Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 09-002495- -00004-0000
Fecha: 2010-10-13 15:16:54 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 400 OPOSIOBSERVTER Folios: 58

FORMULARIO ÚNICO DE OPOSICIÓN

① OPOSICIÓN A :

- [x] Patente de Invención.
- [ ] Patente de Modelo de Utilidad.
- [ ] Diseño Industrial.
- [ ] Esquema de Trazado para Circuitos Integrados.
- [ ] Marcas de Productos o Servicios.
- [ ] Marca Colectiva.
- [ ] Marca de Certificación.
- [ ] Lema Comercial.

② SOLICITUD PUBLICADA

Numero del expediente: 09 002.495
Solicitante: WYETH
Apoderado: ÁLVARO CORREA ORDÓÑEZ
Título de la nueva creación o denominación del signo: COMPOSICIÓN LIQUIDAS DE FENILEFRINA DE ESTABILIDAD MEJORADA
Gaceta: 618

③ OPOSICIÓN PRESENTADA POR:

SOLICITANTE

Nombre: PROCAPS S.A.
Dirección: CALLE 80 No. 78b-201
Nacionalidad o Domicilio: COLOMBIA
Lugar de Constitución: BARRANQUILLA
Teléfono: 371 99 00 Fax: 373 08 18
E-mail:

IDENTIFICACIÓN
C.C. [ ] NIT [X]
C.E. [ ] Otro [ ]
Cual
Número 890.106.527-5

REPRESENTANTE O APODERADO

Nombre: ELIANA ISAURA MORENO BOHORQUEZ
Dirección: CARRERA 13 No. 119-95
Teléfono: (571)213 12 13 Fax: (571)612 19 79
E-mail: negocios@optimum-co.com

IDENTIFICACIÓN
C.C. [X] NIT [ ]
C.E. [ ] Otro [ ]
Cual
Número 51'975.664 TP 83823

④ FUNDAMENTOS DE LA OPOSICIÓN:

Art.14, 16, 18, 20 y 30 de la Decisión 486 de la CAN
Causal: No cumple con los requisitos de patentabilidad.
Signo opositor:
Justificación:
La presente solicitud no cumple con los requisitos de patentabilidad dado que lo revelado, ya se encontraba en el estado de la técnica o es posible derivarlo de la misma tal y como se demostrará en el capítulo "Fundamento de Hechos".

⑤ **Comprobante de pago No.** _____ **Fecha** _____

⑥ **ANEXOS**

- [x] Comprobante de pago de la tasa.
- [x] Poderes, si fuere el caso.
- [x] Pruebas de los fundamentos de la oposición.
- [ ] Documentos que acrediten el legítimo interés, si fuere el caso.
- [x] Documento que acredita la existencia y representación legal de las partes, cuando sean personas jurídicas.

⑦

NOMBRE: ELIANA ISAURA MORENO BOHORQUEZ

FIRMA:

C.C. 51'975.664 **TP.** 83823

Instrucciones para el diligenciamiento del presente formulario, ver reverso de esta página.

Optimum

Derecho de la Competencia, Propiedad Industrial y Comercio Exterior

Señora Jefe,

DIVISIÓN DE NUEVAS CREACIONES

Superintendencia de Industria y Comercio

E. S. D.

Referencia	: Expediente N° 09 002.495
Asunto	: Oposición a la solicitud de patente de Invención titulada *"COMPOSICIONES LÍQUIDAS DE FENILEFRINA DE ESTABILIDAD MEJORADA"*
Solicitante	: WYETH.
Opositora	: PROCAPS S.A.

Publicada en la Gaceta de la Propiedad Industrial

N° 618 del 19 de julio de 2010

Yo, *ELIANA ISAURA MORENO BOHORQUEZ*, abogada en ejercicio, identificada como aparece al pie de su firma, con tarjeta profesional No. 83823 del Consejo Superior de la Judicatura, en mi condición de apoderada de la sociedad *PROCAPS S.A.* conformada bajo las leyes de la República de Colombia y domiciliada en la ciudad de Barranquilla, Colombia, atentamente manifiesto que estando dentro del término de ley y por orden expresa de mi representada, presento oposición a la concesión del registro de la Patente de Invención titulada *"COMPOSICIONES LÍQUIDAS DE FENILEFRINA DE ESTABILIDAD MEJORADA"*, cuyo titular es WYETH, y pido a Usted declarar fundada esta oposición y en consecuencia negar el registro de la patente solicitada.

1. INTERÉS PARA ACTUAR

Conforme a lo dispuesto en el artículo 42 de la Decisión 486 de 2000 de la CAN, estando dentro del término estipulado por la ley, manifiesto el legítimo interés de nuestra representada para oponerse al registro de la patente de la referencia, atendiendo a que la solicitud pretendida no cumple con los requisitos dispuestos en la ley como se analizará más adelante y de ser concedida afectaría directamente la comercialización de algunos productos de mi representada, que contienen, en particular **FENILEFRINA**. Por lo tanto, solicito respetuosamente a ese Despacho se sirva tener en cuenta la presente oposición dentro del trámite administrativo que se surte en esta Superintendencia.

2. FUNDAMENTOS DE HECHOS

2.1. La solicitud objeto de la presente fue presentada el 14 de enero de 2009, reivindicando prioridad bajo la solicitud US20060487120 del 2006-07-14; y fue publicada en Colombia, en la Gaceta de la Propiedad Industrial **N° 618 del 19 de julio de 2010**, cuya publicación internacional corresponde a la WO2008008364 del 2008-01-17.

2.2. La solicitud colombiana 09 002.495 objeto de la presente oposición, se refiere a una composición farmacéutica líquida oral que comprende: (a) fenilefrina o una sal farmacéuticamente aceptable de esta; y (b) polietilenglicol sustancialmente libre de aldehído, en donde el polietilenglicol sustancialmente libre de aldehído tiene menos de 20 ppm de contenido total de aldehído y mantiene dicho nivel de contenido de aldehído durante al menos seis meses; en donde el polietilenglicol

sustancialmente libre de aldehído tiene menos de 10 ppm de contenido total de aldehído y mantiene dicho nivel de contenido de aldehído durante al menos un año; comprende adicionalmente al menos un segundo agente activo seleccionado del grupo que consiste de agentes analgésicos, descongestionantes, expectorantes, anti-tusivos, antipiréticos, anti-inflamatorios, supresores de tos y antihistaminas; en donde el segundo agente activo se selecciona del grupo que consiste de drogas anti-inflamatorias no esteroides (NSAIDS), derivados de ácido propiónico, ibuprofeno, naproxeno, cetoprofen, flurbiprofen, zomepirac, sulindac fenoprofen, suprofen, fluprofen, fenbufen; derivados de ácido acético, tolmetin sódico, indometacin, derivados de ácido fenámico, meclofenamato de sodio de ácido mefenámico, derivados de ácido bifenil carboxílico, diflunisal, flufenisal, oxicamos, piroxicam, sudoxicam, isoxicam, clorfeniramina, bromfeniramina; dexclorfeniramina, dexbromfeniramina, triprolidina, clorciclizina, difenhidramina, doxilamina, tripelenamina, ciproheptatina, bromodifenhidramina, fenindamina, pirilamina, azatadina, acrivastina, astemizol, azelastina, cetirizina, ebastina, fexofenadina, ketotifen, carbinoxamina, desloratadina, loratadina, feniramina, tonzilamina, mizolastina, terfenadina, clofendianol, caramifen, dextrometorfan, difenhidramina, codeina, hidrocodona, pseudoefedrina, efedrina, fenilefrina, fenilpropenolamina, hidrato de terpin, guaifenesina, potasio, guaicolsulfonato de potaio, inhibidores 2 Cox, Celecoxib, Rofecoxib, Valdecoxib, aspirina, acetaminofén, fenacetin, sales de salicilatos y combinaciones de estos.

2.3. En primera instancia, se debe advertir que las reivindicaciones también se refieren a un método de tratamiento y no sólo a la composición farmacológica o a un método de fabricación mediante la cual se obtenga un producto tangible y según la legislación, decisión 486 de la Comunidad Andina de Naciones, Artículo 14.- "*Los Paises Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento (...)*", los usos no están contemplados como patentables; y, Artículo

20.- "*No serán patentables (...) d) los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales*". Solo serán patentables los productos o procedimientos. Por lo tanto a luz de la norma, dicha materia referente al uso y a un método de tratamiento no seria patentable.

2.4.Ahora bien, con base en el artículo 14 de la Decisión 486 de la CAN consagra lo siguiente: "*Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial*". Así las cosas, las invenciones objeto de patente deben ser nuevas y tener nivel inventivo. Bien, pues antes de la fecha de prioridad de esta solicitud se encuentran los siguientes documentos que afecta la patentabilidad de la presente solicitud:

- D1: WO03047502 publicada el 12 de junio de 2003.

2.5.Ahora bien, el documento D1, particularmente en la descripción revela una forma farmacéutica que sustancialmente enmascara el sabor de la composición farmacéutica líquida que contiene una cantidad farmacéuticamente eficaz de un medicamento de sabor desagradable disuelto o dispersado en una base de excipiente acuoso que comprende dicha base excipiente polivinilpirrolidona y/o copolividona, y polietilenglicol de alto peso molecular. Según se indica en el documento D1 se revela el enmascarado del sabor de la composición líquida que comprende al menos un medicamento de sabor desagradable, que comprende según la reivindicación 1 un excipiente polivinilpirrolidona y/o copolividona, y polietilenglicol de alto peso molecular y en la cláusula 19 define que la fenilefrina es uno de los medicamentos de sabor desagradable. Según D1, los edulcorantes

como el sorbitol (reivindicaciones 10 y 11) y agentes de viscosidad tales como glicerina, son parte de la misma (cláusula 10 y 13). Con base en ello y con el conocimiento medio de cualquier persona versada en la materia puede llegar de manera evidente a conformar una composición farmacéutica liquida oral que comprende: (a) fenilefrina o una sal farmacéuticamente aceptable de esta; y (b) polietilenglicol sustancialmente libre de aldehído. Así las cosas, como lo evidencia dicho documento D1, la presente solicitud no comprende altura o nivel inventivo pues lo revelado se deriva de manera evidente a partir del estado de la técnica.

2.6. Por lo tanto, este documento objeto de oposición a la luz del documento D1 carece evidentemente de ALTURA INVENTIVA.

2.7. En consecuencia y de acuerdo a lo descrito anteriormente, se deriva que la solicitud colombiana 09 002.495 no puede pretender un monopolio por patente toda vez que lo que pretende no cumple con dos de los tres requisitos necesarios para su protección.

2.8. Que por consiguiente, respecto a la solicitud pretendida se tiene que:

2.8.1. CARENCIA DE ALTURA INVENTIVA. Según la Decisión 486 de la Comunidad Andina de Naciones, Artículo 18.- *"Se considerará que una invención tiene nivel inventivo, si para una persona del oficio normalmente versada en la materia técnica correspondiente, esa invención no hubiese resultado obvia ni se hubiese derivado de manera evidente del estado de la técnica."*. A la fecha de prioridad, 14 de julio de 2004, a partir del documento D1 en combinación con el conocimiento medio de una persona versada en la materia, puede llegar de manera evidente a una composición farmacéutica líquida oral que comprende: (a) fenilefrina o una sal farmacéuticamente aceptable de esta; y (b) polietilenglicol sustancialmente libre de aldehído, sobre el cual busca protección en el capítulo reivindicatorio.

2.8.2. CARENCIA DE APLICACIÓN INDUSTRIAL La Decisión 486 de la CAN consagra en su artículo 14 lo siguiente: *"Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial"*. La presente solicitud carece de aplicación Industrial ya que como se demostró anteriormente, algunas cláusulas reclaman el método terapéutico y estos no son aplicables industrialmente porque primero no se obtiene un producto o proceso; y segundo no es reproducible o repetible a escala industrial. Por lo tanto, el objeto de la presente invención referido a los usos y métodos terapéuticos, no cumplen con el requisito de la aplicación industrial.

2.9. Dado lo anterior, es posible deducir que la solicitud y lo reivindicado no es objeto de patentabilidad pues es contrario a lo que dicta la Decisión 486 de la Comunidad Andina de Naciones, Artículo 14.- *"Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial."*. La solicitud pretendida no cumple con dos de los tres requisitos de patentabilidad.

2.10. Por todo lo anterior, atentamente solicito a usted que se sirva declarar fundada *"COMPOSICIONES LÍQUIDAS DE FENILEFRINA DE ESTABILIDAD MEJORADA"*, cuyo titular es WYETH, solicitud Colombiana que apareció publicada en la Gaceta de la Propiedad Industrial N° 618 **del 19 de julio de 2010**.

3. PRUEBAS

De conformidad con lo dispuesto por las normas vigentes, solicito a usted tener como prueba en este asunto los siguientes:

- D1: WO03047502 publicada el 12 de junio de 2003.

4. FUNDAMENTO DE DERECHO

Fundamento esta observación en las normas legales siguientes:

4.1. Numeral 1 del artículo 586 del Código de Comercio.

4.2. Artículo 42 de la Decisión 486 de la Comisión del Acuerdo de Cartagena.

4.3. En las demás normas concordantes.

5. ANEXOS

Para los efectos correspondientes anexo al presente escrito los siguientes documentos:

1. Poder para actuar en el presente.
2. Documento que acredita al representante legal de **PROCAPS S.A.**
3. Recibo de caja del respectivo pago de tasa.
4. Copias de los documentos:

- D1: WO03047502 publicada el 12 de junio de 2003.

Optimum

Derecho de la Competencia, Propiedad
Industrial y Comercio Exterior

6. NOTIFICACIONES

Para efectos de notificaciones que por disposición del artículo 50 del Decreto 01 de 1984 debe hacer su Despacho, informo que mi representada y la suscrita recibiremos notificaciones en la Secretaría de su Despacho o en mis oficinas situadas en la Carrera 13 Nº 119-95, Of. 104 de esta ciudad de Bogotá.

Señor Superintendente,

ELIANA ISAURA MORENO BOHORQUEZ
C.C. 51'975.664 de Bogotá
T.P.A. 83823 del C.S. de la J.

Carrera 13 Nº 119-95, Of. 104 Tel. (571) 2 13 12 13 - 6 20 50 21 - Fax. (571) 6 12 19 79
E-mail: negocios@optimum-co.com - www.optimum-co.com
Bogotá Colombia

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 10 - 86,171
FECHA : OCTUBRE 13 DE 2010

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
GYNOPHARM S.A.	CONSIGNACION	BANCO DE BOGOTA	062754387	355160934	01/10/2010	885,000.00

***** C O N C E P T O *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-04 PRESENTACION DE OBSERVACIONES	12 MARCAS Y LEMAS COMERCIALES	295,000.00
		TOTAL : $	295,000.00

SON: DOSCIENTOS NOVENTA Y CINCO MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

12

PROCAPS

PODER ESPECIAL

Yo, **WALTER TANAKA TATEKAWA,** mayor de edad y vecino de la ciudad de Barranquilla (Colombia), identificado como aparece al pie de mi firma, quien en el presente documento actúa en calidad de Representante Legal de la sociedad **PROCAPS S.A.** sociedad legalmente constituida y domiciliada en la ciudad de Barranquilla (Colombia), por el presente documento otorgo a la doctora **ELIANA ISAURA MORENO BOHORQUEZ,** abogada en ejercicio, identificada como aparece al pie de su firma, con tarjeta profesional No. 83823 **del C.S. de la J.,** poder especial, amplio y suficiente, para formular oposiciones u observaciones a la solicitud de patente No. 09 002.495, titulada **"COMPOSICIONES LÍQUIDAS DE FENILEFRINA DE ESTABILIDAD MEJORADA",** cuyo titular es **WYETH,** publicada en la gaceta No. 618 del 19 de julio de 2010.

Nuestro apoderado queda facultado, de manera expresa, para realizar todo tipo de actos necesarios para llevar a cabo el trámite de la oposición, incluyendo, sin limitación, preparar y presentar solicitudes, hacer declaraciones, pagar tasas, contribuciones e impuestos, recabar los títulos o certificados. Asimismo quedan autorizados para impugnar administrativamente todo lo que fuere resuelto en el expediente a que se hace expresa referencia en el presente poder, con todas las facultades generales y específicas que fuera requerido para ella.

De la misma manera, además de las facultades que le confiere la naturaleza del presente mandato, se encuentran facultados para recibir, desistir, transigir, sustituir, y reasumir el presente poder, incoar acciones, interponer recursos y demás facultades conferidas por la ley.

Dado y Firmado en Barranquilla (Colombia) a los 28 días del mes de Septiembre de 2010.

PROCAPS S.A.

C.C. N° 16'251.923
NIT: 890.106.527-5
Representante Legal

Acepto:

ELIANA ISAURA MORENO BOHORQUEZ
C.C. 51'975.664 de Bogotá
T.P.A. 83823 del C.S. de la J.

NOTARIA TERCERA DEL CIRCULO DE BARRANQUILLA

DILIGENCIA DE RECONOCIMIENTO

Ante el Notario Tercero de Barranquilla se presento: WALTER TANAKA TAKEKAWA

identificado con: CC 16.691.923 PALMIRA

Y declaro que el contenido del anterior Documento es cierto y suya la firma que lo refrenda.

Barranquilla: 01 OCT. 2010

NOTARIA TERCERA DEL CIRCULO DE BARRANQUILLA • REPUBLICA DE COLOMBIA • NOTARIA

Marina L. Rojas Zambrano
NOTARIO ENCARGADO

03-8028605 024802 PROCAPS S.A.
Barranquilla, 06 de Sep/bre de 2010 Hr:16:45:53

No. 14904762

********** Pag. 1
C A M A R A D E C O M E R C I O
D E B A R R A N Q U I L L A
08**********

CERTIFICADO DE EXISTENCIA Y REPRESENTACION LEGAL O DE INSCRIPCION DE DOCUMENTOS.
PROCAPS S.A.----------
NIT: 890.106.527-5.

EL SUSCRITO SECRETARIO DE LA CAMARA DE COMERCIO DE BARRANQUILLA, CON FUNDAMENTO EN LAS INSCRIPCIONES DEL REGISTRO MERCANTIL:

C E R T I F I C A

Que por Escritura Pública No. 1,190 del 22 de Julio de 1976, otorgada en la Notaria Tercera de Barranquilla, inscrito(as) en esta Cámara de Comercio, el 28 de Julio de 1976 bajo el No. 6,070 del libro respectivo, fue constituida la sociedad----------
limitada denominada "PRODUCTORA DE CAPSULAS DE GELATINAS LIMITADA PROCAPS LIMITADA".----------

C E R T I F I C A

Que por Escritura Pública No. 1,307 del 28 de Junio de 1979, otorgada en la Notaria Tercera de Barranquilla, inscrito(as) en esta Cámara de Comercio, el 23 de Julio de 1979 bajo el No. 10,039 del libro respectivo, la sociedad antes mencionada----------
se transformo en sociedad anonima bajo la denominacion social de "PRODUCTORA DE CAPSULAS DE GELATINA S.A." PROCAPS S.A.".----------

C E R T I F I C A

Que por Escritura Pública No. 3,810 del 31 de Dic/bre de 1980, otorgada en la Notaria Primera de Barranquilla, inscrito(as) en esta Cámara de Comercio, el 30 de Enero de 1981 bajo el No. 12,705 del libro respectivo, la sociedad antes mencionada----------
se transformo en sociedad de responsabilidad limitada bajo al razon social de "PRODUCTORA DE CAPSULAS DE GELATINA LIMITADA "PROCAPS LI - MITADA".----------

C E R T I F I C A

Que por Escritura Pública No. 3,755 del 10 de Nov/bre de 1983, otorgada en la Notaria Unica de Soledad, inscrito(as) en esta Cámara de Comercio, el 22 de Nov/bre de 1983 bajo el No. 17,922 del libro respectivo, la sociedad antes mencionada----------
se transformo en sociedad anonima bajo la denominacion social de "PRODUCTORA DE CAPSULAS DE GELATINA S.A. "PROCAPS S.A.".----------

C E R T I F I C A

Que por Escritura Pública No. 3,615 del 06 de Dic/bre de 1996, otorgada en la Notaria 2a. de Barranquilla, inscrito(as) en esta Cámara de Comercio, el 20 de Dic/bre de 1996 bajo el No. 67,218 del

********** C O N T I N U A **********

CERTIFICADO DE EXISTENCIA Y REPRESENTACION LEGAL O DE INSCRIPCION DE DOCUMENTOS.
PROCAPS S.A.
NIT: 890.106.527-5.

libro respectivo, la sociedad antes mencionada----------
cambio de razon social, por la denominacion LABORATORIOS PROCAPS S.A
. ----------

C E R T I F I C A

Que por Escritura Pública No. 3,775 del 18 de Dic/bre de 1996, otorgada en la Notaria 2a. de Barranquilla, inscrito(as) en esta Cámara de Comercio, el 23 de Enero de 1997 bajo el No. 67,704 del libro respectivo, la sociedad antes mencionada----------
cambio de razon social, por la denominacion PROCAPS S.A. ----------

C E R T I F I C A

Que dicha sociedad ha sido reformada por las siguientes escrituras y/o documentos privados:

Numero	aaaa/mm/dd	Notaria	No. Insc o Reg	aaaa/mm/dd
39	1979/01/18	Notaria 3a. de Barranquilla.	9,452	1979/01/24
992	1981/04/30	Notaria 1a. de Barranquilla.	13,112	1981/05/
1,464	1982/08/27	Notaria Unica de Soledad	15,533	1982/09/08
2,744	1983/08/18	Notaria Unica de Soledad	17,416	1983/08/26
3,826	1984/07/16	Notaria Unica de Soledad	19,554	1984/07/27
3,835	1985/08/26	Notaria Unica de Soledad	22,230	1985/09/04
2,260	1986/09/10	Notaria Unica de Soledad.	24,995	1986/09/15
1,849	1989/07/11	Notaria 2a. de Barranquilla.	33,909	1989/07/13
444	1990/02/21	Notaria 2a. de Barranquilla.	36,101	1990/03/16
3,090	1991/12/17	Notaria 2a. de Barranquilla.	43,993	1992/01/28
269	1993/02/01	Notaria 2a. de Barranquilla.	48,428	1993/02/16
2,342	1993/07/28	Notaria 2a. de Barranquilla.	50,582	1993/08/10
3,652	1993/11/09	Notaria 2a. de Barranquilla	51,798	1993/11/22
3,615	1996/12/06	Notaria 2a. de Barranquilla	67,218	1996/12/20
89	1997/01/16	Notaria 2a. de Barranquilla	67,704	1997/01/23
2,070	1997/07/17	Notaria 2a. de Barranquilla	70,627	1997/07/31
2,281	1997/08/04	Notaria 2a. de Barranquilla	70,813	1997/08/14
765	1999/04/22	Notaria 3a. de Barranquilla	80,628	1999/04/23
459	2001/02/21	Notaria 2a. de Barranquilla	91,502	2001/02/23
2,608	2001/10/05	Notaria 2a. de Barranquilla	95,771	2001/11/08
1,730	2004/07/29	Notaria 2. de Barranquilla	112,999	2004/08/26
416	2005/03/03	Notaria 2. de Barranquilla	116,364	2005/03/10
1,613	2005/07/28	Notaria 2. de Barranquilla	119,322	2005/08/18
710	2009/05/05	Notaria 3 a. de Barranquilla	150,130	2009/06/30
1,054	2009/06/25	Notaria 3 a. de Barranquilla	150,130	2009/06/30

C E R T I F I C A

Que de acuerdo con la(s) escritura(s) arriba citada(s), la sociedad se rige por las siguientes disposiciones:
DENOMINACION O RAZON SOCIAL:
PROCAPS S.A.----------
SIGLA: PROCAPS.
DOMICILIO PRINCIPAL: Barranquilla.
NIT No: 890.106.527-5.
MATRICULA MERCANTIL: 24,802.

********** C O N T I N U A **********

·03-06028605 024802 PROCAPS S.A.
Barranquilla, 06 de Sep/bre de 2010 Hr:16:45:53

No. 14904763

********** Pag. 2
C A M A R A D E C O M E R C I O
D E B A R R A N Q U I L L A
08**********

CERTIFICADO DE EXISTENCIA Y REPRESENTACION LEGAL O DE INSCRIPCION DE DOCUMENTOS.
PROCAPS S.A.----------
NIT: 890.106.527-5.

C E R T I F I C A

Direccion para notificaciones judiciales:
CL 80 No 78 B - 201.
De la ciudad de Barranquilla.

C E R T I F I C A

DURACION: El término de duración de la sociedad se fijó hasta el 18 de Agosto de 2073.

C E R T I F I C A

OBJETO SOCIAL: El objeto principal de la sociedad sera: a) La fabicacion, importacion y comercializacion de alimentos procesados y suplementos dietarios. b)La fabricacion de capsulas y otros productos similares a partir de materiales tales como gelatinas u otros de distinta naturaleza, que puedan ser utilizados como envases o recipientes de productos y sustancias quimicas, farmaceuticas, alimenticias y cosmeticas, para uso y consumo humano y veterinario. c) La investigacion, desarrollo y fabricacion de toda clase de productos y sustancias quimicas, farmaceuticas, alimenticias y cosmeticas para uso y consumo humano, animal y vegetal. d) La compra y venta de materias primas, insumos y productos intermedios necesarios para los procesos de fabricacion de sustancias quimicas, farmaceuticas, alimen ticias y cosmeticas, asi como la comercializacion interna y externa de los productos terminados. e) La compra, venta, importacion, exportacion y distribucion de toda clase de elementos instrumentales y equipos medicos, quirurgicos, odontologicos y hospitalarios para la salud humana y animal. f) La compra, venta, exportacion, fabricacion, importacion, distribucion de dulces, confites, galletas y todo tipo de golosinas o alimentos para el consumo humano. g) Actuar como representante o agente de personas naturales y juridicas, nacionales y extranjeras en la realizacion de operaciones o transacciones relacionadas con la industria farmaceutica y en especial con cualquiera de las actividades descritas en los literales a), b), c), d) y e) antes descritos. h) Prestar los servicios de asesorias y consultoria en las areas administrativas, de mercadeo, analisis clinico, asistencia tecnica, investigacion, costos y produccion, exportaciones, importaciones, ventas, relacionadas con iguales o similares actividades a las que constituyen el objeto de PROCAPS S.A., asi como los de publicidad y promocion de productos quimicos, alimenticios, cosmeticos y

********** C O N T I N U A **********

farmaceuticos para uso humano, animal o industrial. i) Adquirir, operar, administrar y explotar, a cualquier titulo, empresa o establecimientos dedicados a la investigacion, desarrollo, fabricacion o comercializacion de productos quimicos, farmaceuticos, alimenticios, hospitalarios o cosmeticos. En desarrollo de su objeto principal, la sociedad podra tomar interes social como accionista, socio o fundador de empresas que tengan igual o similar objeto, comprar, vender, importar y exportar maquinarias, insumos y repuestos requeridos para el desarrollo de sus actividades; tomar dinero en prestamo, financiar y garantizar las operaciones comerciales que celebre con terceros relativas a su objeto; celebrar y ejecutar todo tipo de actos y contratos necesarios para desarrollar sus operaciones; girar, aceptar, otorgar y protestar todo tipo de titulos valores e instrumentos negociables, comprar, vender y constituir gravamenes sobre bienes muebles e inmuebles, designar representantes apoderados en el pais y en el exterior y, en general, realizar cualquier acto o negocio que sea necesario o conveniente para el desarrollo de su objeto social y para la mejor proteccion de sus intereses corporativos y la de sus socios. La sociedad podra garantizar el cumplimiento de sus obligaciones adquiridas por terceros o por sus socios, para lo cual podra inclusive constituir gravamenes reales sobre sus bienes de cualquier naturaleza.----------

C E R T I F I C A

CAPITAL	Nro Acciones	Valor Acción
Autorizado		
$**********2,000,000,000	**********2,000,000	**********1,000
Suscrito		
$**********1,234,071,000	**********1,234,071	**********1,000
Pagado		
$**********1,234,071,000	**********1,234,071	**********1,000

C E R T I F I C A

ADMINISTRACION: La direccion y administracion de la sociedad corresponderá a la Asamblea General de Accionistas, a la Junta Directiva, al Presidente, al Vicepresidente y a un Gerente General. Corresponde a la Junta Directiva las siguientes funciones y atribuciones entre otras: Autorizar cualquier acto o contrato cuya cuantia sea superior al equivalente en pesos Colombianos a doscientos cincuenta mil dolares de los Estados Unidos de America (US$250.000), liquidados a la tasa de cambio representativa del mercado vigente el dia en que se surta la transacion. Cuando se trate de operaciones en virtud de las cuales la sociedad garantice obligaciones de terceros o de los socios, se requerira que la operacion sea aprobada con el voto de por lo menos 2/3 partes de los integrantes de la Junta Directiva.
La sociedad tendra un Presidente , quien ejercera la representacion legal de la sociedad y tendra las siguientes atribuciones entre otras: Ejecutar las decisiones de la Asamblea General de Accionistas y de la Junta Directiva. Ejercer la Representacion Legal de la sociedad en todos los actos y contratos que se

********** C O N T I N U A **********

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requieran para el desarrollo del objeto social, de conformidad con lo previsto en las leyes y en los presentes estatutos. Constituir apoderados judiciales y extrajudiciales, recibir notificaciones, absolver interrogatorios de parte, confesar obligaciones de la sociedad, transigir, disistir y allanar a la sociedad en cualquier asunto judicial. Aprobar y celebrar en nombre de la socieda todo acto o contrato cuya cuantia sea igual o inferior al equivalente en pesos colombianos a doscientos cincuenta mil dolares de los Estados Unidos de America (US$250.000), liquidados a la tasa de cambio representativa del mercado vigente el dia en que se surta la transacion o celebracion del acto. Las demas funciones que le correspondan como Representante Legal por disposicion de la ley, de estos estatutos o de la Junta Directiva. El Presidente tendra un suplente, designado por la Junta Directiva, quien reemplazara al Presidente en sus faltas temporales, absolutas o meramente accidentales, con entidades facultades y sin que sea necesario para ello acreditar la ausencia del principal. La sociedad tendra un Vicepresidente designado por la Junta Directiva, quien tambien ejercera la representacion legal de la sociedad, pudiendo ejercerla conjunta o separadamente con el Presidente. El vicepresidente tendra las siguentes facultades entre otras. Ejecutar dentro de su competencia las decisiones de la Asamblea General de Accionistas, de la Junta Directiva y del Presidente. Ejercer la representacion legal de la sociedad en todos los actos y contratos que se requieran para el desarrollo del objeto social, de conformidad con lo previsto en las leyes y en los presentes estatutos. Constituir apoderados judiciales y extrajudiciales, recibir notificaciones, absolver interrogatorios de parte, confesar obligaciones de la sociedad, transigir, desistir y allanar a la sociedad en cualquier asunto judicial. Aprobar y celebrar en nombre de la sociedad todo acto o contrato cuya cuantia sea igual o inferior al equivalente en pesos colombianos a ciento cincuenta mil dolares de los Estados Unidos de America (US$150.000), liquidados a la tasa de cambio representativa del mercado vigente el dia en que se surta la aprobacion o celebracion del acto, siempre que no se trate de enajenar bienes inmuebles o cualquier otro activo fijo de la sociedad, inclusive de naturaleza muebles, acciones, cuotas o partes de interes inversiones y todo tipo de derechos de la sociedad, o de constituir gravamenes sobre cualquiera de los anteriores, facultades que radican exclusiva y privativamente en cabeza del Presidente. Las demas funciones que le corresponda como Representante legal por disposicion de la ley, de estos estatutos o de la Junta Directiva. El Vicepresidente tendra (1) suplente, designado por la Junra Directiva, quien lo reemplazara conjunta o separadamente en sus faltas temporales, absolutas o meramente accidentales, con identicas facultades y sin que sea necesario para

ello acreditar la ausencia del principal. La sociedad tendra un (1) Gerente General, con su respectivo Suplente, designados por la Junta Directiva. El Suplente reemplazara al Gerente General, en sus faltas temporales, absolutas o meramente accidentales, quien junto con el gerente general, llevaran la representacion legal de la sociedad, con identicas facultades, pudiendolas ejercer conjunta o separadamente con el Presidente y Vicepresidente, con identicas facultades que el Gerente General y sin que sea necesario para ello acreditar la ausencia del titular. El Gerente General tendra las siguientes facultades entre otras: Ejercer la representacion legal de la sociedad, en todos los actos y contratos que se requieran para el desarrollo del objeto social, de conformidad con lo previsto en las leyes y en los presentes estatutos. Aprobar y celebrar en nombre de la sociedad todo acto o contrato cuya cuantia sea igual o inferior al equivalente en pesos Colombianos a Cincuenta Mil dolares de los Estados Unidos de America (US$50.000), liquidados a la tasa de cambio representativa del mercado vigente el dia en que se surta la aprobacion o celebracion del acto, siempre que no se trate de enajenar a cualquier titulo bienes inmuebles o cualquier otro activo fijo de la sociedad, inclusive de naturaleza mueble, acciones, cuotas o partes de interes, inversiones y todo tipo de derechos de la sociedad o de constituir gravamenes sobre cualquiera de las anteriores facultades que radican exclusiva y privativamente en cabeza del Presidente. ----------

C E R T I F I C A

Que según Acta No. 116 del 27 de Junio de 1997 correspondiente a la Asamblea de Accionistas en Barranquilla, de la sociedad:
PROCAPS S.A.----------
cuya parte pertinente se inscribió en esta Cámara de Comercio, el 15 de Agosto de 1997 bajo el No. 70,838 del libro respectivo, y según Acta No. 127 del 22 de Marzo de 2000 correspondiente a la Asamblea de Accionistas en Barranquilla, de la sociedad:
PROCAPS S.A.----------
cuya parte pertinente se inscribió en esta Cámara de Comercio, el 29 de Mayo de 2000 bajo el No. 87,250 del libro respectivo, fueron hechos los siguientes nombramientos:

CLASE: JUNTA DIRECTIVA

Principales

1. Minski Gontovnik Ruben	CC.*******7,463,982
2. Minski Gontovnik Meyer	CC.*******7,461,324
3. Minski Gontovnik Jose	CC.*******8,671,834

Suplentes

1. Minski Zirberblum Elliot	CC.******72,219,541
2. Minski Deitel Daniel	.**********
3. Minski Sharon	PA.*990,212,082,805

C E R T I F I C A

********** C O N T I N U A **********

03 6028605 024802 PROCAPS S.A.
Barranquilla, 06 de Sep/bre de 2010 Hr:16:45:53

No. 14904765

CAMARA DE COMERCIO DE BARRANQUILLA

C A M A R A D E C O M E R C I O
D E B A R R A N Q U I L L A
08**********

CERTIFICADO DE EXISTENCIA Y REPRESENTACION LEGAL O DE INSCRIPCION DE DOCUMENTOS.
PROCAPS S.A.----------
NIT: 890.106.527-5.

Que según Acta No. 116 del 27 de Junio de 1997 correspondiente a la Asamblea de Accionistas en Barranquilla, de la sociedad: PROCAPS S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 15 de Agosto de 1997 bajo el No. 70,838 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre	Identificación
Presidente.	
Minski Gontovnik Ruben	CC.*******7,463,982
Suplente del Presidente	
Minski Minski Abraham	CC.*********802,575
Vicepresidente	
Minski Gontovnik Meyer	CC.*******7,461,324
Suplente del vicepresidente	
Minski Gontovnik Jose	CC.*******8,671,834

C E R T I F I C A

Que según Acta No. 11 del 01 de Febrero de 2001 correspondiente a la Junta Directiva en Barranquilla, de la sociedad: PROCAPS S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 12 de Febrero de 2001 bajo el No. 91,273 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre	Identificación
Gerente General.	
Uribe Ochoa Guillermo Luis	CC.******70,073,754

C E R T I F I C A

Que según Acta No. 406 del 02 de Sep/bre de 2004 correspondiente a la Junta Directiva en Barranquilla, de la sociedad: PROCAPS S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 09 de Sep/bre de 2004 bajo el No. 113,263 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre	Identificación
Suplente del Gerente.	
Tanaka Tatekawa Walter	CC.******16,251,923

C E R T I F I C A

Que según Acta No. 124 del 29 de Marzo de 1999 correspondiente a la Asamblea de Accionistas en Barranquilla, de la sociedad: PROCAPS S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 04 de Agosto de 1999 bajo el No. 82,226 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre	Identificación

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Revisor Fiscal Ppal.
Vargas Pertuz Ana Isabel CC.******32,696,645

C E R T I F I C A

Que según Acta No. 151 del 31 de Marzo de 2009 correspondiente a la Asamblea de Accionistas en Barranquilla, de la sociedad: PROCAPS S.A. cuya parte pertinente se inscribió en esta Cámara de Comercio, el 30 de Julio de 2009 bajo el No. 151,129 del libro respectivo, fueron hechos los siguientes nombramientos:

Cargo/Nombre Identificación

Suplente del Revisor Fiscal.
Duarte Diaz David CC.******73,115,965

C E R T I F I C A

Que por Escritura Pública No. 2,784 del 07 de Dic/bre de 2007, otorgada en la Notaria 2 a. de Barranquilla cuya parte pertinente se inscribió en esta Cámara de Comercio, el 20 de Dic/bre de 20 bajo el No. 3,492 del libro respectivo,---------- y las inscripciones 3.492-1, 3.493, 3.494, 3.495, 3.496, 3.497, ---- 3.498, 3.499, 3.500, 3.501, 3.502, 3.503, 3.504, 3.505, 3.506, ----- 3.507, Consta que RUBEN MINSKI GONTOVNIK, C.C. No. 7.463.982, ------ obrando como Presidente y Representante Legal de la sociedad C.I. NATURMEGA S.A., que obrando en su condicion de Presidente y ------- Representante Legaql de la sociedad PROCAPS S.A., el presidente --- debidamente facultado por los Estatutos Sociales y por el Maximo Organo Social, otorga los siguientes poderes: Otorgar poder -------- general, amplio y suficiente a los doctores JOSEFINA DEL CARMEN ---- MIELES BUELVAS CC.No.33.138.497; a MARCELA CARVAJALINO PAGANO ------ CC.No.22.579.748; CRISTINA VIOLI FRANCESCHINI CC.No.22.463.716, con las facultades que se transcriben a continuacion: a.- Para que ----- representen a la sociedad PROCAPS S.A, ante todo tipo de ---------- autoridades administrativas y jurisdiccionales, en asuntos de ------ naturaleza civil, laboral, comercial, penal, aduanera, cambiaria, tributaria, policiva, administrativa y fiscal. b.- Contestar y ----- presentar demandas, requerimientos, recursos, pedir y aportar ------ pruebas, recibir, notificarse, ejercer la accion de tutela, -------- tramitar incidente de desacato, comparecer en los procesos que ----- cursen contra la sociedad, allanarse en nombre de la sociedad en los asuntos que sean necesarios, transigir, desistir, sustituir, renunciar y reasumir el poder. c.- La facultad expresa de ---------- conciliar, por tanto pueden llegar a acuerdos conciliatorios, ------ transaccionales, judiciales o extrajudiciales o extrajudiciales, cualquiera que sea su cuantia, para lo cual las apoderadas deben aportar la autorizacion simple y escrita del Representante legal de la sociedad. d.- Podran presentar solicitudes de devolucion y/o compensacion de impuestos, ventas y rentas, recibir los pagos por las devoluciones y adelantar todo tramite o proceso administrativo ante la DIAN, de tal forma que en ningun momento quede sin -------- representacion legal de la sociedad. PODERES ESPECIALES: a.- Se ---- confiere poder especial amplio y suficiente a las personas que se determinan seguidamente, que conforman el grupo A y B, para, para

********** C O N T I N U A **********

No. 14904766

CAMARA DE COMERCIO DE BARRANQUILLA

C A M A R A D E C O M E R C I O
D E B A R R A N Q U I L L A
08**********

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que conjuntamente suscriban contratos de suministros de mercancias y servicios con entidades oficiales, hasta la suma de OCHOCIENTOS MIL DOLARES DE LOS ESTADOS UNIDOS DE AMERICA (US800.000.00), ------- liquidados a la tasa representativa del mercado vigente en el dia que se realice la respectiva transaccion. Grupo A. WALTER NANAKA TATEKAWA CC.No.16.251.923, CLAUDIA TANGARIFE CASTILLO ---------- CC.No.41.660.293, CARMEN ALICIA FLOREZ CC.No.22.434.044, IVAN ------ VILLAREAL CAMACHO CC.No.91.201.749, CARMEN ALICIA HERRERA ---------- DIAZGRANADOS CC.No.22.377.540, DAVID ANTONIO CHARRIS GIRALDO ------- CC.No.19.341.274, RICARDO DORADO HURTADO CC.No.79.715.772, JAIME RRERO LLINAS CC.No.19.300.593. b.- Se confiere poder especial ----- amplio y suficiente al senor WILLIAM ALBERTO BARROS CERRA ---------- CC.No.8.715.941, para que en nombre y representacion de PROCAPS ---- S.A., suscriban declaraciones cambiarias, aduaneras y tributarias a que este obligada la sociedad, en el giro normal de sus negocios y operaciones sociales, por tanto quedan facultados para firmarlas, como tambien los demas documentos relacionados con ellas, ---------- notificarse, aportar y solicitar las pruebas que sean necesarias. c.-Otorgar poder especial amplio y suficiente al senor MARLON ----- TATIS PAREDES CC.No.72.176.874 y al senor WILLIAM ALBERTO BARROS CERRA CC.No.8.715.941, para que en nombre y representacion de ------ PROCANPS S.A., suscriban las declaraciones, reportes y cualquier documento relacionado con los tramites o registros de Comercio ----- Exterior y o cualquier entidad del Estado que haga sus veces: d) Otorgar poder especial amplio y suficiente a la doctora CARMEN ----- ALICIA HERRERA DIAZGRANADOS, CC.No.22.377.540 y al doctor WALTER TANAKA TATEKAWA, CC.No.16.251.923, para que en nombre y ---------- representacion de PROCAPS S.A.; endosen los titulos valores de la sociedad hasta por la suma de UN MIL MILLONES DE PESOS ---------- (1.000.000.000.00) M.L. CUARTO: EI representante legal de la ------- sociedad PROCAPS S.A.; doctor RUBEN MINSKI GONTOVNIK, manifiesta que la presente reforma fue aprobada por la Asamblea General ------- Extraordinaria de Accionista de PROCAPS S.A., con observancia de las disposiciones legales y estatutarias.----------

C E R T I F I C A

Que por Escritura Pública No. 1,933 del 16 de Sep/bre de 2008, otorgada en la Notaria 2 a. de Barranquilla cuya parte pertinente se inscribió en esta Cámara de Comercio, el 06 de Octubre de 2008 bajo el No. 3,748 del libro respectivo,----------
Consta que el señor RUBEN MINSKI GONTOVNIK, C.C. No. 7.463.982, que comparece en su condicion de Presidente y Representante Legal de la Sociedad PROCAPS S.A., confiere por medio de este instrumento ------ publico Poder especial Amplio y Suficiente a la doctora MILENA -----

********** C O N T I N U A **********

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ESCAFFI PARDO, C.C. No. 32.758.420, para que en nombre y ---------- representacion de PROCAPS S.A., suscriba declaraciones cambiarias, aduaneras y tributarias a que este obligada la sociedad en el giro normal de sus negocios y operaciones sociales, por tanto queda ----- facultada para firmar, como tambien los demas documentos ---------- relacionados con ellas, notificarse, aportar y solicitar las ------- pruebas que sean necesarias.----------

C E R T I F I C A

Que por Documento Privado del 09 de Abril de 2010, otorgado en Barranquilla inscrito en esta Cámara de Comercio, el 20 de Abril de 2010 bajo el Nro 4,201 del libro respectivo,----------
Consta que el señor RUBEN MINSKI GONTOVNIK, C.C. No. 7.463.982, ---- quien obra en el caracter de Presidente y/o Representante legal de la sociedad PROCAPS S.A., que por medio de este instrumento -------- publico, otorga Poder Especial Amplio y Suficiente a la Doctora ---- MONICA DE HART DE OCHOA, identificada con C.C. No. 32.676.025, para que en nombre y representacion de la sociedad, Endose las Facturas Nacionales e Internacionales hasta por la suma de UN MIL MILLONES DE PESOS ($1.000.000.000.00)M.L. La doctora Monica de Hart de Ochoa, queda facultada para realizar todo acto o tramite necesario para el cabal cumplimiento del presente mandato.----------

C E R T I F I C A

Que por Documento Privado del 10 de Junio de 2010, otorgado en Barranquilla inscrito en esta Cámara de Comercio, el 13 de Julio de 2010 bajo el Nro 4,228 del libro respectivo,----------
consta que el señor RUBEN MISNKI GONTOVNIK, cc. No. 7.463.982 en su condicion de Presidente y representante legal de PROCAPS S.A., ----- confiere poder especial, amplio y suficiente al señor RICARDO DORADO HURTADO cc. No. 79.715.772 para que represente a la sociedad, ante el INVIMA, Fondo Nnacional de estupefacientes e ICA, con el fin que gestione, tramite o presente las diferentes solicitudes y ---------- peticiones de la empresa, segun la competencia de estas entidades. Por lo anterior, el Señor RICARDO DORADO HURTADO, queda facultado para presentar, gestionar, tramitar y firmar las diferentes -------- solicitudes y peticiones de la empresa, segun la competencia de ---- estas entidades, como tambien presentar y firmar todo los ---------- documentos relacionados con estas solicitudes, notificarse de ------ cualquier acto administrativo que expidan, aportar y solicitar las pruebas que sean necesarias, desistir, y en general a realizar todo tramite o acto necesario de tal forma que la sociedad en ningun ---- momento quede sin representacion legal ante estas entidades, en ---- cumplimiento fiel al mandato otorgado.----------

C E R T I F I C A

Que por Documento Privado del 03 de Agosto de 2010, otorgado en Barranquilla inscrito en esta Cámara de Comercio, el 24 de Agosto de 2010 bajo el Nro 4,258 del libro respectivo,----------
consta que RUBEN MINSKI GONTOVNIK, varón, mayor de edad, de ésta

********** C O N T I N U A **********

No. 14904767

CAMARA DE COMERCIO DE BARRANQUILLA

CAMARA DE COMERCIO
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vecindad, identificado con la cédula de ciudadanía No.7.463.982, expedida en Barranquilla, en mi condición de Representante legal y/o Presidente de la sociedad PROCAPS S. A., conforme a las -------- facultades otorgadas por los Estatutos Sociales, todo lo cual ------ demuestro con el certificado de existencia y representación legal expedido por la Cámara de Comercio de Barranquilla, que adjunto a este escrito, me permito manifestarles que confiero poder especial, amplio y suficiente al señor MARIO LÓPEZ LEON, varón, mayor de ----- edad, de esta vecindad, identificado con la cédula de ciudadanía .72.311.558, expedida en Puerto Colombia (Atlántico), para que en nombre y representación de la sociedad, realice los siguientes ----- actos: 1. Endosar las Facturas Nacionales e Internacionales de esas compañías hasta por la suma de UN MIL MILLONES DE PESOS ---------- ($1.000.000.000.00) Moneda Legal. 2. Suscribir Declaraciones ------- Cambiarias, Aduaneras y Tributarias a las que esta obligada la ----- sociedad en el giro ordinario de sus negocios, quedando facultado para notificarse, aportar y solicitar pruebas relacionados con las declaraciones Cambiarias. El señor MARIO LÓPEZ LEÓN, queda --------- facultado para notificarse, aportar y solicitar pruebas, presentar escritos en caso que resulte necesario en general a realizar todo acto, diligencia o tramite que considere indispensable para el ----- cabal cumplimiento del presente mandato.----------

C E R T I F I C A

Que en esta Cámara de Comercio no aparecen inscripciones posteriores de documentos referentes a reforma, disolución, liquidación o nombramientos de representantes legales de la expresada sociedad.

C E R T I F I C A

Que su última Renovación fue el: 30 de Marzo de 2010.

La información sobre embargos de establecimiento se suministra en Certificados de Matrícula, la de contratos sujetos a registro, en Certificados Especiales.

C E R T I F I C A

Que los actos de registro aquí certificados quedan en firme cinco días hábiles despues de la correspondiente inscripción, siempre que, dentro de dicho término, no sean objeto de los recursos de reposición ante esta entidad, y/o de apelación para ante la Superintendencia de Industria y Comercio.

CERTIFICADO DE EXISTENCIA Y REPRESENTACION LEGAL O DE INSCRIPCION DE DOCUMENTOS.

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CAMARA DE COMERCIO DE BARRANQUILLA

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 June 2003 (12.06.2003)

PCT

(10) International Publication Number
WO 03/047502 A1

(51) International Patent Classification[7]: A61K

(21) International Application Number: PCT/PH02/00008

(22) International Filing Date: 31 May 2002 (31.05.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/017,697 7 December 2001 (07.12.2001) US

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(81) Designated States *(national)*: AU, BR, CA, CN, ID, IL, IN, JP, KP, KR, MX, NZ, PH, SG, VN, ZA.

(84) Designated States *(regional)*: European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/047502 A1

(54) Title: TASTE MASKED AQUEOUS LIQUID PHARMACEUTICAL COMPOSITION

(57) Abstract: A substantially taste masked liquid pharmaceutical composition containing a pharmaceutically effective amount of an unpleasant tasting drug dissolved or dispersed in an aqueous excipient base said excipient base comprising polyvinyl pyrrolidone and/or copolyvidone, and high molecular weight polyethylene glycol.

TASTE MASKED AQUEOUS LIQUID PHARMACEUTICAL COMPOSITION

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a liquid drug composition, and more particularly to a substantially taste masked aqueous liquid pharmaceutical composition that contains an otherwise unpleasant tasting drug.

Description of Related Art

The most convenient and commonly employed route of drug delivery has been by oral ingestion, either in liquid or solid formats. The unpalatable taste of most drugs is generally not a problem with solid dosage formats, which are intended to be swallowed whole. In the case of capsules, the hard gelatin shell prevents the drug from being tasted during the short transit time in the mouth. Tablets, on the other hand, can be coated with sugar or film forming polymers for tastemasking.

Many children and some adults however have difficulty swallowing solid dosage formats, and in this case, the drug is given in liquid form, either as syrup or suspension. Most drugs however are bitter, and this can lead to poor patient compliance. Because the threshold for bitterness is low, only a very small amount of dissolved drug is needed for perception of bitterness.

The prior art has shown extensive use of one or a combination of different flavoring methodologies to mask the bitter taste of drugs. For example, a flavor can be selected that complements the taste of the preparation, or a flavor with a longer intensity and stronger taste than the drug can be used. High levels of sweetening agents are often used to overwhelm bitterness with sweetness. The taste buds may also be anesthesized by menthol or mint flavors. These approaches are generally not very effective in masking the taste of a bitter drug, and a flavoring system that works with one drug usually does not apply to another drug.

The prior art also indicates that taste masking could also be achieved by increasing the viscosity of liquid preparations. Various combinations of viscosity modifiers for taste masking exist in the patent literature. For example, US patent 5,616,621 provides taste masked liquid preparations by increasing the viscosity with a combination of polyethylene glycol and sodium carboxymethylcellulose; US patent 5,658,919 discloses taste masking of acetaminophen suspension using a suspending system consisting of xanthan gum and a mixture of cellulosic polymers. The increase in viscosity is assumed to limit the contact of the drug with the tongue, presumably by slowing down salivary water uptake into the viscous liquid medicament, which can lead to dilution and dissolution of the ingested medication. This approach is only moderately successful in reducing bitterness especially at high drug loading. While bitterness may be reduced at the onset, bitter aftertaste becomes prominent after swallowing because thick preparations are more difficult to wash down thus leaving behind some residual viscous liquid medicament in the mouth after swallowing. This bitter aftertaste is more prominent with water intake due to the reduction in viscosity and dilution of the residual liquid medicament and subsequent dissolution of the drug in the mouth.

Several other approaches have been pursued to address the unpleasant taste of a drug in a liquid format. US patent 5,730,997 illustrates the use of a hyperosmotic liquid using a sugar derivative and maltose syrup for taste masking. US patent 5,154,926 claims reduction of the bitter taste of acetaminophen syrup by using a water-soluble macromolecule with a polyhydric alcohol and/or polymer of a polyhydric alcohol of MW 300-400. US patents 5,763,449 and 5,962,461 teach the use of a combination of povidone, C_3-C_6 polyol and ammonium glycyrrhizinate for taste masking. EP application 1025858 A1 discloses relief of bitterness of basic drugs by combining propylene glycol with povidone and/or copolyvidone.

The disclosure that follows illustrates another, more general solution to the problem of bad taste in liquid compositions containing either dissolved or dispersed drugs.

SUMMARY OF THE INVENTION

The present invention provides a taste masked oral liquid composition comprising at least one therapeutically effective amount of a bitter-tasting drug. The drug is dissolved or dispersed in an aqueous taste masking excipient base comprising a high molecular weight (MW) polyethylene glycol, a polyvinyl pyrrolidone and/or copolyvidone. The taste masked liquid composition has substantially reduced bitter taste and aftertaste.

In preferred embodiments of the invention, the oral pharmaceutical liquid composition comprises about 0.1 to about 10 weight percent of at least one bitter-tasting drug wherein the bitter-tasting drug is an aromatic compound with hydrophilic groups that can form hydrogen bonds such as hydroxyl, carboxylic or amine groups; about 0.5 to about 10 weight percent of polyvinyl pyrrolidone and/or copolyvidone; about 0.05 to about 10 weight percent polyethylene glycol of MW 4000-6000; about 30-90% of a sweetening composition; about 0 to 0.4% of a viscosity-building agent; about 0-20% of a polyhydric alcohol, and 0.1-0.5% of a flavoring agent. The liquid composition is adjusted to a pH between 2.5 to 8.

DETAILED DESCRIPTION OF THE INVENTION

The present invention contemplates a taste masked liquid composition where the liquid composition is a syrup, a ready-to-use suspension, or extemporaneously prepared liquid syrup or suspension such as, for example, dry powder for reconstitution with water, liquid concentrate for dilution, dispersible tablet or capsule. In the case of extemporaneously prepared syrup or suspension, the concentration of ingredients are based on the reconstituted product.

The liquid pharmaceutical composition of the present invention contains at least one normally bitter tasting drug as active ingredient. The bitter-tasting drugs are present at therapeutically effective amounts in the dosage form. These amounts differ depending

on the drug and prescribed dosage regimens. For instance, liquid preparations intended for infants generally contain high drug concentrations to enable small doses and reduced dosing frequency. The amount of drug in the composition is from about 0.02 to about 15 percent by weight, preferably from about 0.1 to about 10 percent by weight of the total composition. In the case of dry powder for reconstitution with water, the drug may be present as uncoated or coated particles. Coated drug particles are not usually perfectly sealed. After reconstitution, some amount of drug can leach out through the coating into the liquid phase during storage, which can result in some bitterness in the product.

Bitter tasting drugs that may be used with the liquid composition are aromatic compounds with hydrophilic groups that can form hydrogen bonds such as hydroxyl, carboxylic or amine groups. These drugs may be selected from but not limited to the group consisting of analgesics, decongestants, antitussives, expectorants, antihistamines, mucolytics, laxatives, vasodilators, anti-arrhythmics, anti-diarrhea drugs , anti-hypertensives, antibiotics, narcotics, bronchodilators, anti-inflammatory drugs, cardiovascular drugs, tranquilizers, antipsychotics, antitumor drugs, sedatives, antiemetics, anti-nauseants, anti-convulsant, neuromuscular drugs, hypoglycemic agents, diuretics, antispasmodics, uterine relaxants, antiobesity drugs, antianginal drugs, and antiviral drugs. Combinations of these drugs can also be used.

Particular unpleasant tasting drugs include but are not limited to acetaminophen, ibuprofen, phenylpropanolamine hydrochloride, pseudoephedrine hydrochloride, phenylephrine hydrochloride, diphenhydramine hydrochloride, guaifenesin, dextromethorphan hydrobromide, chlorpheniramine maleate, brompheniramine maleate, terfenadine, loratadine, descarboethoxyloratadine, bromhexine hydrochloride, ambroxol hydrochloride, salbutamol sulphate, amoxicillin, ampicillin, cloxacillin, flucloxacillin, cephalexin, and combinations thereof.

One embodiment of the present invention contains acetaminophen from about 1 to about 15 weight percent, preferably from about 2 to about 10 weight percent of total composition. A second embodiment of the invention contains guaifenesin from about

0.5 to about 10 weight percent, preferably from about 1 to about 5 weight percent of total composition. If suspensions of these drugs are to be prepared, the drug should preferably be micronized with more than 80% of the particles having a particle size less than or equal to 10 microns and not more than 15% having particle sizes greater than or equal to 50 microns.

In the present invention, the normally bitter drug is dissolved or dispersed in an aqueous taste masking excipient base comprising a polyvinyl pyrrolidone and/or copolyvidone, and a high MW polyethylene glycol. The taste masked liquid composition has substantially reduced bitter taste and aftertaste.

A contemplated composition contains about 0.1 to about 30 weight percent polyvinyl pyrrolidone (PVP) and/or copolyvidone, preferably about 0.5 to about 10 weight percent, more preferably about 1 to about 7 weight percent of total composition. The PVP can either be water-soluble or water-insoluble. PVP is commercially available from a number of suppliers. The water-soluble PVPs or povidone sold under the Trademark KOLLIDON K25, K30, K90 having molecular weights of 28,000-34,000, 44,000-54,000, and 1,000,000-1,500,000, respectively, are preferred for use, with the K25 and K30 being most preferred. Water-insoluble PVPs referred to as crospovidone or crospolyvidone are crosslinked insoluble polyvinyl pyrrolidone. Crospovidone is available from BASF under the Trademark KOLLIDON CL, KOLLIDON CL-M, CROSPOVIDONE M. Copolyvidone is a copolymer of vinyl pyrrolidone and vinyl acetate available from BASF under the Tradename KOLLIDON VA 64. In the present invention, water-soluble PVPs, water-insoluble PVPs, and copolyvidone may be used either singly or in combination.

The disclosure of Volker Bühler's book, *Kollidon*, BASF Aktiengesellshaft, Ludwigshafen, Germany (1992) teaches the use of PVP as both a solubilization aid for several drugs as well as for specifically masking the bitter taste of acetaminophen. This book teaches that PVP forms complexes with aromatic compounds particularly those with hydrophilic groups that can form hydrogen bonds such as hydroxyl, carboxyl, and amine groups. See also Horn et al., *J. Pharm. Sci.*, 71:1021-126 (1982).

It is thought that PVP forms a complex with acetaminophen reducing its bitter taste. An exemplary formulation for an oral liquid PVP- and acetaminophen syrup composition is provided in page 113, Table 81 of the above Bühler's text. This formulation contains 5 weight percent of fully dissolved acetaminophen and 20 weight percent Kollidon K25.

Consistent with Bühler's disclosure, we have found that the addition of PVP improves the taste of an acetaminophen suspension. The bitterness reduction however is still not significant to eliminate the bitterness especially the bitter aftertaste.

We have now surprisingly found that the bitterness of an acetaminophen suspension especially the bitter aftertaste can be significantly improved by using a high molecular weight polyethylene glycol (PEG) with PVP and/or copolyvidone. This despite the fact that polyethylene glycol is known to increase the solubility of acetaminophen. Thus, the amount of dissolved acetaminophen would have been theoretically higher when polyethylene glycol is used with PVP and/or copolyvidone in an acetaminophen suspension, which in turn should have increased the bitterness, and yet on contrary, significant reduction in bitterness especially on the bitter aftertaste was achieved. The improvement is more prominent when water intake follows swallowing of the medication. The molecular weight of polyethylene glycol is critical to its contribution to taste masking when combined with PVP and/or copolyvidone. Liquid polyethylene glycol with MW 400-600 has no effect on tastemasking, only the semisolid/solid polyethylene glycol of MW $\geq$ 900 works. The higher the molecular weight, the lower the level of polyethylene glycol required. The preferred polyethylene glycol molecular weight is about 2000 to about 8000, more preferably the molecular weight is about 4000 to about 6000. The amount of polyethylene glycol is from about 0.01 to about 25 weight percent, preferably from about 0.05 to about 10 weight percent, and more preferably from about 0.1 to about 5 weight percent.

We have also surprisingly found that the taste masking effect of high molecular weight polyethylene glycol and PVP and/or copolyvidone are not limited to suspensions but also to fully dissolved drugs (syrups) such as for example Guaifenesin or lower levels

of acetaminophen. The mechanism by which debittering is achieved is unknown. However, without wishing to be bound by theory, it is believed that a complex is formed between the drug and PVP and/or copolyvidone, with the high molecular weight polyethylene glycol potentiating debittering by competing with unbound drug for taste receptors of bitterness.

The taste masked liquid composition of the present invention may contain additional ingredients used in the drug industry, herein referred to as additives. Additives include well-known components, but are not limited to sweetening agents, flavors, colorants, antioxidants, chelating agents, viscosity-building agents, surfactants, pH modifiers, bulking agents, acidifiers, cosolvents, and mixtures thereof.

Representative sweetening agents include but not limited to:

(1) Water-soluble sweetening agents such as monosaccharides, disaccharides, sugar alcohols, and polysaccharides, e.g., glucose, fructose, invert sugar, sorbitol, sucrose, maltose, xylose, ribose, mannose, corn syrup solids, xylitol, mannitol, maltodextrins, and mixtures thereof. In general, water-soluble sweetening agents selected from sugar, invert sugar, sorbitol, mannitol, and mixtures thereof are useful at amounts of about 20 to about 95 weight percent, with amounts of about 30 to about 90 weight percent being preferred, and about 40 to about 85 weight percent being more preferred.

(2) Water-soluble artificial sweeteners and dipeptide-based sweeteners such as saccharin salts, acesulfame-K, sucralose, aspartame, and mixtures thereof. In general, these sweeteners are used in combination with water-soluble sweetening agents to enhance sweetness.

Flavors that may optionally be added to the taste masked liquid excipient base of the present invention are those known in the pharmaceutical art. For example, synthetic flavor oils, and/or naturally derived oils from plants, flowers, leaves, and so forth, and combinations thereof are useful. In general, amounts of about 0.05 to about 5 weight

percent of the total composition are useful with amounts of about 0.1 to about 1.5 weight percent being preferred and about 0.2 to about 1 weight percent being most preferred.

The taste masked liquid composition of the present invention may optionally contain viscosity-building agents from 0 to about 7 weight percent of total composition, preferably from about 0.05 to about 5 weight percent, and most preferably from about 0.1 to about 3 weight percent. The viscosity-building agents may be selected from but not limited to xanthan gum, carrageenan, tragacanth, guar gum, pectin, carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxypropylcellulose, methylcellulose, microcrystalline cellulose and carboxymethylcellulose sodium blends, and mixtures thereof. The viscosity-building agent provides both body and mouthfeel to the preparation. The viscosity-building agent must be selected carefully to ensure compatibility with the drug and the other components of the formulations.

A cosolvent may optionally be used to dissolve or rapidly disperse additives, or as a solubilizer for the drugs. Ethanol and polyhydric alcohols such as glycerin, propylene glycol, low molecular weight polyethylene glycols, and mixtures thereof are generally employed as cosolvents.

In the case of dry powders for reconstitution, the powders or granules may optionally contain anti-caking agents to improve the flow properties of dry powders during processing and prevent the powders from caking during storage. The anti-caking agents may be selected from but not limited to colloidal silicon dioxide, tribasic calcium phosphate, powdered cellulose, magnesium trisilicate, starch, and mixtures thereof.

The invention will now be described with respect to the following specific examples.

Experiment 1

The effective amount of crospovidone needed to reduce the bitterness of a liquid suspension containing acetaminophen was determined by evaluating compositions containing 0, 2.5%, 5% and 10% crospovidone.

Table 1: Acetaminophen Suspension

Ingredient	Example 1-A (g/100 ml)	Example 1-B (g/100 ml)	Example 1-C (g/100 ml)	Example 1-D (g/100 ml)
Acetaminophen	5	5	5	5
Xanthan gum	0.3	0.3	0.3	0.3
Sucrose	55	55	55	55
70% Sorbitol Solution	10	10	10	10
Invert Sugar	20	20	20	20
Glycerin	5	5	5	5
Crospovidone (Kollidon CL-M)	0	2.5	5	10
Sodium Benzoate	0.2	0.2	0.2	0.2
Sorbitan Monolaurate	0.05	0.05	0.05	0.05
Disodium Edetate	0.2	0.2	0.2	0.2
Sucralose	0.2	0.2	0.2	0.2
Saccharin sodium	0.13	0.13	0.13	0.13
Coloring	0.006	0.006	0.006	0.006
Flavoring	0.3	0.3	0.3	0.3
Citric Acid	0.1	0.1	0.1	0.1
Sodium Citrate Dihydrate	0.295	0.295	0.295	0.295
Purified Water	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL
pH	5 - 6	5 - 6	5 - 6	5 - 6

The acetaminophen suspensions were prepared in the following manner:

Sucrose syrup containing sodium benzoate was prepared. The hot syrup was cooled down to 30°C. The sucrose syrup, sorbitol and invert sugar were blended together to form Phase A. Sorbitan monolaurate was added to the mixture to form Phase B. Phase B was stirred for 15 minutes.

The required amount of crospovidone (for Examples 1-B, 1-C and 1-D) was dispersed into Phase B. The admixture was stirred for 30 minutes after which acetaminophen was added. The resulting admixture was stirred for one hour to form Phase C.

Xanthan gum was dispersed in glycerin. The resulting dispersion was added to Phase C. The admixture was stirred for 15 minutes to form Phase D.

An aqueous solution of citric acid and sodium citrate dihydrate was prepared to form Phase E. An aqueous solution of disodium edetate, saccharin sodium and sucralose was prepared to form Phase F.

Phases E and F were added to Phase D. The admixture was stirred for one hour and then homogenized in a colloid mill. Color and flavor were added to the homogenized bulk, which was stirred for two more hours before adjusting to the desired volume with purified water. The suspensions were allowed to stand for 24 hours before tasting.

The viscosity of the samples were determined using a Brookfield Model DV – I+ viscometer using a number 3 spindle at 30 rpm. The viscosity of samples containing 0, 2.5%, 5% and 10% crospovidone did not differ significantly from each other.

Three rounds of taste tests were done. Example 1-A was compared to Example 1-B in the first round. Example 1-B was compared to Example 1-C in round 2. Example 1-C was compared to Example 1-D in round 3. Ten respondents were asked to taste 2.5 ml of each sample in random order. The respondents were asked to drink water and take unsalted crackers between samples to remove traces of the first sample tasted. Each respondent was asked to pick a preference based on reduced bitterness. The results are presented in Tables 2, 3 and 4.

Table 2: Taste Comparison: Example 1-A vs 1-B

Example	PVP (% w/v)	No. of Respondents who prefer sample
1-A	0	None
1-B	2.5	10 out of 10

Table 3: Taste Comparison: Example 1-B vs I-C

Example	PVP (% w/v)	No. of Respondents who prefer sample
1-B	2.5	2 out of 9
1-C	5	7 out of 9

Table 4: Taste Comparison: Example 1-C vs 1-D

Example	PVP (% w/v)	No. of Respondents who prefer sample
1-C	5	5 out of 10
1-D	10	5 out of 10

The results show that there is an optimum level of PVP required for taste masking, beyond which no further taste improvement is achieved. The taste masking effect is independent of product viscosity, which was not significantly different for the PVP range tested.

Experiment 2

The effect of adding a high molecular weight polyethylene glycol on the taste of a liquid suspension containing acetaminophen was determined by evaluating compositions containing 0, 0.5%, 2.5%, and 5% polyethylene glycol 4000.

Table 5: Acetaminophen Suspension

Ingredient	Example 2-A (g/100 ml)	Example 2-B (g/100 ml)	Example 2-C (g/100 ml)	Example 2-D (g/100 ml)
Acetaminophen	5	5	5	5
Xanthan gum	0.3	0.3	0.3	0.3
Sucrose	55	55	55	55
70% Sorbitol Solution	10	10	10	10
Invert Sugar	20	20	20	20
Glycerin	5	5	5	5
Polyethylene glycol (MW = 4000)	0	0.5	2.5	5
Sodium Benzoate	0.2	0.2	0.2	0.2
Sorbitan Monolaurate	0.05	0.05	0.05	0.05
Disodium Edetate	0.2	0.2	0.2	0.2
Sucralose	0.2	0.2	0.2	0.2
Saccharin sodium	0.13	0.13	0.13	0.13

Coloring	0.006	0.006	0.006	0.006
Flavoring	0.3	0.3	0.3	0.3
Citric Acid	0.1	0.1	0.1	0.1
Sodium Citrate Dihydrate	0.295	0.295	0.295	0.295
Purified Water	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL
pH	5 - 6	5 - 6	5 - 6	5 - 6

The acetaminophen suspensions were prepared in the following manner:

Sucrose syrup containing sodium benzoate was prepared. The hot syrup was cooled down to 30°C. The sucrose syrup, sorbitol and invert sugar were blended together to form Phase A. Sorbitan monolaurate was added to the mixture to form Phase B. Phase B was stirred for 15 minutes.

The required amount of polyethylene glycol (for Examples 2-B, 2-C and 2-D) was dissolved in water to form Phase C. Phase C solution was added to Phase B. The admixture was stirred for 30 minutes after which acetaminophen was added. The resulting admixture was stirred for one hour to form Phase D.

Xanthan gum was dispersed in glycerin. The resulting dispersion was added to Phase D. The admixture was stirred for 15 minutes to form Phase E.

An aqueous solution of citric acid and sodium citrate dihydrate was prepared to form Phase F. An aqueous solution of disodium edetate, saccharin sodium and sucralose was prepared to form Phase G.

Phases F and G were added to Phase E. The admixture was stirred for one hour and then homogenized in a colloid mill. Color and flavor were added to the homogenized bulk which was stirred for two more hours before adjusting to the desired volume with purified water. The suspensions were allowed to stand for 24 hours before tasting.

The viscosity of the samples were determined using a Brookfield Model DV – I+ viscometer using a number 3 spindle at 30 rpm. The viscosity of samples containing 0, 0.5%, 2.5% and 5% w/v PEG did not differ significantly from each other.

Three rounds of taste tests were done comparing Example 2-A with Example 2-B, Example 2-C, and Example 2-D, respectively. Ten respondents were asked to taste 2.5 ml of each sample in random order. The respondents were asked to drink water take unsalted crackers between samples to remove traces of the first sample tasted. Each respondent was asked to pick a preference based on reduced bitterness. The results are shown in Tables 6, 7 and 8.

Table 6: Taste Comparison of Example 2-A vs 2-B

Example	PEG 4000 (% w/v)	No. of Respondents who prefer sample
2-A	0	2 out of 10
2-B	0.5	4 out of 10 *No difference: 4 out of 10*

Table 7: Taste Comparison of Example 2-A vs 2-C

Example	PEG 4000 (% w/v)	No. of Respondents who prefer sample
2-A	0	5 out of 10
2-C	2.5	5 out of 10

Table 8: Taste Comparison of Example 2-A vs 2-D

Example	PEG 4000 (% w/v)	No. of Respondents who prefer sample
2-A	0	None
2-D	5	10/10

Results show that a minimum amount of polyethylene glycol is required to achieve significant taste improvement. When used singly for taste masking, amounts of about 2.5 to about 5% w/v high molecular weight polyethylene glycol were found to be effective. These amounts in typical formulations, however, exceed acceptable daily intake levels, thus limiting the use of polyethylene glycol singly to achieve taste masking.

Experiment 3

The effect of combining crospovidone and high molecular weight polyethylene glycol on the taste of a liquid suspension containing acetaminophen was determined. The taste of a sample containing crospovidone and polyethylene glycol 4000 was compared with a

sample containing only crospovidone, and a sample containing only polyethylene glycol 4000, respectively.

Table 9: Acetaminophen Suspension

Ingredient	Example 3-A (g/100 ml)	Example 3-B (g/100 ml)	Example 3-C (g/100 ml)
Acetaminophen	5	5	5
Xanthan gum	0.3	0.3	0.3
Sucrose	55	55	55
70% Sorbitol Solution	10	10	10
Invert Sugar	20	20	20
Glycerin	5	5	5
Polyethylene glycol (MW = 4000)	0	0.5	0.5
Crospovidone (Kollidon CL-M)	5	0	5
Sodium Benzoate	0.2	0.2	0.2
Sorbitan Monolaurate	0.05	0.05	0.05
Disodium Edetate	0.2	0.2	0.2
Sucralose	0.2	0.2	0.2
Saccharin sodium	0.13	0.13	0.13
Coloring	0.006	0.006	0.006
Flavoring	0.3	0.3	0.3
Citric Acid	0.1	0.1	0.1
Sodium Citrate Dihydrate	0.295	0.295	0.295
Purified Water	q.s. to 100 mL	q.s. to 100 mL	q.s. to 100 mL
pH	5 - 6	5 - 6	5 - 6

The acetaminophen suspensions were prepared in the following manner:

Sucrose syrup containing sodium benzoate was prepared. The hot syrup was cooled down to 30°C. The sucrose syrup, sorbitol and invert sugar were blended together to form Phase A. Sorbitan monolaurate was added to the mixture to form Phase B. Phase B was stirred for 15 minutes.

The required amount of polyethylene glycol (for Examples 3-B and 3-C) was dissolved in water to form Phase C. Phase C solution was added to Phase B. The required amount of crospovidone (for Examples 3-A and 3-C) was added to Phase B.

The admixture was stirred for 30 minutes after which acetaminophen was added. The resulting admixture was stirred for one hour to form Phase D.

Xanthan gum was dispersed in glycerin. The resulting dispersion was added to Phase D. The admixture was stirred for 15 minutes to form Phase E.

An aqueous solution of citric acid and sodium citrate dihydrate was prepared to form Phase F. An aqueous solution of disodium edetate, saccharin sodium and sucralose was prepared to form Phase G.

Phases F and G were added to Phase E. The admixture was stirred for one hour and then homogenized in a colloid mill. Color and flavor were added to the homogenized bulk which was stirred for two more hours before adjusting to the desired volume with purified water. The suspensions were allowed to stand for 24 hours before tasting.

Two rounds of taste tests were done comparing Example 3-C with Example 3-A, and Example 3-C with Example 3-B, respectively. Eleven respondents were asked to taste 2.5 ml of each sample in random order. The respondents were asked to drink water and take unsalted crackers between samples to remove traces of the first sample tasted. Each respondent was asked to pick a preference based on reduced bitterness.

The formulation containing crospovidone and polyethylene glycol (Example 3-C) was preferred over the formulation containing only crospovidone (Example 3-A) by 10 of 11 respondents. The same formulation containing crospovidone and polyethylene glycol (Example 3-C) was also preferred over the formulation containing only polyethylene glycol (Example 3-B) by 9 of 11 respondents. These results indicate that significant taste masking effect was achieved when polyvinyl pyrrolidone is used in combination with a high molecular weight polyethylene glycol, and that a significantly lower level of PEG is required for tastemasking in the presence of polyvinyl pyrrolidone than when using PEG alone.

Experiment 4

This example describes the production of a liquid taste masked suspension containing the analgesic acetaminophen.

Table 10: Acetaminophen Suspension

Ingredient	Example 4-A (g/100 ml)	Example 4-B (g/100 ml)
Acetaminophen	5	5
Xanthan gum	0.3	0.3
Sucrose	55	55
Sorbitol Solution	10	10
Invert Sugar	20	20
Glycerin	5	5
Crospovidone (Kollidon CL)	2.5	2.5
Polyethylene Glycol 4000	0.25	0
Sodium Benzoate	0.2	0.2
Sorbitan Monolaurate	0.05	0.05
Disodium Edetate	0.2	0.2
Sucralose	0.2	0.2
Saccharin sodium	0.13	0.13
Coloring	0.006	0.006
Flavoring	0.3	0.3
Citric Acid	0.1	0.1
Sodium Citrate Dihydrate	0.295	0.295
Purified Water	q.s.	q.s.
pH	5 - 6	5 - 6

The acetaminophen suspensions were prepared in the following manner:

Sucrose syrup containing sodium benzoate was prepared. The hot syrup was cooled down to 30°C. The sucrose syrup, sorbitol and invert sugar were blended together to form Phase A, which was then divided into two portions.

A solution of polyethylene glycol (for Example 4-A) in water was prepared. The resulting solution was added to one portion of Phase A. The admixture was stirred for 15 minutes after which sorbitan monolaurate was added directly to the admixture to form Phase B. Crospovidone was dispersed into Phase B. The admixture was stirred

for 30 minutes after which acetaminophen was added. The resulting admixture was stirred for one hour to form Phase C.

Xanthan gum was dispersed in glycerin. The resulting dispersion was added to the second portion of Phase A. The admixture was stirred for 15 minutes to form phase D.

An aqueous solution of citric acid and sodium citrate dihydrate was prepared to form Phase E. An aqueous solution of disodium edetate, saccharin sodium and sucralose was prepared to form Phase F.

Phases C, E and F were added to Phase D. The admixture was stirred for one hour and then homogenized in a colloid mill. Color and flavor were added to this homogenized bulk which was stirred for two more hours before adjusting to the desired volume with purified water. The suspensions were allowed to stand for 24 hours before tasting.

Seven respondents were asked to taste 2.5 ml each of Example 4-A and Example 4-B in random order. The respondents were asked to drink water after each medication, and take unsalted crackers between samples to remove traces of the first sample tasted.

All respondents perceived either a sweet aftertaste or no aftertaste for the formulation containing crospovidone and PEG (Example 4-A), while 5 of 7 respondents detected bitter aftertaste in the formulation containing crospovidone only (Example 4-B). The result shows the significant reduction/elimination of bitterness when high MW polyethylene glycol is used with PVP.

Example 4-A was further compared to Calpol Six Plus (UK, Glaxo Wellcome), a commercial acetaminophen suspension containing the same drug concentration which is relatively good-tasting among the other brands in the market. Seven of seven respondents preferred Example 4-A to Calpol Six Plus. All the respondents perceived bitterness in Calpol Six Plus.

Experiment 5

The effect of the molecular weight of polyethylene glycol on the taste of a liquid suspension containing acetaminophen was determined.

Table 11: Acetaminophen Suspension

Ingredient	Example 5-A (g/100 ml)	Example 5-B (g/100 ml)	Example 5-C (g/100 ml)
Acetaminophen	5	5	5
Xanthan gum	0.3	0.3	0.3
Sucrose	55	55	55
Sorbitol Solution	10	10	10
Invert Sugar	20	20	20
Glycerin	5	5	5
Crospovidone (Kollidon CL-M)	5	5	5
Polyethylene Glycol (MW=4000)	0.5	0	0
Polyethylene Glycol (MW=1450)	0	0.5	1
Sodium Benzoate	0.2	0.2	0.2
Sorbitan Monolaurate	0.05	0.05	0.05
Disodium Edetate	0.2	0.2	0.2
Sucralose	0.2	0.2	0.2
Saccharin sodium	0.13	0.13	0.13
Coloring	0.006	0.006	0.006
Flavoring	0.3	0.3	0.3
Citric Acid	0.1	0.1	0.1
Sodium Citrate Dihydrate	0.295	0.295	0.295
Purified Water	q.s.	q.s.	q.s.
pH	5 - 6	5 - 6	5 - 6

The acetaminophen suspensions were prepared in the following manner:

Sucrose syrup containing sodium benzoate was prepared. The hot syrup was cooled down to 30°C. The sucrose syrup, sorbitol and invert sugar were blended together to form Phase A.

A solution of polyethylene glycol in water was prepared. The resulting solution was added to Phase A. The admixture was stirred for 15 minutes after which sorbitan monolaurate was added directly to the admixture to form Phase B. Crospovidone was

dispersed into Phase B. The admixture was stirred for 30 minutes after which acetaminophen was added. The resulting admixture was stirred for one hour to form Phase C.

Xanthan gum was dispersed in glycerin. The resulting dispersion was added to the second portion of Phase C. The admixture was stirred for 15 minutes to form phase D. An aqueous solution of citric acid and sodium citrate dihydrate was prepared to form Phase E. An aqueous solution of disodium edetate, saccharin sodium and sucralose was prepared to form Phase F.

Phases E and F were added to Phase D. The admixture was stirred for one hour and then homogenized in a colloid mill. Color and flavor were added to this homogenized bulk which was stirred for two more hours before adjusting to the desired volume with purified water.

The viscosity of the samples were determined using a Brookfield Model DV – I+ viscometer using a number 3 spindle at 30 rpm. The samples had the same viscosity.

Two rounds of taste tests were done comparing Example 5-A with Example 5-B, and Example 5-A with Example 5-C, respectively. Ten respondents were asked to taste 2.5 ml of each sample in random order. The respondents were asked to drink water after each medication, and take unsalted crackers between samples to remove traces of the first sample tasted. Each respondent was asked to pick a preference based on reduced bitterness.

Seven out of ten respondents preferred Example 5-A (5% crospovidone + 0.5% PEG 4000) over Example 5-B (5% crospovidone + 0.5% PEG 1450), and one respondent found no difference between the two products. On the other hand, Example 5-A (5% crospovidone + 0.5% PEG 4000) and Example 5-C (5% crospovidone + 1% PEG 1450) were equally preferred. Thus, the higher the molecular weight of PEG, the lower the level required for taste masking.

Those ordinarily skilled in the art should be able to run routine experiments to determine the optimum levels of polymer (PVP and/or copolyvidone) and polyethylene glycol required for achieving maximum taste masking of a given unpleasant-tasting drug.

Experiment 6

This example describes the production of a liquid taste masked suspension containing a high dose of the analgesic acetaminophen.

Table 12: Acetaminophen Suspension

Ingredient	Example 6-A g/100 ml	Example 6-B g/100 ml
Acetaminophen	10	10
Xanthan gum	0.3	0.3
Sucrose	54	54
Sorbitol Solution	10	10
Invert Sugar	20	20
Glycerin	5	5
Crospovidone (Kollidon CL-M)	5	5
Polyethylene Glycol 4000	1	0
Sodium Benzoate	0.2	0.2
Sorbitan Monolaurate	0.05	0.05
Disodium Edetate	0.2	0.2
Sucralose	0.4	0.4
Saccharin sodium	0.26	0.26
Coloring	0.006	0.006
Flavoring	0.4	0.4
Citric Acid	0.1	0.1
Sodium Citrate Dihydrate	0.295	0.295
Purified Water	q.s.	q.s.
pH	5 - 6	5 - 6

The acetaminophen suspension was prepared in the same manner as Experiment 4. The suspensions were allowed to stand for 24 hours before tasting.

Seven respondents were asked to taste 1.0 ml each of Example 6-A and Example 6-B in random order. The respondents were asked to drink water after each medication, and take unsalted crackers between samples to remove traces of the first sample tasted.

All respondents perceived either a sweet aftertaste or no aftertaste for Example 6-A (5% crospovidone + 1% PEG 4000), while 7 of 7 respondents detected bitter aftertaste in Example 6-B (5% crospovidone only) illustrating the significant reduction/elimination of bitterness when high MW polyethylene glycol is used with PVP.

A blind taste was conducted on one hundred mothers comparing Example 6-A with Calpol Infant Drops (UK, Glaxo Wellcome) which contains the same drug concentration. Calpol Infant Drops is a commercial acetaminophen suspension that is relatively good tasting among other brands in the market. Seventy four percent of mothers preferred Example 6-A to Calpol Infant Drops, showing the superior taste masking of a formulation containing PVP and high molecular weight PEG.

Experiment 7

This example describes the production of a liquid taste masked syrup containing the expectorant Guaifenesin.

Table 13: Guaifenesin Syrup

Ingredient	Example 7-A g/100 ml	Example 7-B g/100 ml
Guaifenesin	2	2
Sucrose	51	51
Sorbitol Solution	30	30
Glycerin	7.5	7.5
Povidone (Kollidon K30)	2.5	2.5
Polyethylene Glycol 4000	1.25	0
Sodium Benzoate	0.2	0.2
Sucralose	0.1	0.1
Flavoring	0.3	0.3
Citric Acid	3.7	3.7
Purified Water	q.s. to 100 mL	q.s. to 100 mL
pH	3 - 4	3 - 4

The Guaifenesin solution was prepared in the following manner:

Sucrose syrup containing sodium benzoate was prepared. The hot syrup was cooled down to 30°C. The sucrose syrup, glycerin and sorbitol were blended together to form Phase A.

An aqueous solution of polyethylene glycol (for Example 7-A) was prepared. An aqueous solution of Guaifenesin was prepared. The solutions were combined and stirred for 15 minutes to form Phase B.

Povidone was dissolved in water. The resulting solution was added to phase A. The admixture was stirred for 15 minutes to form Phase C. Phase B was added to Phase C to form Phase D.

An aqueous solution of citric acid was prepared to form phase E. An aqueous solution of sucralose was prepared to form Phase F. Phases E and F were added to Phase D. The admixture was stirred for one hour and the flavor added. The resulting admixture was stirred for two more hours to achieve homogeneity, and then purified water was added to adjust to the final volume. The syrups were allowed to stand for 24 hours before tasting.

Eleven respondents were asked to taste 1 ml each of Example 7-A and Example 7-B in random order. The respondents were asked to drink water after tasting each sample, and rest between samples taking unsalted crackers to remove traces of the first sample tasted. Each respondent was asked to pick a preference based on reduced bitterness.

Eight out of eleven respondents preferred Example 7-A (2.5% PVP + 1.25% PEG 4000) to Example 7-B (2.5% PVP). The result illustrates the significant reduction/elimination of bitterness in syrups when high MW polyethylene glycol is used with PVP.

Experiment 8

This example describes the preparation of Amoxicillin Trihydrate granules for reconstitution with water.

Table 14: Amoxicillin Trihydrate Granules

Ingredient	Example 8-A g/100 mL	Example 8-B g/100 mL
Amoxicillin Trihydrate	13	13
Sucrose	45	45
Sorbitan Monolaurate	0.06	0.06
Povidone (Kollidon K30)	2.5	2.5
Polyethylene Glycol 4000	0.50	0
Methylparaben	0.10	0.10
Propylparaben	0.02	0.02
Sodium Citrate Anhydrous	0.10	0.10
Precipitated Silica	1.2	1.2
Color	0.004	0.004
Flavoring	0.80	0.80
Purified Water	q.s. to 100 mL	q.s. to 100 mL

The Amoxicillin dry powder was prepared by sieving all the excipients prior to use. The screened excipients were premixed for 10 minutes. Amoxicillin Trihydrate was added to the excipient premix. The resulting powders were mixed for another 10 minutes.

The equivalent weight of granules for 100 mL of reconstituted product was weighed and placed into a bottle. Water was then added to the powders to a volume of 100 mL. The powder-water mixture was shaken until a visually homogeneous suspension was obtained.

Example 8-A was compared to Example 8-B. Ten respondents were requested to taste 1 mL of each sample in random order. Each respondent was requested to drink water after each medication, and take unsalted crackers between samples to remove traces of the

first sample tasted. Each respondent was asked to pick a preference based on reduced bitterness.

Eight out of ten respondents preferred Example 8-A to Example 8-B, illustrating the significant reduction/elimination of bitterness in extemporaneously prepared liquid suspensions when high MW polyethylene glycol is used with PVP.

Experiment 9

This example describes the preparation of Cloxacillin Sodium granules for reconstitution with water.

Table 15: Cloxacillin Sodium Granules

Ingredient	Example 9-A g/100 mL	Example 9-B g/100 mL
Cloxacillin	2.5	2.5
Sucrose	45	45
Sorbitan Monolaurate	0.06	0.06
Copolyvidone	2.5	2.5
Polyethylene Glycol 4000	1	0
Methylparaben	0.10	0.10
Propylparaben	0.02	0.02
Sodium Citrate Anhydrous	0.10	0.10
Precipitated Silica	1.2	1.2
Color	0.004	0.004
Flavoring	0.80	0.80
Purified Water	q.s. to 100 mL	q.s. to 100 mL

The Cloxacillin dry powder was prepared by sieving all the excipients prior to use. The screened excipients were premixed for 10 minutes. Cloxacillin Sodium was added to the excipient premix. The resulting powders were mixed for another 10 minutes.

The equivalent weight of granules for 100 mL of reconstituted product was weighed and placed into a bottle. Water was added to the powders to a volume of 100 mL. The

powder-water mixture was shaken until a visually homogeneous suspension was obtained.

Example 9-A was compared to Example 9-B. Eight respondents were requested to taste 1 mL of each sample in random order. Each respondent was requested to drink water after each medication, and take unsalted crackers between samples to remove traces of the first sample. Each respondent was asked to pick a preference based on reduced bitterness.

Seven out of ten respondents preferred Example 9-A to Example 9-B. The result illustrates the significant reduction/elimination of bitterness in extemporaneously prepared liquid suspensions when high molecular weight polyethylene glycol is used with Copolyvidone.

Experiment 10

This example describes the production of a liquid tastemasked syrup containing the antitussive Dextromethorphan Hydrobromide.

Table 16: Dextromethorphan Hydrobromide Syrup

Ingredient	grams per 100 ml
Dextromethorphan Hydrobromide	0.3
Sucrose	60
Povidone (Kollidon K25)	2.5
Polyethylene Glycol 6000	0.25
Sodium Benzoate	0.2
Sucralose	0.2
Saccharin sodium	0.13
Flavoring	0.3
Citric Acid	0.64
Sodium Citrate Dihydrate	2.66
Purified Water	q.s. to 100 mL
pH	4.5 – 5.5

The Dextromethorphan Hydrobromide syrup was prepared in the following manner:

Sucrose syrup containing sodium benzoate was prepared. The hot syrup was cooled down to 30°C to form Phase A.

A solution of polyethylene glycol in water was prepared. Dextromethorphan Hydrobromide was dissolved in this solution. The admixture was stirred for 15 minutes to form Phase B. Phase B was then added to Phase A and stirred for 15 minutes to form Phase C. Povidone was added directly into Phase C and stirred for one hour to form Phase D.

An aqueous solution of citric acid and sodium citrate dihydrate was prepared to form phase E. An aqueous solution of saccharin sodium and sucralose was prepared to form Phase F. Phases E and F were added to Phase D. The admixture was stirred for one hour and the flavor added. The resulting admixture was stirred for two more hours to achieve homogeneity, and then purified water was added to adjust to the final volume.

The formulation has an acceptable taste with no bitterness.

Experiment 11

This example describes the production of a liquid taste masked syrup containing the antihistamine Diphenhydramine Hydrochloride.

Table 17: Diphenhydramine Hydrochloride Syrup

Ingredient	grams per 100 ml
Diphenhydramine Hydrochloride	0.3
Sorbitol	40
Glycerin	30
Povidone (Kollidon K25)	5.0
Polyethylene Glycol 8000	2.25
Sodium Benzoate	0.2
Sucralose	0.2
Saccharin sodium	0.13
Flavoring	0.3
Citric Acid	0.64

Sodium Citrate Dihydrate	2.66
Purified Water	q.s. to 100 mL
pH	4.5 – 5.5

The Diphenhydramine Hydrochloride syrup was prepared in the following manner:

The sorbitol and glycerin were blended together to form Phase A.

A solution of polyethylene glycol in water was prepared. Diphenhydramine Hydrochloride was dissolved in this solution. The admixture was stirred for 15 minutes to form Phase B. Phase B was then added to Phase A and stirred for 15 minutes to form Phase C. Povidone was added directly into Phase C and stirred for one hour to form Phase D.

An aqueous solution of citric acid and sodium citrate dihydrate was prepared to form phase E. An aqueous solution of saccharin sodium and sucralose was prepared to form Phase F. Phases E and F were added to Phase D. The admixture was stirred for one hour and the flavor added. The resulting admixture was stirred for two more hours to achieve homogeneity, and then purified water was added to adjust to the final volume.

The formulation has an acceptable taste with no bitterness.

Experiment 12

This example describes the production of a liquid taste masked syrup containing the antihistamine Brompheniramine Maleate.

Table 18: Brompheniramine Maleate Syrup

Ingredient	grams per 100 ml
Brompheniramine maleate	0.08
Sorbitol Solution	40
Glycerin	30

Povidone (Kollidon K25)	2.5
Polyethylene Glycol 3350	2.25
Sodium Benzoate	0.2
Sucralose	0.2
Saccharin sodium	0.13
Flavoring	0.3
Citric Acid	0.05
Purified Water	q.s. to 100 mL
pH	3 - 4

The Brompheniramine Maleate syrup was prepared in the following manner:
The sorbitol and glycerin were blended together to form Phase A.

A solution of polyethylene glycol in water was prepared. Brompheniramine maleate was dissolved in this solution. The admixture was stirred for 15 minutes to form Phase B. Phase B was then added to Phase A and stirred for 15 min to form Phase C. Povidone was added directly into Phase C and stirred for one hour to form Phase D.

An aqueous solution of citric acid was prepared to form phase E. An aqueous solution of saccharin sodium and sucralose was prepared to form Phase F. Phases E and F were added to Phase D. The admixture was stirred for one hour and the flavor added. The resulting admixture was stirred for two more hours to achieve homogeneity, and then purified water was added to adjust to the final volume.

The formulation has an acceptable taste with no bitterness.

CLAIMS

We claim:

1. A liquid pharmaceutical composition or an extemporaneously prepared liquid pharmaceutical composition, comprising:
at least one unpleasant tasting drug;
polyethylene glycol of molecular weight at least 900, and
polyvinyl pyrrolidone and/or copolyvidone.

2. The method according to Claim 1, wherein said liquid pharmaceutical composition has a pH from about 2.5 to about 8.

3. The liquid pharmaceutical composition according to Claim 1, wherein the unpleasant drug is an aromatic compound with a hydrophilic group(s) that can form hydrogen bonds such as hydroxyl, carboxylic or amine groups.

4. The liquid pharmaceutical composition according to Claim 1 wherein the bitter drug is present at about 0.02 to about 15 percent by weight.

5. The liquid pharmaceutical composition according to Claim 1, wherein the amount of polyethylene glycol is from about 0.05 to about 10 weight percent.

6. The liquid pharmaceutical composition according to Claim 5, wherein the amount of polyethylene glycol is from about 0.1 to about 5 weight percent.

7. The liquid pharmaceutical composition according to Claim 1, wherein said polyethylene glycol is of molecular weight of from about 2000 to about 8000.

8. The liquid pharmaceutical composition according to Claim 1, wherein the polyvinyl pyrrolidone and/or copolyvidone is present at about 0.1 to about 30 weight percent.

9. The liquid pharmaceutical composition according to Claim 8, wherein the polyvinyl pyrrolidone and/or copolyvidone is present at about 1 to about 7 weight percent.

10. The liquid pharmaceutical compositions according to Claim 1, further comprising a sweetening agent and/or a viscosity building agent.

11. The liquid pharmaceutical composition according to Claim 10, wherein the said sweetening agent is selected from the group consisting of sugar, invert sugar, glucose, fructose, sorbitol, mannitol, xylitol, a high intensity artificial sweetener, a dipeptide sweetener, and combinations thereof.

12. The liquid pharmaceutical composition according to Claim 10, wherein said sweetening agent is present at about 30 to about 90 weight percent.

13. The liquid pharmaceutical composition according to Claim 10, wherein the said viscosity-building agent is selected from the group consisting of glycerin, xanthan gum, carrageenan, tragacanth, guar gum, pectin, carboxymethylcellulose, hydroxypropyl methylcellulose, methylcellulose, microcrystalline cellulose and carboxymethylcellulose blends, and mixtures thereof.

14. The liquid pharmaceutical composition according to Claim 10, wherein said viscosity building agent is present in an amount from about 0.1 to about 3 weight percent.

15. The liquid pharmaceutical composition according to Claim 1, wherein said composition is used to treat fever, infection, headache, pain, inflammation, excess mucus or phlegm, coughing, allergies, allergic diseases, nausea, vomiting, and motion sickness.

16. The liquid pharmaceutical composition according to Claim 15, wherein said unpleasant tasting drug is selected from the group consisting of an analgesic, an anti-inflammatory drug, an antihistamine, a decongestant, anti-infective, a mucolytic, an antitussive, an expectorant, and combinations thereof.

17. The liquid pharmaceutical composition according to Claim 16, wherein said analgesic or said anti-inflammatory drug is selected from the group consisting of acetaminophen, ibuprofen, naproxen, mefenamic acid, ketoprofen, celecoxib, rofecoxib, and tramadol, and combinations thereof.

18. The liquid pharmaceutical composition according to Claim 16, wherein said antihistamine is selected from the group consisting of loratadine, descarboethoxyloratadine, diphenhydramine, brompheniramine, chlorpheniramine, terfenadine, cetirizine, and combinations thereof.

19. The liquid pharmaceutical composition according to Claim 16, wherein said decongestant is selected from phenylpropanolamine, pseudoephedrine, phenylephrine, and combinations thereof.

20. The liquid pharmaceutical composition according to Claim 16, wherein said anti-infective is selected from amoxicillin, ampicillin, cloxacillin, flucloxacillin, penicillin, cephalexin, and combinations thereof.

21. The liquid pharmaceutical composition according to Claim 16, wherein said mucolytic is selected from the group consisting of ambroxol, carbocisteine, and bromhexine, and combinations thereof.

22. The liquid pharmaceutical composition according to Claim 16, wherein said antitussive or said expectorant is selected from the group consisting of caramiphen, dextromethrophan hydrobromide, codeine phosphate, codeine sulfate, guaifenesin, and combinations thereof.

23. The liquid pharmaceutical composition according to Claim 22, wherein said guaifenesin is present in an amount of about 1 to about 5 weight percent.

24. The liquid pharmaceutical composition according to Claim 23, further comprising at least one additional drug selected from the group consisting of a bronchodilator, a mucolytic, an antitussive, and combinations thereof.

25. The liquid pharmaceutical composition according to Claim 24, wherein said bronchodilator is selected from the group consisting of salbutamol, terbutaline, theophylline, and combinations thereof.

26. The liquid pharmaceutical composition according to Claim 24, wherein said antitussive is selected from the group consisting of caramiphen, dextromethrophan hydrobromide, codeine phosphate, codeine sulfate, and combinations thereof.

27. The liquid pharmaceutical composition according to Claim 24, wherein said mucolytic is selected from the group consisting of ambroxol, carbocisteine, and bromhexine, and combinations thereof.

28. The liquid pharmaceutical composition according to Claim 17, wherein said acetaminophen is present in an amount of about 1 to about 10 weight percent.

29. The liquid pharmaceutical composition according to Claim 28, further comprising at least one additional drug selected from the group consisting of an analgesic, an anti-inflammatory drug, an antihistamine, a decongestant, an antitussive, an expectorant, a mucolytic, and combinations thereof.

30. The liquid pharmaceutical composition according to Claim 29 wherein said analgesic or said anti-inflammatory agent is selected from the group consisting ibuprofen, naproxen, mefenamic acid, ketoprofen, celecoxib, rofecoxib, tramadol, and combinations thereof.

31. The liquid pharmaceutical composition according to Claim 29, wherein said antihistamine is selected from the group consisting of loratadine, descarboethoxyloratadine, diphenhydramine, brompheniramine, chlorpheniramine, terfenadine, cetirizine, and combinations thereof.

32. The liquid pharmaceutical composition according to Claim 29, wherein the decongestant is selected from the group consisting of phenylpropanolamine, pseudoephedrine, phenylephrine, and combinations thereof.

33. The liquid pharmaceutical composition according to Claim 29, wherein said antitussive or said expectorant is selected from the group consisting of caramiphen, dextromethrophan hydrobromide, codeine phosphate, codeine sulfate, guaifenesin, and combinations thereof.

34. The liquid pharmaceutical composition according to Claim 29, wherein said mucolytic is selected from the group consisting of ambroxol, carbocisteine, and bromhexine, and combinations thereof.

35. A liquid pharmaceutical composition comprising:
5 g acetaminophen, 0.3 g xanthan gum, 55 g sucrose, 10 g 70% sorbitol solution, 20 g invert sugar, 5 g glycerin, 2.5 to 5 g crospovidone, 0 to 2.5 g polyethylene glycol with an average molecular weight between 1000 to 4000, 0.2 g sodium benzoate, 0.05 g sorbitan monolaurate, 0.2 g edetate disodium, 0.2 g sucralose, 0.13 g saccharin sodium, 0 to 0.006 g FD&C or D&C color, 0.2 to 0.4 g flavor, water to a volume of 100 mL, citric acid-sodium citrate dihydrate to a pH of 5 to 6.

36. A liquid pharmaceutical composition comprising:
10 g acetaminophen, 0.3 g xanthan gum, 54 g sucrose, 10 g 70% sorbitol solution, 20 g invert sugar, 5 g glycerin, 5 to 10 g crospovidone, 0 to about 1 g polyethylene glycol with an average molecular weight between 1000 to 4000, 0.2 g sodium benzoate, 0.05 g sorbitan monolaurate, 0.2 g edetate disodium,

0.4 g sucralose, 0.26 g saccharin sodium, 0 to 0.006 g FD&C or D&C color, 0.2 to 0.4 g flavor, water to a volume of 100 mL, citric acid-sodium citrate dihydrate to a pH of 5 to 6.

37. A liquid pharmaceutical composition comprising :
2 to 4 g guaifenesin, 51 g sucrose, 30 g 70% sorbitol solution, 7.5 g glycerin, 2.5 g to 5 g povidone, 0 to 1.5 g polyethylene glycol with an average molecular weight between 1000 to 4000, 0.2 g sodium benzoate, 0.1 g sucralose, from about 0.2 to about 0.4 g flavor, water to a volume of 100 mL, citric acid to a pH of 3 to 4.

38. A liquid pharmaceutical composition comprising :
0.3 g dextromethorphan hydrobromide, 60 g sucrose, 20 g invert sugar, 2.5 g to 5 g povidone, from about 0 to 1 g polyethylene glycol with an average molecular weight between 1000 to 6000, 0.2 g sodium benzoate, 0.2 g sucralose. 0.13 g saccharin sodium, 0.2 to about 0.4 g flavor, water to a volume of 100 mL, citric acid-sodium citrate dihydrate to a pH of 4.5 to 5.5.

39. A liquid pharmaceutical composition comprising :
0.3 g diphenhydramine hydrochloride, 40 g 70% sorbitol solution, 30 g glycerin, 2.5 g to 5 g povidone, 0 to 2.25 g polyethylene glycol with an average molecular weight between 1000 to 8000, 0.2 g sodium benzoate, 0.2 g sucralose. 0.13 g saccharin sodium, 0.2 to 0.4 g flavor, water to a volume of 100 mL, citric acid-sodium citrate dihydrate to a pH of 4.5 to 5.5.

40. A liquid pharmaceutical composition comprising :
0.08 g brompheniramine maleate, 40 g 70% sorbitol solution, 30 g glycerin, 2.5 g to 5 g povidone, 0 to 2.25 g polyethylene glycol with an average molecular weight between 1000 to 8000, 0.2 g sodium benzoate, 0.2 g sucralose. 0.13 g saccharin sodium, 0.2 to 0.4 g flavor, water to a volume of 100 mL, citric acid-sodium citrate dihydrate to a pH of 3 to 4.

41. A ready-to-use powder or granules for reconstitution wherein after reconstitution to 100 mL with water, the liquid pharmaceutical composition comprises:

3.25 to 13 g amoxicillin trihydrate, 45 g sucrose, 0.06 g sorbitan monolaurate, 0.5 to 2.5 g povidone and/or copolyvidone, 0.1 to about 0.5 g polyethylene glycol with an average molecular weight between 1000 to 8000, 0.10 g methylparaben, 0.02 propylparaben, 0 to 0.004 g FD&C or D&C color, 0.20 to 1 g flavor, 1.2 g precipitated silica, and sodium citrate to pH 4-6.

42. A ready-to-use powder or granules for reconstitution wherein after recontitution to 100 mL with water, the liquid pharmaceutical composition comprises:

2 to 10 g cloxacillin sodium, 45 g sucrose, 0.06 g sorbitan monolaurate, 0.5 to 2.5 g povidone and/or copolyvidone, 0.1 to about 0.5 g polyethylene glycol with an average molecular weight between 1000 to 8000, 0.10 g methylparaben, 0.02 propylparaben, 0 to 0.004 g FD&C or D&C color, 0.20 to 1 g flavor, 1.2 g precipitated silica, and sodium citrate to pH 4-6.

43. A method for preparing a taste-masked liquid pharmaceutical composition, comprising combining:

at least one unpleasant-tasting drug;

polyethylene glycol with a molecular weight of at least 900;

polyvinyl pyrrolidone and/or a copolyvidone; and

an aqueous liquid excipient base.

44. The method according to Claim 43, wherein said polyethylene glycol has an average molecular weight of from about 2000 to about 8000.

45. The method according to Claim 43, wherein said polyethylene glycol has an average molecular weight of from about 4000 to about 6000.

46. The method according to Claim 43, wherein said liquid pharmaceutical composition further comprises one or more additives selected from the group consisting of sweetening agents, flavors, colorants, antioxidants, chelating agents, viscosity-building agents, surfactants, pH modifiers, bulking agents, acidifiers, cosolvents, anticaking agents, and mixtures thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/PH02/00008

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: A61K 9/08; A61K 47/30, 47/32

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)
PEG, PVP, COPOLYVIDONE

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT, Medline

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1025858 A (EISAI CO LTD.) 9 March 2000 Entire document	1-46
X	WO 95/23595 A (THE PROCTOR AND GAMBLE COMPANY) 8 September 1995 Entire document	1-46
X	WO 95/19792 A (THE PROCTOR AND GAMBLE COMPANY) 27 July 1995 Entire document	1-46

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

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"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
13 November 2002	25 NOV 2002
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer NICOLE HOWARD Telephone No : (02) 6283 2245

INTERNATIONAL SEARCH REPORT

International application No.
PCT/PH02/00008

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95/19759 A (THE PROCTOR AND GAMBLE COMPANY) 27 July 1995 Entire document	1-46
X	EP 441307 A (SHOWA YAKUHIN KAKO CO., LTD.) 14 August 1991 Entire document	1-46
X	WO 95/04527 A (SCHERER CORPORATION) 16 February 1995 Entire document	1-46

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/PH02/00008

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
EP	1025858	JP	2000136134	WO	200012135		
WO	9519759	AU	16075/95	BR	9506564	CA	2181241
		CN	1138827	CZ	9602104	EP	741560
		FI	962948	HU	74909	NO	963052
		NZ	279443	PL	315635	SK	961/96
		US	5484606	WO	9519792		
EP	441307	CA	2035693	JP	3232816	US	5154926
WO	9504527	AU	76299/94	BR	9407178	CA	2168732
		EP	713390	US	5505961		
WO	9519792	HU	74909	US	5484606	AU	16075/95
		BR	9506564	CA	2181241	CN	1138827
		CZ	9602104	EP	741560	FI	962948
		NO	963052	NZ	279443	PL	315635
		SK	961/96	WO	9519759		
WO	9523595	AU	19357/95	CA	2184365	US	5510389

END OF ANNEX

Industria y Comercio
SUPERINTENDENCIA

2020
Bogotá, D.C.,

Doctor:
Álvaro Correa Ordoñez
Apoderado

Oficio N°: 0U 0305

ASUNTO:

Radicación PCT Nº	09-2495
Trámite	011
Evento	378
Actuación	440
Folios	009

Con fundamento en lo previsto por el artículo 43 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica que la oposición presentada por la doctora Eliana Isaura Moreno Bohórquez, en su calidad de apoderada de Procaps S.A., reúne los requisitos formales exigidos por la ley al momento de su presentación.

En cumplimiento de lo dispuesto en la citada norma, se le concede el término de sesenta (60) días hábiles siguientes a la fecha de notificación del presente oficio, para que haga valer sus argumentaciones y presente pruebas.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única Nº 10 de 2001.

JOSÉ LUÍS SALAZAR LÓPEZ
Director de Nuevas Creaciones (E).

07 ENE. 2011

El anterior oficio fue notificado por fijación en lista de fecha, _____.

202088

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Industria y Comercio
SUPERINTENDENCIA

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 09 002495

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCIÓN**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **618** DE

FECHA **19 DE JULIO 2010** EL TÉRMINO HÁBIL SEÑALADO POR LA LEY

EXPIRA EL **13 DE OCTUBRE DE 2010**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI ___X___ NO _____