date

ACKNOWLEDGMENT

State of Massachusetts
ss:
County of Essex }

On the 24th day of April 2006, before me, personally appeared Tianning YU, proved to me through satisfactory evidence of identity which was MA drivers license to be the person whose name is signed on the preceding or attached document, and acknowledged that ~~he~~/she executed the same, of ~~his~~/her own free will and for the purposes set forth.

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Diane R. Driscoll
Notary Public

TRADUCCIÓN OFICIAL No. 525/07 de un documento escrito en inglés, el cual para su identificación se sella con el sello del Traductor. Esta es una Traducción Oficial efectuada el día 29 de noviembre de 2007 por la Sra. María Teresa Lara, c.c. 41.568.055 de Bogotá, Traductora Oficial según Resolución No. 01016 del 2 de octubre de 1998, expedida por el Ministerio de Justicia.

= =

Cesión a WYETH del invento titulado "UN MÉTODO DE CROMATOGRAFÍA DE PARTICIÓN DÉBIL". Certificación notarial suscrita por Barbara A. Kiely, Notario Público del estado de Nueva Jersey, y legalizaciones subsiguientes.

AM101950 L1

DECLARACIÓN JURAMENTADA

Yo, Michelle L. McGowan, Asociada para Legalizaciones, Wyeth, certifico por la presente que la copia adjunta ha sido comparada con la Cesión original (para la U.S.S.N. 60/660,437 y cualquier equivalente legal de la misma en un país extranjero, para el invento titulado: "UN MÉTODO DE CROMATOGRAFÍA DE PARTICIÓN DÉBIL"), fechada el 14 de julio de 2005 de Paul R. Brown, Jonathan Coffman, Ranganathan Godavarti, Tim Iskra, Brian D. Kelley, Suresh Vunnum, Shujun Sun y Tianning Yu a Wyeth y que la citada copia es fiel copia del original.

Dado a los 28 días del mes de agosto de 2007, en Madison, Nueva Jersey, Estados Unidos de América.

Wyeth

(Fdo.) Michelle L. McGowan

Michelle L. McGowan
Asociada para Legalizaciones

PARA USO EN COLOMBIA

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 01016
DE MINJUSTICIA

RECONOCIMIENTO

Estado de Nueva Jersey)
)
Condado de Morris)

A los 28 días del mes de agosto de 2007, ante mi personalmente compareció Michelle L. McGowan, Asociada para Legalizaciones de Wyeth, a quien conozco y de quien me consta que es la persona descrita en el instrumento anterior y quien lo suscribió, y reconoció ante mi haber suscrito el mismo.

(Fdo.) Barbara A. Kiely
Notario Público

(Sello notarial en relieve)

[Sello] Barbara A. Kiely ID. 33893
Notario Público de Nueva Jersey
Mi comisión expira el 20 de junio de 2009

Expediente No: AM101950
Patente

Cesión de Invento

En virtud del pago por la CESIONARIA al CEDENTE de contraprestación válida y valiosa, el recibo de la cual se reconoce por la presente, el CEDENTE:

(1) Nombre Completo del Inventor: Paul R. BROWN
Residencia: 94 Medowood Road, North Andover, Massachusetts 01845
Ciudadanía: Estados Unidos de América

(2) Nombre Completo del Inventor: Jonathan COFFMAN
Residencia: 20 Sawmill Lane, Hampstead, New Hampshire 03841
Ciudadanía: Estados Unidos de América

(3) Nombre Completo del Inventor: Ranganathan GODAVARTI
Residencia: 27 Dolores Drive, Burlington, Massachusetts 01803
Ciudadanía: India

(4) Nombre Completo del Inventor: Tim ISKRA
Residencia: 40 Kings Way Unit 601C, Waltham, Massachusetts 02451
Ciudadanía: Estados Unidos de América

---

(5) Nombre Completo del Inventor: Brian D. KELLEY
Residencia: 108 Blakely Road, Medford, Massachusetts 02155
Ciudadanía: Estados Unidos de América

---

(6) Nombre Completo del Inventor: Suresh VUNNUM
Residencia: 6 Oak Street, Burlington, Massachusetts 01803
Ciudadanía: India

---

(7) Nombre Completo del Inventor: Shujun SUN
Residencia: 43 Peabody Drive, Brentwood, New Hampshire 03833
Ciudadanía: Estados Unidos de América

---

(8) Nombre Completo del Inventor: Tianning YU
Residencia: 4 Amherst Street, Arlington, Massachusetts 02474
Ciudadanía: República Popular China

---

por la presente vende, cede y traspasa a la CESIONARIA:

Wyeth
Five Giralda Farms
Madison, Nueva Jersey 07940

y a los sucesores, cesionarios y representantes legales de la CESIONARIA, todo derecho, título e interés para los Estados Unidos y sus posesiones territoriales y en todos los países extranjeros, incluidos todos los derechos a reclamar prioridad, en y sobre el invento titulado:

UN MÉTODO DE CROMATOGRAFÍA DE PARTICIÓN DÉBIL

e inventado por el CEDENTE y los siguientes inventores adicionales, en caso de haberlos:

y el cual se encuentra en la Solicitud Provisional de los E.U. No. 60/660,437 presentada el: 11 de marzo de 2005

[ ] Yo, el suscrito CEDENTE, por la presente autorizo y solicito la inserción anterior del número de solicitud y la fecha de presentación, una vez se conozcan,

[marcar también si se están cediendo solicitud(es) extranjera(s)]

[X] y cualquier equivalente legal de las mismas en un país extranjero,

incluyendo el derecho a reclamar prioridad, incluidas todas y cada una de las mejoras allí divulgadas, y en y sobre todas las Patentes que hayan de obtenerse para dicho invento en virtud de la solicitud anterior o cualquier solicitud provisional, no provisional, de continuación, divisional, de renovación o sustituta de la misma posteriormente presentada, y respecto de Patentes, cualquier reemisión o reexamen de las mismas.

El CEDENTE pacta por el presente que no se ha hecho ni se hará ni se realizará ninguna cesión, venta, acuerdo o gravamen que pudiese entrar en conflicto con esta cesión.

El CEDENTE autoriza a la CESIONARIA a presentar solicitudes y recibir Patentes para dicho invento en cualquiera de dichos países en su propio nombre, o en nombre del CEDENTE, a su elección.

El CEDENTE pacta y acuerda suscribir u obtener cualquier garantía adicional necesaria del título sobre dicho invento y cualquier Patente que pueda expedirse para el mismo y, en cualquier momento, a solicitud y por cuenta de la CESIONARIA, entregar cualquier testimonio en cualquier interferencia, litigio o proceso relacionado con el mismo y otorgar todos los documentos que puedan ser necesarios o convenientes para perfeccionar el

título sobre dicho invento o cualquier Patente que pueda otorgarse para el mismo a la CESIONARIA, sus sucesores, cesionarios u otros representantes legales y, en cualquier momento, a solicitud y por cuenta de la CESIONARIA suscribir cualquier continuación, continuación en parte, solicitud divisional, de renovación o sustituta de la misma, y en cuanto a Patentes y reemisión o reexamen de las mismas, o cualquier otra solicitud adicional de Patente para dicho invento o cualquier parte del mismo, todas las cuales solicitudes y cualesquiera Patentes que se expidan sobre las mismas son por la presente cedidas a la CESIONARIA, y hará todos los juramentos o declaraciones lícitos, y realizará todo los actos lícitos requeridos para adquirir las mismas, sin otra compensación, pero por cuenta de la CESIONARIA, sus sucesores, cesionarios u otros representantes legales.

El CEDENTE autoriza y solicita al Comisionado de Patentes expedir todas y cada una de las Patentes de los Estados Unidos para dicho invento, resultantes de cualquiera de las anteriores solicitudes a su CESIONARIA.

(Fdo.) Paul R. Brown
Paul R. BROWN

14 julio 2005
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Paul R. BROWN, a quien conozco como la misma persona descrita en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Jonathan Coffman — 14 julio 2005
Jonathan COFFMAN — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Jonathan COFFMAN, a quien conozco como la misma persona descrita en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Ranganathan Godavarti — 14 julio 2005
Ranganathan GODAVARTI — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Ranganathan GODAVARTI, a quien conozco como la misma persona descrita

en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Tim Iskra
Tim ISKRA

14 julio 2005
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Tim ISKRA, a quien conozco como la misma persona descrita en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Brian D. Kelley
Brian D. KELLEY

14 julio 2005
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Brian D. KELLEY, a quien conozco como la misma persona descrita en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello]

DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Suresh Vunnum — 14 julio 2005
Suresh VUNNUM — Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Suresh VUNNUM, a quien conozco como la misma persona descrita en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello]

DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

(Fdo.) Shujun Sun
Shujun SUN

14 julio 2005
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Shujun SUN, a quien conozco como la misma persona descrita en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

[Sello]

DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 0574
DE MINJUSTICIA

(Fdo.) Tianning Yu
Tianning YU

14 julio 2005
Fecha

RECONOCIMIENTO

Estado de Massachusetts }
ss:
Condado de Essex }

A los 14 días del mes de julio de 2005, compareció personalmente ante mí Tianning YU, a quien conozco como la misma persona descrita en el instrumento anterior y quien lo otorgó, y reconoció haber otorgado el mismo, por su propia voluntad y para los propósitos allí señalados.

(Fdo.) Diane R. Driscoll
Notario Público

245

[Sello] DIANE R. DRISCOLL
Notario Público
Estado de Massachusetts
Mi comisión expira el
21 de mayo de 2010

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. País: Estados Unidos de América
2. Este documento público ha sido firmado por: Barbara A. Kiely
3. actuando en calidad de: Notario Público de Nueva Jersey
4. lleva el sello/timbre de: Barbara A. Kiely, Notario

CERTIFICADO

5. en Trenton, Nueva Jersey
6. el día 4 de septiembre de 2007
7. por Bradley Abelow, TESORERO DE NUEVA JERSEY
8. No. A301930
9. Sello/Timbre: 10. Firma

(Sello del Estado de Nueva Jersey) (Fdo.) Bradley Abelow

= =

La anterior es traducción fiel y completa del documento en referencia, de la cual se deja copia en este archivo para su confrontación.

María Teresa Lara R.
c.c. 41.568.055 de Bogotá
Traductora Oficial según
Resolución No. 01016 del
2 de octubre de 1998, del
Ministerio de Justicia

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 01016
DE MINJUSTICIA

APOSTILLE

(CONVENTION DE LA HAYE DU 5 OCTOBRE 1961)

1. COUNTRY: UNITED STATES OF AMERICA

2. THIS PUBLIC DOCUMENT HAS BEEN SIGNED BY:
BARBARA A KIELY

3. ACTING IN THE CAPACITY OF:
NOTARY PUBLIC OF NEW JERSEY

4. BEARS THE SEAL/STAMP OF:
BARBARA A KIELY, NOTARY

CERTIFIED

5. AT TRENTON, NEW JERSEY

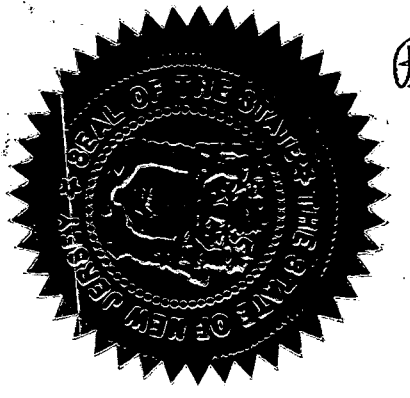
6. THE 4TH DAY OF SEPTEMBER 2007

7. BY: Bradley Abelow, NEW JERSEY TREASURER

8. NO. A301930

9. SEAL/STAMP:

10. SIGNATURE



Bradley Abelow

AM101950 L1

AFFIDAVIT

I, Michelle L. McGowan, Legalization Associate, Wyeth, do hereby certify that the attached copy has been compared with the original Assignment (for U.S.S.N. 60/660,437, and any legal equivalent thereof in a foreign country, for the invention entitled: "A METHOD OF WEAK PARTITIONING CHROMATOGRAPHY") dated July 14,2005 from Paul R. Brown, Jonathan Coffman, Ranganathan Godavarti, Tim Iskra, Brian D. Kelley, Suresh Vunnum, Shujun Sun and Tianning Yu to Wyeth and that the said copy is a true copy of the original.

Dated this 28th day of August, 2007, at Madison, New Jersey, United States of America.

Wyeth

Michelle L. McGowan
Legalization Associate

TO BE USED IN COLOMBIA

ACKNOWLEDGMENT

State of New Jersey)
)
County of Morris)

On this 28th day of August, 2007, before me personally appeared Michelle L. McGowan, Legalization Associate of Wyeth, to me known and known to me to be the individual described in and who executed the foregoing instrument, and she acknowledged to me that she executed the same.

Notary Public

Barbara A. Kiely ID. 33893
Notary Public of New Jersey
My Commission Expires June 20, 2009

Assignment of Invention

In consideration of the payment by ASSIGNEE to ASSIGNOR of good and valuable consideration, the receipt of which is hereby acknowledged,
ASSIGNOR:

(1) Full Name of Inventor: Paul R. BROWN
Residence: 94 Medowood Road, North Andover, Massachusetts 01845
Citizenship: United States of America

---

(2) Full Name of Inventor: Jonathan COFFMAN
Residence: 20 Sawmill Lane, Hampstead, New Hampshire 03841
Citizenship: United States of America

---

(3) Full Name of Inventor: Ranganathan GODAVARTI
Residence: 27 Dolores Drive, Burlington, Massachusetts 01803
Citizenship: India

---

(4) Full Name of Inventor: Tim ISKRA
Residence: 40 Kings Way Unit 601C, Waltham, Massachusetts 02451
Citizenship: United States of America

---

(5) Full Name of Inventor: Brian D. KELLEY
Residence: 108 Blakely Road, Medford, Massachusetts 02155
Citizenship: United States of America

---

(6) Full Name of Inventor: Suresh VUNNUM
Residence: 6 Oak Street, Burlington, Massachusetts 01803
Citizenship: India

---

(7) Full Name of Inventor: Shujun SUN
Residence: 43 Peabody Drive, Brentwood, New Hampshire 03833
Citizenship: United States of America

---

(8) Full Name of Inventor: Tianning YU
Residence: 4 Amherst Street, Arlington, Massachusetts 02474
Citizenship: ~~United States of America~~ People's Republic of China

---

hereby sells, assigns and transfers to ASSIGNEE: TYu July 14, 2005

Wyeth
Five Giralda Farms
Madison, New Jersey 07940

and the successors, assigns and legal representatives of the ASSIGNEE the entire right, title and interest for the United States and its territorial possessions and in all foreign countries, including all rights to claim priority, in and to the invention entitled:
A METHOD OF WEAK PARTITIONING CHROMATOGRAPHY

and invented by ASSIGNOR and the following additional inventors, if any:

and which is found in U.S. Provisional Application No. 60/660,437 filed on: March 11, 2005

☐ I/we the ASSIGNOR signing below, hereby authorize and request insertion above of the application number and filing date, when they become known,

[also check if foreign application(s) is(are) also being assigned]

☒ and any legal equivalent thereof in a foreign country,

including the right to claim priority, including any and all improvements disclosed therein, and in and to all Letters Patent to be obtained for said invention by the above application or any subsequently filed provisional, nonprovisional, continuation, divisional, renewal, or substitute thereof, and as to Letters Patent any reissue or re-examination thereof.

ASSIGNOR hereby covenants that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this assignment.

ASSIGNOR authorizes ASSIGNEE to make applications for and to receive Letters patent for said invention in any of said countries in its own name, or in ASSIGNOR's name, at its election.

ASSIGNOR covenants and agrees to execute or procure any further necessary assurance of the title to said invention and any Letters Patent which may issue therefore and to, at any time, upon the request and at the expense of ASSIGNEE deliver any testimony in any interference, litigation or proceeding related thereto and execute all papers that may be necessary or desirable to perfect the title to said invention or any Letters Patent which may be granted therefore in ASSIGNEE, its successors, assigns or other legal representatives, and that to, at any time, upon the request and at the expense of ASSIGNEE execute any continuation, continuation-in-part, divisional, renewal or substitute thereof, and as to Letters Patent and reissue or re-examination thereof, or any other additional applications of Letters Patent for said invention or any part thereof, all of which applications and any Letters Patent issuing thereon are hereby assigned to ASSIGNEE, and will make all rightful oaths or declarations, and do all lawful acts requisite for procuring the same therein, without further compensation, but at the expense of ASSIGNEE, its successors, assigns or other legal representatives.

ASSIGNOR authorizes and requests the Commissioner of Patents to issue any and all Letters Patent of the United States for said invention, resulting from any of the aforesaid applications to its ASSIGNEE.

Paul R. BROWN

14 July 2005
Date

ACKNOWLEDGMENT

State of Massachusetts)
ss:
County of Essex)

On the 14th day of July 2005, Paul R. BROWN personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Jonathan COFFMAN

14 JULY 2005
Date

ACKNOWLEDGMENT

State of Massachusetts)
ss:
County of Essex)

On the 14th day of July 2005, Jonathan COFFMAN personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Ranganathan GODAVARTI — 14 Jul 2005 — Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 14th day of July 2005, Ranganathan GODAVARTI personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Tim ISKRA — 14 JUL 2005 — Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 14th day of July 2005, Tim ISKRA personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Brian D. KELLEY

14 July 05
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 14th day of July 2005, Brian D. KELLEY personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Suresh VUNNUM

14 July 05
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 14th day of July 2005, Suresh VUNNUM personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Shujun SUN

July 14, 2005
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 14th day of July 2005, Shujun SUN personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

Tianning YU

July 14, 2005
Date

ACKNOWLEDGMENT

State of Massachusetts }
ss:
County of Essex }

On the 14th day of July 2005, Tianning YU personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he/she executed the same, of his/her own free will and for the purposes set forth.

Diane R. Driscoll
Notary Public

DIANE R. DRISCOLL
Notary Public
Commonwealth of Massachusetts
My Commission Expires
May 21, 2010

US 20070060741A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2007/0060741 A1**

Kelley et al. (43) **Pub. Date: Mar. 15, 2007**

(54) **METHOD OF WEAK PARTITIONING CHROMATOGRAPHY**

(75) Inventors: **Brian D. Kelley**, Medford, MA (US); **James E. Booth**, Andover, MA (US); **Paul Brown**, Andover, MA (US); **Jon Coffman**, Hampstead, NH (US); **Ranganathan Godavarti**, Burlington, MA (US); **Tim Iskra**, Derry, NH (US); **Shujun Sun**, Brentwood, NH (US); **Mary B. Switzer**, North Andover, MA (US); **Suresh Vunnum**, Burlington, MA (US); **Tianning Yu**, Arlington, MA (US)

Correspondence Address:
WilmerHale/Wyeth
60 STATE STREET
BOSTON, MA 02109 (US)

(73) Assignee: **Wyeth**, Madison, NJ

(21) Appl. No.: **11/372,054**

(22) Filed: **Mar. 10, 2006**

Related U.S. Application Data

(60) Provisional application No. 60/660,437, filed on Mar. 11, 2005.

Publication Classification

(51) **Int. Cl.**
C07K 16/00 (2006.01)

(52) **U.S. Cl.** **530/387.1**; 530/412

(57) **ABSTRACT**

This invention relates to methods of using weak partitioning chromatography for the purification of a product from a load fluid containing one or more impurities. Further, the invention relates to methods of weak partitioning chromatography defined by operating conditions which cause a medium to bind least 1 mg of product per mL of medium, or alternatively, defined by a partition coefficient of at least 0.1.

TRADUCCIÓN OFICIAL No. 524/07 de un documento escrito en inglés, el cual para su identificación se sella con el sello del Traductor. Esta es una Traducción Oficial efectuada el día 29 de noviembre de 2007 por la Sra. María Teresa Lara, c.c. 41.568.055 de Bogotá, Traductora Oficial según Resolución No. 01016 del 2 de octubre de 1998, expedida por el Ministerio de Justicia.

= =

Poder otorgado por WYETH respecto de la solicitud de patente titulada "UN MÉTODO DE CROMATOGRAFÍA DE PARTICIÓN DÉBIL". Certificación notarial suscrita por Michelle L. McGowan, Notario Público del estado de Nueva Jersey, y legalizaciones subsiguientes.

EL PODER Y LA CERTIFICACIÓN NOTARIAL NO SE TRADUCEN POR ENCONTRARSE EN INGLÉS Y ESPAÑOL EN EL DOCUMENTO ORIGINAL.

(Fdo.) Michelle L. McGowan
Notario Público

(Sello) MICHELLE L. McGOWAN
Notario Público, Estado de Nueva Jersey
No. 2108903
Habilitada en el Condado de Morris
La comisión expira el 9 de febrero de 2011

(Sello notarial
en relieve)

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. País: Estados Unidos de América
2. Este documento público ha sido firmado por: Michelle L. McGowan
3. actuando en calidad de: Notario Público de Nueva Jersey
4. lleva el sello/timbre de: Michelle L. McGowan, Notario

CERTIFICADO

5. en Trenton, Nueva Jersey

6. el día 21 de agosto de 2007

7. por Bradley Abelow, TESORERO DE NUEVA JERSEY

8. No. A300700

9. Sello/Timbre:

(Sello del Estado de Nueva Jersey)

10. Firma

(Fdo.) Bradley Abelow

= =

La anterior es traducción fiel y completa del documento en referencia, de la cual se deja copia en este archivo para su confrontación.

MARIA TERESA LARA R.
TRADUCTORA OFICIAL
RESOLUCION No. 01016
DE MINJUSTICIA

María Teresa Lara R.
c.c. 41.568.055 de Bogotá
Traductora Oficial según
Resolución No. 01016 del
2 de octubre de 1998, del
Ministerio de Justicia

APOSTILLE

(CONVENTION DE LA HAYE DU 5 OCTOBRE 1961)

1. COUNTRY: UNITED STATES OF AMERICA

2. THIS PUBLIC DOCUMENT HAS BEEN SIGNED BY:
MICHELLE L MC GOWAN

3. ACTING IN THE CAPACITY OF:
NOTARY PUBLIC OF NEW JERSEY

4. BEARS THE SEAL/STAMP OF:
MICHELLE L MC GOWAN, NOTARY

CERTIFIED

5. AT TRENTON, NEW JERSEY

6. THE 21ST DAY OF AUGUST 2007

7. BY: Bradley Abelow, NEW JERSEY TREASURER

8. NO. A300700

9. SEAL/STAMP:

10. SIGNATURE

Bradley Abelow

BAKER & McKENZIE

AM101950 Colombia

Raisbeck, Lara, Rodríguez & Rueda
Av. 82 No. 10 - 62 6th Floor
Bogotá, Colombia

NIT: 860.068.840-3
Tel: +57 1 634 1500
Fax: +57 1 376 2211
www.bakernet.com

309

80047

POWER OF ATTORNEY

The undersigned.

WYETH

with offices at

Five Giralda Farms, Madison, NJ 07940,
United States of America

declares that it hereby grants to

ALVARO CORREA-ORDOÑEZ and/or
OLGA GEORGETTE OTERO and/or
RICARDO METKE and/or
JUAN PABLO CONCHA

all members of the law firm Raisbeck, Lara, Rodriguez & Rueda, with domicile at Av. 82 No. 10 – 62, 6Th floor, of Bogotá D. C., Colombia, and for so long as they remain members of the law firm, a full and sufficient power of attorney with respect to Colombian patent application(s) based on PCT/US2006/008919 and entitled "A METHOD OF WEAK PARTITIONING CHROMATOGRAPHY" and to obtain patent protection thereof, for which purpose I (we) authorize the said attorneys to represent me (us) before any authorities or persons, with or without jurisdiction, specially those administrative, administrative contentious and judicial, as well as before Arbitration Court, in all matters concerning the following: a) Obtainment of a patent(s) based upon said patent application(s), including filing of assignments, change of name or address, voluntary cancellation; and defending oppositions, cancellations, nullity, writ mandamus, and in general the civil, penal, an administrative processes relating to those rights.

I hereby ratify all lawful actions previously taken on behalf of this company by the aforementioned attorneys with respect to the mentioned matters.

Done and subscribed in

On the 17 day of August 2007

Signature of the person issuing the Power

WYETH

Michael P. Straher
Assistant Secretary

PODER DE ABOGADO

La abajo firmada,

WYETH

con oficinas en

Five Giralda Farms, Madison, NJ 07940,
Estados Unidos de América

declara por el presente que otorga a

ALVARO CORREA-ORDOÑEZ y/o
OLGA GEORGETTE OTERO y/o
RICARDO METKE y/o
JUAN PABLO CONCHA

Todos miembros de la firma de abogados Raisbeck, Lara, Rodríguez & Rueda, con domicilio en la Av. 82 No. 10 – 62 Piso 6 en Bogotá D. C., Colombia, y hasta tanto ellos continúen siendo miembros de la firma, poder especial amplio y suficiente con respecto a la solicitud(es) de patente en Colombia basada(s) en PCT/US2006/008919 y titulada "UN METODO DE CROMATOGRAFIA DE PARTICION DEBIL",
y para obtener la protección de patente de la misma, a cuyo efecto autorizo (amos) a los dichos apoderados para que me (nos) representen ante cualesquiera autoridades o personas, ejerzan o no jurisdicción, especialmente ante las del orden administrativo, contencioso-administrativo y judicial, así como los tribunales de arbitramento, en todo lo concerniente a los siguientes asuntos: a) Obtención de la(s) patente(s) de invención basada(s) en la mencionada solicitud de patente, incluyendo presentación de traspasos, cambio de nombre o dirección, cancelación voluntaria; y defensa en oposiciones, cancelaciones, nulidades, la tutela, y en general procesos civiles, penales, administrativos relacionados con estos derechos.

Igualmente, ratifico todo lo actuado en derecho hasta el momento en nombre de esta compañía por cualquiera de los mencionados apoderados en los casos mencionados.

Dado y firmado en

A los 17 días del mes de agosto de 2007

Firma de la persona que firma el Poder

NOTARIAL CERTIFICATION

On this 17 day of **August** 2007 , the undersigned Notary

CERTIFIES

1. That **Michael P. Straher** set his hand on the foregoing document.

2. That the grantor is to me personally known and that he/she has legal capacity to execute the instrument.

3. That the grantor has executed the foregoing document as

Assistant Secretary

of the judicial person **WYETH**

4. That the judicial person **WYETH** having its home office in
Five Giralda Farms, Madison, NJ 07940,
United States of America

is duly organized, has present legal existence and that the purposes for which the power of attorney is granted are within the scope of its corporate purposes.

5. That the grantor has in fact the referred to authority and that his/her representation is legal.

6. That I have based certifications 3, 4 and 5 above on the following authentic documents for such purpose exhibited to me and which I mention specifically, giving their dates and their origin or source:
Minutes of the Board of Directors Meeting held on April 26, 2007.

Notary Public
MICHELLE L. McGOWAN
Notary Public, State of New Jersey
No. 2108903
Qualified in Morris County
Commission Expires Feb. 9, 2011

CERTIFICACION NOTARIAL

A los 17 días del mes de agósto de 2007 , el suscrito Notario

DA FE

1 Que Michael P. Straher suscribió de su puño y letra el documento que antecede.

2. Que conozco al otorgante y que éste tiene capacidad legal para el otorgamiento.

3 Que el otorgante ha suscrito el referido documento en su carácter de
Subsecretario
de la persona jurídica **WYETH**

4 Que la persona jurídica **WYETH** con sede en
Five Giralda Farms, Madison, NJ 07940,
Estados Unidos de América

está legalmente constituida, que tiene existencia legal actual y que el acto para el cual se otorga el poder está comprendido entre los que constituyen su objeto social.

5 Que el otorgante tiene efectivamente la representación que ostenta y que ésta es legítima.

6. Que he basado las certificaciones 3, 4 y 5 anteriores en los siguientes documentos auténticos que al efecto se me exhibieron y que menciono específicamente con expresión de sus fechas y de su origen o procedencia:
Actas de la reunión de la Junta Directiva celebrada el 26 de abril de 2007

El Notario Público

~~PAG~~ 312

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: Belinda Lew
Wilmer Cutler Pickering Hale and Dorr LLP
The Willard Office Building
1455 Pennsylvania Avenue, NW
Washington, DC 20004

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 0036119.00179WO1	Date of mailing *(day/month/year)* 10 SEP 2007
International application No. PCT/US 06/08919	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
Applicant Wyeth	International filing date *(day/month/year)* 10 March 2006 (10.03.2006)

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35

   For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: Belinda Lew
Wilmer Cutler Pickering Hale and Dorr LLP
The Willard Office Building
1455 Pennsylvania Avenue, NW
Washington, DC 20004

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing *(day/month/year)*	10 SEP 2007
Applicant's or agent's file reference 0036119.00179WO1	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US 06/08919	International filing date *(day/month/year)* 10 March 2006 (10.03.2006)
Applicant Wyeth	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35

   For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

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	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/220 (January 2004) *(See notes on accompanying sheet)*

~~RAR-1~~ 317

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 0036119.00179WO1	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US 06/08919	International filing date *(day/month/year)* 10 March 2006 (10.03.2006)	(Earliest) Priority Date *(day/month/year)* 11 March 2005 (11.03.2005)
Applicant Wyeth		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out 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))

   b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No. III)

4. With regard to the **title**,

   ☒ the text is approved as submitted by the applicant

   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   ☒ the text is approved as submitted by the applicant

   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

   a. the figure of the **drawings** to be published with the abstract is Figure No. _____

   ☐ as suggested by the applicant

   ☐ as selected by this Authority, because the applicant failed to suggest a figure

   ☐ as selected by this Authority, because this figure better characterizes the invention

   b. ☒ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 06/08919

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8)- C07K 1/00, 14/00, 16/00 (2007.01)
USPC- 530/355
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC 530/355

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC-435/183; Google: keywords: weak partitioning chromatography ; ion exchange chromatography and weak for ion exchange chromatography and partition coefficient

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST: DB=PGPB,USPT,USOC,EPAB,JPAB

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ——— Y	US 5,429,746 A (SHADLE et al) 04 July 1995 (04.07.1995), entire document	1, 87, 90, 93, 96, 99, 102, 105, 108, 111, 114, 117, 120 ——— 2-86, 88-89, 91-92, 94-95, 97-98,100-101, 103-104, 106-107, 109-110, 112-113, 115-116, 118-119, 121-122
Y	US 4,029,583 A (CHANG et al) 14 June 1977 (14.06.1977), col 1, ln 13-32; col 10, ln 24-35	2-86, 88-89, 91-92, 94-95, 97,98, 100-101, 103-104, 106-107, 109-110, 112-113, 115-116, 118-119, 121-122

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 April 2007 (17.04.2007)	10 SEP 2007

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2005)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: Belinda Lew
Wilmer Cutler Pickering Hale and Dorr LLP
The Willard Office Building
1455 Pennsylvania Avenue, NW
Washington, DC 20004

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	10 SEP 2007
Applicant's or agent's file reference 0036119.00179WO1	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 06/08919	10 March 2006 (10.03.2006)	11 March 2005 (11.03.2005)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - C07K 1/00, 14/00, 16/00 (2007.01)
USPC - 530/355

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 43*bis*.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 66.1*bis*(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	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	17 April 2007 (17.04.2007)	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 06/08919

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/US 06/08919

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	1-122	YES
	Claims	none	NO
Inventive step (IS)	Claims	none	YES
	Claims	1-122	NO
Industrial applicability (IA)	Claims	1-122	YES
	Claims	none	NO

2. Citations and explanations:

Claims 1, 87, 90, 93, 96, 99, 102, 105, 108, 111, 114, 117 and 120 lack an inventive step under PCT Article 33(3) as being obvious over US 5,429,746 A to Shadle et al (hereinafter 'Shadle').

Regarding Claims 1 and 87, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50) a method of recovering purified protein or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind at a load ratio ranging dependent on the support or resin used, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography.

Regarding Claims 90, 93, 96, 99, 102, 105, and 108, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle further discloses (col 14, Table 2; col 15, Table 3) that the passing of the load fluid through a medium at operating conditions causes the medium to bind at a load ratio ranging from 9.1 grams of product/ 1 liter of medium to 16 grams of product/1L medium and is dependent on the support or resin used. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium is dependent on the type of support or resin used in the chromatography and that operating conditions are identified as the screening conditions.

Regarding Claim 111, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be an ion exchange resin with operating conditions that include pH levels and ionic strengths, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that operating conditions were identified as the screening conditions.

Regarding Claim 114, 117 and 120, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be a hydrophobic interaction chromatography resin with operating conditions that include pH levels, ionic strengths, salt concentrations, phosphate concentrations, and glycine concentrations and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography which can include immobilized metal affinity chromatography resin with operating conditions that include the use of HEPES and calcium concentrations as well as counterligand levels and that operating conditions could also be identified as the screening conditions.

Claims 2-86, 88-89, 91-92, 94-95, 97-98, 100-101, 103-104, 106-107, 109-110, 112-113, 115-116, 118-119 and 121-122 lack an inventive step as being obvious over Shadle in view of US 4,029,583 A to Chang et al (hereinafter 'Chang').

Regarding Claims 2 and 88, Shadle discloses (col 3, ln 43-54; col 13, ln 24-50) a method of recovering purified protein or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art to combine the teachings of Shadle and Chang to develop a method of recovering purified protein from a load fluid including one or more impurities comprising the steps of passing the load fluid through a medium at operating conditions defined by a partition coefficient of at least 0.1 and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 06/08919

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
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Box V 2. Citations and explanations

Regarding Claims 3 and 89, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50) a method of recovering purified protein or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind at a load ratio ranging from 9-16g/liter and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art to combine the teachings of Shadle and Chang to develop a method of recovering purified protein from a load fluid including one or more impurities comprising the steps of passing the load fluid through a medium at operating conditions which cause the medium to bind at any load ratio dependent on the type of resin used, and defined by a partition coefficient of at least 0.1 and finally recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash.

Regarding Claims 4-10, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method wherein the operating conditions comprise of pH levels, ionic strengths, salt concentrations, glutamine, phosphate, arginine, glycine and counter ligand concentrations (inactive virus from an antibody solution after antibody purification). It would have been obvious to one skilled in the art that the operating conditions are screening conditions for optimum purification and that the operating condition could also include imidazole concentrations, calcium, excipient and HEPES concentrations, depending on the product being purified or isolated, through general knowledge in the art and through routine expermination and design choice, in light of Shadle and Chang.

Regarding Claims 11-14, Shadle discloses (col 7, ln 52-63; col 11, ln 63-68 to col 12, ln 1; col 2, ln 33-36; col 12, ln 60-68 to col 13, ln 1-5) a method wherein the screening step includes column binding studies under gradient or isocratic elution. It would have been obvious to skilled in the art that the binding studies could be batch studies or column binding studies, through general knowledge in the art in light of Shadle and Chang.

Regarding Claims 15-21, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 19, ln 30-31; col 20, Table 2) the operating conditions can cause the medium to bind at least 5 mg of protein product per ml of medium to 477 grams of protein product in up to 416 liters of medium.

Regarding Claims 22-26, Chang discloses (col 1, ln 13-32; col 10, ln 24-40) the passing of a load fluid through a medium defined by partition coefficients that can range in smaller or larger value depending on the solutes used. It would have been obvious to one skilled in the art that the partition coefficient would have been dependent on the polarity of the solutes/solvents used and that it can range from 0.2 to over 20, based on general knowledge in the art in light of Shadle and Chang.

Regarding Claim 27-28, claim 1 is obvious over Shadle and claim 23 is obvious over Shadle and Chang as described above. Chang further discloses (col 1, ln 46-48) the product of can be protein selected form hormones, lipoproteins and nucleic acids. Chang does not teach that the product can be an antibody. Shadle discloses (col 24, ln 66-68) that the product can be an antibody.

Regarding Claims 29-34, claim 1 is obvouos over Shadle as described above. Shadle also discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8) that the medium can be an ion exchange medium, an anion exchange resin or a cation exchange resin or a hydrophobic interaction chromatography resin. It would have been obvious to one skilled in the art the medium can also be a hydroxyapatite resin or an immobilized metal affinity chromatography resin.

Regarding Claims 35 and 36, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 10, ln 10-14; col 10, ln 41-44; col 12, ln 8-10; col 26, ln 22-24) that one or more impurities can be host cell proteins, host DNA, IgG aggregates, Protein A, and Viruses.

Regarding Claims 37-47, Shadle discloses (col 18, Table 7; col 20, Table 9) that the impurities comprised of Protein A had a cumulative concentration of not more than 11ng or 138ng/mg product, depending on the operating conditions used in the chromatography. It would have been obvious to one skilled in the art that, by modifying the operating conditions through routine experimentation, one could obtain not more than 100 to 500 ng of host cell impurity per mg of product or not more than 10 ng, 50 ng or 100 ng of protein A per mg of product or not more than 1 ng of nucleic acid per mg of product or product variants that are not more than 0.5% to 10% of the purified product.

Regarding Claims 48-56, Shadle discloses (col 18, Table 7; col 20, Table 9) that the impurities comprised of Protein A had a cumulative concentration of not more than 11 ng or 138 ng/mg product, depending on the operating conditions used in the chromatography. Shadle further discloses (col 9, ln 60-65) an antibody purification that is virally inactive and > 97% pure. It would have been obvious to one skilled in the art that a >97% pure product would have a greater than 1 or 2 log removal value for viruses, host cell proteins and Protein A, based on general knowledge in the art at the time the invention was made.

Regarding Claims 57, 59-61, Shadle discloses (col 10, ln 61-68 to col 11, ln 1-35) that the product containing fluid is eluted from a Protein A column using an elution buffer of low ionic strength, the pH and conductivity of the product containing fluid is adjusted using an equilibration buffer which results in the load fluid being passed through an ion exchange medium. It would have been obvious to one skilled in the art that the wash with the Equilibration buffer or neutralization buffer could result in no more than 20 mM, 40 mM, 60 mM or 80 mM of the ionic strength of the product containing fluid, based on general knowledge in the art at the time the invention was made.

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WRITTEN OPINION OF THE
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Supplemental Box

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Regarding Claims 58 and 62-63, Shadle discloses (col 2, ln 1-8) that the load fluid can pass through an ion exchange medium that can be an anion exchange resin or a cation exchange resin. It would have been obvious that the use of the cation exchange resin would not need diafiltration and that the pKa of the anionic charged groups would be 2 to 5 and the pKa for the cationic charged groups would be 6.5-10, based on general knowledge in the art at the time the invention was made.

Regarding Claim 64-66, Shadle discloses (col 10 , ln 67-68 to col 11, ln 1-3) that the elution buffer is a PBS buffer (phosphate buffered saline) with 0.1M glycine. It would have been obvious to one skilled in the art that the elution buffer may be comprised of zwitterions at pH of 4 to 9 and that the zwitterions could include glycine, a substituted glycine or any of the zwitterions in the claimed invention, through general knowledge in the art at the time the invention was made.

Regarding Claims 67-70, Shadle discloses (col 2, ln 1-8) a method of recovering purified protein from a load fluid comprising the steps of passing the load fluid through an ion exchange medium that can be an anion exchange resin or a cation exchange resin. It would have been obvious to one skilled in the art that the ionic strength of the load fluid would be no more than 10 mM to 50 mM, based on general knowledge in the art at the time the invention was made.

Regarding Claims 71-73, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 10, ln 10-14; col 10, ln 41-44; col 12, ln 8-10; col 26, ln 22-24) that one or more impurities of the purified product can be host cell proteins, host DNA, IgG aggregates, Protein A, and Viruses. Shadle further discloses (col 9, ln 60-65) that the product is >97% pure.

Regarding Claims 74-81, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 14, Table 2; col 15, Table 3) that the passing of the load fluid through a medium at operating conditions causes the medium to bind at a load ratio ranging from 9.1 grams of product/1 liter of medium to 16 grams of product/1L medium and is dependent on the support or resin used. It would have been obvious to one skilled in the art that the product mass bound to the medium, would have been dependent on the medium and could be at least 10%-30% of the total product mass or at least 10mg to 1000 mg of product per ml of medium, based on general knowledge in the art at the tme the invention was made, as well as through routine experimentation.

Regarding Claims 82 to 86, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 18, ln 55; Table 7) that the concentration of the product in the load fluid is 0.94 grams per liter. It would have been obvious to one skilled in the art that the load fluid could be made up of 5 mg to 100 mg of product per ml of load fluid through general knowledge in the art at the time the invention was made, as well as through routine experimentation.

Regarding Claims 91, 94, 97, 100, 103, 106 and 109, Shadle discloses (col 3, ln 43-54; col 13, ln 24-50; col 24, ln 66-68) a method of recovering purified product, protein or antibody from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art to combine the teachings of Shadle and Chang to develop a method of recovering purified protein from a load fluid including one or more impurities comprising the steps of passing the load fluid through a medium at operating conditions defined by a partition coefficient of at least 0.1 and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash and that operating conditions are identified as the screening conditions.

Regarding Claims 92, 95, 98, 101, 104, 107 and 110, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68) a method of recovering purified product, protein or antibody from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle further discloses (col 14, Table 2; col 15, Table 3) that the passing of the load fluid through a medium at operating conditions causes the medium to bind at a load ratio ranging from 9.1 grams of product/1 liter of medium to 16 grams of product/1L medium and is dependent on the support or resin used. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that the partition coefficient is dependent on the polarity of the solvents can be 0.3 to 20 and that operating conditions would be identified as the screening conditions, based on general knowledge in the art, as well as through routine experimentation.

Regarding Claim 112, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be an ion exchange resin with operating conditions that include pH levels and ionic strengths, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that operating conditions would have been identified as the screening conditions, based general knowledge in the art, as well as through routine experimentation.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 06/08919

Supplemental Box

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Regarding Claim 113, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be an ion exchange resin with operating conditions that include pH levels and ionic strengths, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that the partition coefficient would be dependent on the polarity of the solvents can be 0.3 to 20 and that operating conditions are identified as the screening conditions, based on general knowledge in the art, as well as through routine experimentation.

Regarding Claim 115, 118 and 121 Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be a hydrophobic interaction chromatography resin with operating conditions that include pH levels, ionic strengths, salt concentrations, phosphate concentrations, and glycine concentrations, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used which can include immobilized metal affinity chromatography resin with operating conditions that include the use of HEPES and calcium concentrations as well as counterligand levels and could also be identified as the screening conditions, based on general knowledge in the art, as well as through routine experimentation.

Regarding Claim 116, 119 and 122, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be a hydrophobic interaction chromatography resin with operating conditions that include pH levels, ionic strengths, salt concentrations, phosphate concentrations, and glycine concentrations and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography which could include immobilized metal affinity chromatography resin with operating conditions that include the use of HEPES and calcium concentrations as well as counterligand levels and screening conditions and that the partition coefficient would be dependent on the polarity of the solvents can be 0.3 to 20, based on general knowledge in the art, as well as through routine experimentation.

Claims 1-122 have industrial applicability as defined by PCT Article 33(4), because the subject matter can be made or used in industry

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;
(ii) the claim is cancelled;
(iii) the claim is new;
(iv) the claim replaces one or more claims as filed;
(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers. claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

If a demand for international preliminary examination is made, the written opinion of the International Searching Authority will, except in certain cases where the International Preliminary Examining Authority did not act as International Searching Authority and where it has notified the International Bureau under Rule 66.1*bis*(b), be considered to be a written opinion of the International Preliminary Examining Authority. If a demand is made, the applicant may submit to the International Preliminary Examining Authority a reply to the written opinion 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 (Rule 43*bis*.1(c)).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see the *PCT Applicant's Guide*, Volume II.

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PATENT COOPERATION TREATY

PCT/US2006/008919

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:

PIERONI, Joseph, P.
Fitzpatrick, Cella, Harper & Scinto
30 Rockefeller Plaza
New York, NY 10112-3801
ETATS-UNIS D'AMERIQUE

Date of mailing *(day/month/year)*	
04 October 2007 (04.10.2007)	
Applicant's or agent's file reference	IMPORTANT NOTICE
01997.073400	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2006/008919	10 March 2006 (10.03.2006)	11 March 2005 (11.03.2005)

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
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 01997.073400	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2006/008919	International filing date *(day/month/year)* 10 March 2006 (10.03.2006)	Priority date *(day/month/year)* 11 March 2005 (11.03.2005)
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 44*bis*.3(c) and 93*bis*.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 44*bis* .2).

	Date of issuance of this report 25 September 2007 (25.09.2007)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Simin Baharlou e-mail: pt09.pct@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: Belinda Lew
Wilmer Cutler Pickering Hale and Dorr LLP
The Willard Office Building
1455 Pennsylvania Avenue, NW
Washington, DC 20004

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	10 SEP 2007
Applicant's or agent's file reference 0036119.00179WO1	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 06/08919	10 March 2006 (10.03.2006)	11 March 2005 (11.03.2005)

International Patent Classification (IPC) or both national classification and IPC
IPC(8) - C07K 1/00, 14/00, 16/00 (2007.01)
USPC - 530/355

Applicant Wyeth

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

- [X] 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
- [X] 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
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

FILE NO. 01997.07340.PC
ATTORNEY MAG
DUE DATE 12/10/07
DOCKETED VMG 10/12/07

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 66.1*bis*(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	Date of completion of this opinion	Authorized officer:
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	17 April 2007 (17.04.2007)	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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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:

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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	1-122	YES
	Claims	none	NO
Inventive step (IS)	Claims	none	YES
	Claims	1-122	NO
Industrial applicability (IA)	Claims	1-122	YES
	Claims	none	NO

2. Citations and explanations:

Claims 1, 87, 90, 93, 96, 99, 102, 105, 108, 111, 114, 117 and 120 lack an inventive step under PCT Article 33(3) as being obvious over US 5,429,746 A to Shadle et al (hereinafter 'Shadle').

Regarding Claims 1 and 87, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50) a method of recovering purified protein or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind at a load ratio ranging dependent on the support or resin used, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography.

Regarding Claims 90, 93, 96, 99, 102, 105, and 108, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle further discloses (col 14, Table 2; col 15, Table 3) that the passing of the load fluid through a medium at operating conditions causes the medium to bind at a load ratio ranging from 9.1 grams of product/ 1 liter of medium to 16 grams of product/1L medium and is dependent on the support or resin used. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium is dependent on the type of support or resin used in the chromatography and that operating conditions are identified as the screening conditions.

Regarding Claim 111, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be an ion exchange resin with operating conditions that include pH levels and ionic strengths, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that operating conditions were identified as the screening conditions.

Regarding Claim 114, 117 and 120, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be a hydrophobic interaction chromatography resin with operating conditions that include pH levels, ionic strengths, salt concentrations, phosphate concentrations, and glycine concentrations and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography which can include immobilized metal affinity chromatography resin with operating conditions that include the use of HEPES and calcium concentrations as well as counterligand levels and that operating conditions could also be identified as the screening conditions.

Claims 2-86, 88-89, 91-92, 94-95, 97-98, 100-101, 103-104, 106-107, 109-110, 112-113, 115-116, 118-119 and 121-122 lack an inventive step as being obvious over Shadle in view of US 4,029,583 A to Chang et al (hereinafter 'Chang').

Regarding Claims 2 and 88, Shadle discloses (col 3, ln 43-54; col 13, ln 24-50) a method of recovering purified protein or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art to combine the teachings of Shadle and Chang to develop a method of recovering purified protein from a load fluid including one or more impurities comprising the steps of passing the load fluid through a medium at operating conditions defined by a partition coefficient of at least 0.1 and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash.

----------continued in Supplemental Box----------

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US 06/08919

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
Box V 2. Citations and explanations

Regarding Claims 3 and 89, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50) a method of recovering purified protein or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind at a load ratio ranging from 9-16g/liter and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art to combine the teachings of Shadle and Chang to develop a method of recovering purified protein from a load fluid including one or more impurities comprising the steps of passing the load fluid through a medium at operating conditions which cause the medium to bind at any load ratio dependent on the type of resin used, and defined by a partition coefficient of at least 0.1 and finally recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash.

Regarding Claims 4-10, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method wherein the operating conditions comprise of pH levels, ionic strengths, salt concentrations, glutamine, phosphate, arginine, glycine and counter ligand concentrations (inactive virus from an antibody solution after antibody purification). It would have been obvious to one skilled in the art that the operating conditions are screening conditions for optimum purification and that the operating condition could also include imidazole concentrations, calcium, excipient and HEPES concentrations, depending on the product being purified or isolated, through general knowledge in the art and through routine expermination and design choice, in light of Shadle and Chang.

Regarding Claims 11-14, Shadle discloses (col 7, ln 52-63; col 11, ln 63-68 to col 12, ln 1; col 2, ln 33-36; col 12, ln 60-68 to col 13, ln 1-5) a method wherein the screening step includes column binding studies under gradient or isocratic elution. It would have been obvious to skilled in the art that the binding studies could be batch studies or column binding studies, through general knowledge in the art in light of Shadle and Chang.

Regarding Claims 15-21, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 19, ln 30-31; col 20, Table 2) the operating conditions can cause the medium to bind at least 5 mg of protein product per ml of medium to 477 grams of protein product in up to 416 liters of medium.

Regarding Claims 22-26, Chang discloses (col 1, ln 13-32; col 10, ln 24-40) the passing of a load fluid through a medium defined by partition coefficients that can range in smaller or larger value depending on the solutes used. It would have been obvious to one skilled in the art that the partition coefficient would have been dependent on the polarity of the solutes/solvents used and that it can range from 0.2 to over 20, based on general knowledge in the art in light of Shadle and Chang.

Regarding Claim 27-28, claim 1 is obvious over Shadle and claim 23 is obvious over Shadle and Chang as described above. Chang further discloses (col 1, ln 46-48) the product of can be protein selected form hormones, lipoproteins and nucleic acids. Chang does not teach that the product can be an antibody. Shadle discloses (col 24, ln 66-68) that the product can be an antibody.

Regarding Claims 29-34, claim 1 is obvouos over Shadle as described above. Shadle also discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8) that the medium can be an ion exchange medium, an anion exchange resin or a cation exchange resin or a hydrophobic interaction chromatography resin. It would have been obvious to one skilled in the art the medium can also be a hydroxyapatite resin or an immobilized metal affinity chromatography resin.

Regarding Claims 35 and 36, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 10, ln 10-14; col 10, ln 41-44; col 12, ln 8-10; col 26, ln 22-24) that one or more impurities can be host cell proteins, host DNA, IgG aggregates, Protein A, and Viruses.

Regarding Claims 37-47, Shadle discloses (col 18, Table 7; col 20, Table 9) that the impurities comprised of Protein A had a cumulative concentration of not more than 11ng or 138ng/mg product, depending on the operating conditions used in the chromatography. It would have been obvious to one skilled in the art that, by modifying the operating conditions through routine experimentation, one could obtain not more than 100 to 500 ng of host cell impurity per mg of product or not more than 10 ng, 50 ng or 100 ng of protein A per mg of product or not more than 1 ng of nucleic acid per mg of product or product variants that are not more than 0.5% to 10% of the purified product.

Regarding Claims 48-56, Shadle discloses (col 18, Table 7; col 20, Table 9) that the impurities comprised of Protein A had a cumulative concentration of not more than 11 ng or 138 ng/mg product, depending on the operating conditions used in the chromatography. Shadle further discloses (col 9, ln 60-65) an antibody purification that is virally inactive and > 97% pure. It would have been obvious to one skilled in the art that a >97% pure product would have a greater than 1 or 2 log removal value for viruses, host cell proteins and Protein A, based on general knowledge in the art at the time the invention was made.

Regarding Claims 57, 59-61, Shadle discloses (col 10, ln 61-68 to col 11, ln 1-35) that the product containing fluid is eluted from a Protein A column using an elution buffer of low ionic strength, the pH and conductivity of the product containing fluid is adjusted using an equilibration buffer which results in the load fluid being passed through an ion exchange medium. It would have been obvious to one skilled in the art that the wash with the Equilibration buffer or neutralization buffer could result in no more than 20 mM, 40 mM, 60 mM or 80 mM of the ionic strength of the product containing fluid, based on general knowledge in the art at the time the invention was made.

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

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Supplemental Box

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Prior Supplemental Box

Regarding Claims 58 and 62-63, Shadle discloses (col 2, ln 1-8) that the load fluid can pass through an ion exchange medium that can be an anion exchange resin or a cation exchange resin. It would have been obvious that the use of the cation exchange resin would not need diafiltration and that the pKa of the anionic charged groups would be 2 to 5 and the pKa for the cationic charged groups would be 6.5-10, based on general knowledge in the art at the time the invention was made.

Regarding Claim 64-66, Shadle discloses (col 10 , ln 67-68 to col 11, ln 1-3) that the elution buffer is a PBS buffer (phosphate buffered saline) with 0.1M glycine. It would have been obvious to one skilled in the art that the elution buffer may be comprised of zwitterions at pH of 4 to 9 and that the zwitterions could include glycine, a substituted glycine or any of the zwitterions in the claimed invention, through general knowledge in the art at the time the invention was made.

Regarding Claims 67-70, Shadle discloses (col 2, ln 1-8) a method of recovering purified protein from a load fluid comprising the steps of passing the load fluid through an ion exchange medium that can be an anion exchange resin or a cation exchange resin. It would have been obvious to one skilled in the art that the ionic strength of the load fluid would be no more than 10 mM to 50 mM, based on general knowledge in the art at the time the invention was made.

Regarding Claims 71-73, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 10, ln 10-14; col 10, ln 41-44; col 12, ln 8-10; col 26, ln 22-24) that one or more impurities of the purified product can be host cell proteins, host DNA, IgG aggregates, Protein A, and Viruses. Shadle further discloses (col 9, ln 60-65) that the product is >97% pure.

Regarding Claims 74-81, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 14, Table 2; col 15, Table 3) that the passing of the load fluid through a medium at operating conditions causes the medium to bind at a load ratio ranging from 9.1 grams of product/1 liter of medium to 16 grams of product/1L medium and is dependent on the support or resin used. It would have been obvious to one skilled in the art that the product mass bound to the medium, would have been dependent on the medium and could be at least 10%-30% of the total product mass or at least 10mg to 1000 mg of product per ml of medium, based on general knowledge in the art at the tme the invention was made, as well as through routine experimentation.

Regarding Claims 82 to 86, claim 1 is obvious over Shadle as described above. Shadle also discloses (col 18, ln 55; Table 7) that the concentration of the product in the load fluid is 0.94 grams per liter. It would have been obvious to one skilled in the art that the load fluid could be made up of 5 mg to 100 mg of product per ml of load fluid through general knowledge in the art at the time the invention was made, as well as through routine experimentation.

Regarding Claims 91, 94, 97, 100, 103, 106 and 109, Shadle discloses (col 3, ln 43-54; col 13, ln 24-50; col 24, ln 66-68) a method of recovering purified product, protein or antibody from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art to combine the teachings of Shadle and Chang to develop a method of recovering purified protein from a load fluid including one or more impurities comprising the steps of passing the load fluid through a medium at operating conditions defined by a partition coefficient of at least 0.1 and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash and that operating conditions are identified as the screening conditions.

Regarding Claims 92, 95, 98, 101, 104, 107 and 110, Shadle discloses (col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68) a method of recovering purified product, protein or antibody from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle further discloses (col 14, Table 2; col 15, Table 3) that the passing of the load fluid through a medium at operating conditions causes the medium to bind at a load ratio ranging from 9.1 grams of product/1 liter of medium to 16 grams of product/1L medium and is dependent on the support or resin used. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that the partition coefficient is dependent on the polarity of the solvents can be 0.3 to 20 and that operating conditions would be identified as the screening conditions, based on general knowledge in the art, as well as through routine experimentation.

Regarding Claim 112, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be an ion exchange resin with operating conditions that include pH levels and ionic strengths, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that operating conditions would have been identified as the screening conditions, based general knowledge in the art, as well as through routine experimentation.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:
Prior Supplemental Box

Regarding Claim 113, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be an ion exchange resin with operating conditions that include pH levels and ionic strengths, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography and that the partition coefficient would be dependent on the polarity of the solvents can be 0.3 to 20 and that operating conditions are identified as the screening conditions, based on general knowledge in the art, as well as through routine experimentation.

Regarding Claim 115, 118 and 121 Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be a hydrophobic interaction chromatography resin with operating conditions that include pH levels, ionic strengths, salt concentrations, phosphate concentrations, and glycine concentrations, and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used which can include immobilized metal affinity chromatography resin with operating conditions that include the use of HEPES and calcium concentrations as well as counterligand levels and could also be identified as the screening conditions, based on general knowledge in the art, as well as through routine experimentation.

Regarding Claim 116, 119 and 122, Shadle discloses (col 1, ln 6-7; col 1,ln 65-68; col 2, ln 1-8; col 3, ln 43-54; col 14, ln 27, Table 2; col 13, ln 24-50; col 24, ln 66-68; col 7, ln 5-10; col 7, ln 43-45; col 12, ln 35-45, Table 2; col 10, ln 67-68 to col 11, ln 1; col 9, ln 26; col 11, ln 39-40; col 21, ln 63; col 25, ln 22-25; col 26, ln 40-45) a method of recovering purified protein or antibody or product from a load fluid including one or more impurities, comprising the steps of: passing the load fluid through a medium at operating conditions which cause the medium to bind on the support or resin which can be a hydrophobic interaction chromatography resin with operating conditions that include pH levels, ionic strengths, salt concentrations, phosphate concentrations, and glycine concentrations and recovering the purified product in the column effluent during the load cycle and any essentially isocratic wash. Shadle does not disclose the use of partition coefficients as part of the operating conditions. Chang further discloses (col 1, ln 13-32; col 10, ln 24-35) the passing of a load fluid through a medium defined by partition coefficients. It would have been obvious to one skilled in the art that the load ratio or amount of product per ml of medium would have been dependent on the type of support or resin used in the chromatography which could include immobilized metal affinity chromatography resin with operating conditions that include the use of HEPES and calcium concentrations as well as counterligand levels and screening conditions and that the partition coefficient would be dependent on the polarity of the solvents can be 0.3 to 20, based on general knowledge in the art, as well as through routine experimentation.

Claims 1-122 have industrial applicability as defined by PCT Article 33(4), because the subject matter can be made or used in industry

REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Folio 331

2020
Bogotá D.C.,

Doctor(a)
CORREA ORDOÑEZ ALVARO
Apoderado(a) y/o Representante de
WYETH

REFERENCIA	Radicación No.	07 92447
	Solicitud internacional	PCT/US2006/008919
	Fecha inicio fase nacional	11/10/2007
	Trámite	11
	Evento	378
	Actuación	416
	Oficio No.	5614
	Folios	1

Teniendo en cuenta que la solicitud de privilegio de patente que se tramita bajo el expediente indicado en la referencia, reúne los requisitos de forma establecidos en la Decisión 486 de la Comisión de la Comunidad Andina, el Tratado de Cooperación en Materia de Patentes (PCT), el Reglamento y la Circular Única de la Superintendencia de Industria y Comercio, se envía el extracto de la solicitud a la Oficina de Comunicaciones para efecto de su publicación en la Gaceta de Propiedad Industrial.

Cúmplase
Dado en Bogotá DC, 10 MAR. 2008

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

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