

AS. 134.955

DIRECCIÓN DE NUEVAS CREACIONES
Procedimiento acelerado de exámenes de patente (PPH)

1	NÚMERO DE SOLICITUD ANTE LA SIG	15 258 581		
2	OFICINA DE PRIMERA PRESENTACIÓN (OPP)	USPTO		
3	NÚMERO(S) DE SOLICITUD O PUBLICACIÓN DE LA(S) SOLICITUD(ES) (OPP):	1. 14/254,023 2. 3.		
4	☐ REPRESENTANTE LEGAL ☒ APODERADO			
APELLIDOS CADENA SARMIENTO		NOMBRES JUAN PABLO		
		IDENTIFICACIÓN C.C. 80.410.337 T.P. 57492		
DIRECCIÓN	Calle 70A 4 41	No. TELÉFONO 7442200		
CIUDAD	Bogotá, D.C.	CORREO ELECTRÓNICO notificaciones@bc.com.co		
PAÍS	CO	No. RADICACIÓN O PROTOCOLO DE PODER GENERAL		
5	CONDICIONES PARA ACCEDER A ESTE PROCESO:			
5.1.	DATOS DE PRIORIDAD ☒ SI ☐ NO			
1. US	(33) PAÍS DE ORIGEN	CÓDIGO PAÍS	(31) NÚMERO	(32) FECHA (AAAA/MM/DD)
2. US		US	61/911,201	2013/12/03
3.		US	61/813,064	2013/04/17
4.				
5.2.	DATOS SOLICITUD INTERNACIONAL PCT ☒ SI ☐ NO			
Solicitud Internacional No.		PCT/US2014/034301	Fecha	16.04.2014
Publicación Internacional No.		WO 2014/172423	Fecha	23.10.2014
El solicitante presenta una copia de la(s) reivindicación(es) patentable(s) u otorgable(s) de la solicitud de la Oficina de Primera Presentación que profirió el examen de patentabilidad, junto con una traducción al castellano. ☒ SI ☐ NO				
REQUISITOS PARA EL RECONOCIMIENTO DE LOS RESULTADOS DE EXÁMENES DE PATENTABILIDAD EFECTUADOS A SOLICITUDES EXTRANJERAS				
Para que la Superintendencia de Industria y Comercio pueda reconocer los resultados de exámenes de patentabilidad producidos por otras Oficinas de Propiedad Industrial se debe cumplir con las siguientes condiciones:				
(a) Al momento de solicitar el examen de patentabilidad, si el solicitante pide que se reconozcan exámenes de patentabilidad de otras oficinas extranjeras, deberá aportar junto con el pago de la tasa correspondiente, los siguientes anexos:				
(i) Copia de las resoluciones, fallos o decisiones que han sido relevantes para la determinación de la patentabilidad de la(s) solicitud(es) en la Oficina que haya proferido el examen de patentabilidad que contienen reivindicaciones patentables u otorgables que son la base de la petición, y si es del caso, su traducción al castellano. ☒ SI ☐ NO				
(ii) Copia de todas las reivindicaciones determinadas como patentables u otorgables en la Oficina que profirió el examen de patentabilidad y, si es del caso, su traducción al castellano. ☒ SI ☐ NO				
(iii) Copia de los antecedentes, información o documentos citados por el examinador de la Oficina de Primera Presentación del examen de patentabilidad, en las resoluciones, fallos o decisiones correspondientes, incluyendo la literatura no patente. Los documentos de patente deberán presentarse siempre y cuando no estén disponibles para la Superintendencia de Industria y Comercio mediante el simple acceso a bases de datos gratuitas. ☐ SI ☒ NO				
(iv) Una tabla de correspondencias de las reivindicaciones que han sido determinadas como patentables u otorgables en la solicitud de la Oficina que haya proferido el examen de patentabilidad.				
7	FIRMA DEL SOLICITANTE, DEL APODERADO O DEL REPRESENTANTE LEGAL <i>Junto a cada firma, indicar el nombre del firmante y su calidad (si tal calidad no es obvia al leer el petitorio).</i>			

Señor

DIRECTOR DIVISIÓN DE NUEVAS CREACIONES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

E.

S.

D.

REF: Expediente No. **15.268581** solicitud de patente de invención a favor de **SIGNAL PHARMACEUTICALS LLC** Título **FORMULACIONES FARMACÉUTICAS, PROCESO, FORMAS SÓLIDAS Y MÉTODOS DE USO RELACIONADOS CON 1-ETIL-7-(2-METIL-6-(1H-1,2,4-TRIAZOL-3-IL)PIRIDIN-3-IL)-3,4-DIHIDROPIRAZINO[2,3-b]PIRAZIN-2(1H)-ONA**

PETICION TRAMITE ACELERADO DE PATENTES

JUAN PABLO CADENA SARMIENTO, portador de la tarjeta profesional No. 57.492 del C.S.J., obrando como apoderado de la sociedad solicitante me permito presentar los siguientes documentos para participar en el programa de trámite acelerado de patentes.

- a. Copia de la acción oficial de patentabilidad emitida por la USPTO junto con la traducción al español.
- b. Copia de la respuesta del solicitante el **14 de enero de 2016** junto con las reivindicaciones modificadas y su correspondiente traducción al español.
- c. Copia de la notificación de concesión (notice of allowability) en donde se establece que las reivindicaciones concedidas son las **10 y 12-38** de la respuesta del solicitante radicada el **14 de enero de 2016**.
- d. Notificación de aceptación (notice of allowance) en donde se establece que la solicitud ha sido examinada y aceptada para conceder la patente.
- e. Tabla de correspondencia entre las reivindicaciones concedidas por la USPTO y las reivindicaciones modificadas en Colombia el 7 de diciembre de 2016.

En consecuencia, solicitamos a su Despacho tener en cuenta el examen de patentabilidad y las reivindicaciones concedidas por la USPTO y proceder con la concesión de la patente para la solicitud en Colombia.

Del Señor Director

JUAN PABLO CADENA SARMIENTO

T.P. No. 57.492 del C.SJ.

C.C. 80.410.337 de Usaquén

Calle 70 A No. 4 - 41



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NOTICE OF ALLOWANCE AND FEE(S) DUE

84802 7590 02/04/2016
JONES DAY for Celgene Corporation
222 E. 41ST. STREET
NEW YORK, NY 10017

EXAMINER	
COUGHLIN, MATTHEW P	
ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 02/04/2016

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/254,023	04/16/2014	Anil Menon	10624-345-999	7694
TITLE OF INVENTION: PHARMACEUTICAL FORMULATIONS, PROCESSES, SOLID FORMS AND METHODS OF USE RELATING TO 1-ETHYL-7-(2-METHYL-6-(1H-1,2,4-TRIAZOL-3-YL)PYRIDIN-3-YL)-3,4-DIHYDROPYRAZINO[2,3-b]PYRAZIN-2(1H)-ONE				

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$960	\$0	\$0	\$960	05/04/2016

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

Notice of Allowability	Application No. 14/254,023	Applicant(s) MENON ET AL.	
	Examiner MATTHEW COUGHLIN	Art Unit 1626	AIA (First Inventor to File) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the amendment filed 14 January 2016.
☐ A declaration(s)/affidavit(s) under 37 CFR 1.130(b) was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are 10 and 12-38. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some *c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)	5. ☒ Examiner's Amendment/Comment
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____	6. ☐ Examiner's Statement of Reasons for Allowance
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material	7. ☐ Other _____
4. ☒ Interview Summary (PTO-413), Paper No./Mail Date <u>20160202</u> .	

/MATTHEW COUGHLIN/ Primary Examiner, Art Unit 1626	
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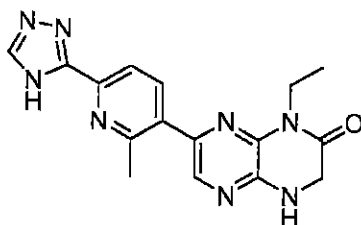
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

1-9. (Canceled)

10. (Currently Amended) A ~~solid~~ crystal form of Compound 1, or a tautomer thereof:



Compound 1

which has an X-ray powder diffraction pattern comprising peaks at approximately 9.8, 12.0 and 17.9 °2θ.

11. (Canceled)

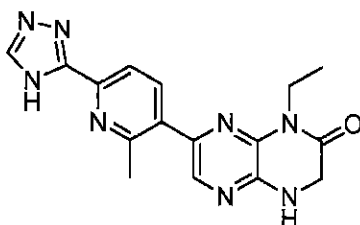
12. (Currently Amended) A pharmaceutical composition comprising ~~Compound 1, or a pharmaceutically acceptable salt, tautomer, isotopologue or stereoisomer thereof~~ the crystal form of claim 10, and one or more pharmaceutically acceptable excipients or carriers, each independently selected from carboxymethyl cellulose, cellulose, lactose, magnesium stearate, starch, and stearic acid.

13. (New) The crystal form of claim 10 which has an X-ray powder diffraction pattern further comprising peaks at approximately 15.9, 25.2 and 27.1 °2θ.

14. (New) The crystal form of claim 10 which has a differential scanning calorimetry thermogram comprising an endotherm with a maximum at approximately 269.6 °C when heated from about 25 °C to about 300 °C.

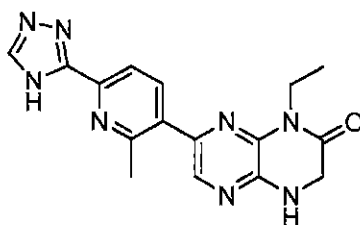
15. (New) The crystal form of claim 10 which is substantially pure.

16. (New) A crystal form of Compound 1, or a tautomer thereof:



Compound 1

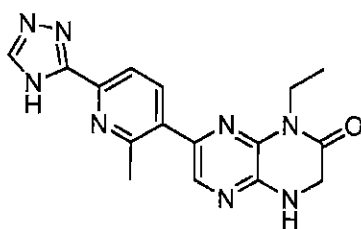
- which has an X-ray powder diffraction pattern comprising peaks at approximately 7.5, 10.4 and 11.7 °2θ.
17. (New) The crystal form of claim 16 which has an X-ray powder diffraction pattern further comprising peaks at approximately 4.9, 8.6 and 17.9 °2θ.
18. (New) The crystal form of claim 16 which has a differential scanning calorimetry thermogram comprising an endotherm with a maximum at approximately 267.8 °C when heated from about 25 °C to about 300 °C.
19. (New) The crystal form of claim 16 which has a differential scanning calorimetry thermogram comprising an exotherm with a maximum at approximately 158.8 °C when heated from about 25 °C to about 300 °C.
20. (New) The crystal form of claim 16 which is substantially pure.
21. (New) A pharmaceutical composition comprising the crystal form of claim 16, and one or more pharmaceutically acceptable excipients or carriers, each independently selected from carboxymethyl cellulose, cellulose, lactose, magnesium stearate, starch, and stearic acid.
22. (New) A crystal form of Compound 1, or a tautomer thereof:



Compound 1

which has an X-ray powder diffraction pattern comprising peaks at approximately 9.3, 11.7 and 19.9 °2θ.

23. (New) The crystal form of claim 22 which has an X-ray powder diffraction pattern further comprising peaks at approximately 7.4, 17.3 and 23.7 °2θ.
24. (New) The crystal form of claim 22 which has a differential scanning calorimetry thermogram comprising an endotherm with a maximum at approximately 270.3 °C when heated from about 25 °C to about 300 °C.
25. (New) The crystal form of claim 22 which has a differential scanning calorimetry thermogram comprising an exotherm with a maximum at approximately 135.9 °C when heated from about 25 °C to about 300 °C.
26. (New) The crystal form of claim 22 which is substantially pure.
27. (New) A pharmaceutical composition comprising the crystal form of claim 22, and one or more pharmaceutically acceptable excipients or carriers, each independently selected from carboxymethyl cellulose, cellulose, lactose, magnesium stearate, starch, and stearic acid.
28. (New) A crystal form of Compound 1, or a tautomer thereof:

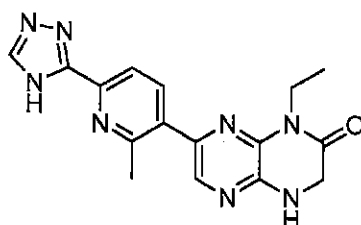


Compound 1

which has an X-ray powder diffraction pattern comprising peaks at approximately 11.0, 20.2 and 21.9 °2θ.

29. (New) The crystal form of claim 28 which has an X-ray powder diffraction pattern further comprising peaks at approximately 18.2, 19.6 and 23.4 °2θ.

30. (New) The crystal form of claim 28 which has a differential scanning calorimetry thermogram comprising an endotherm with a maximum at approximately 269.0 °C when heated from about 25 °C to about 300 °C.
31. (New) The crystal form of claim 28 which is substantially pure.
32. (New) A pharmaceutical composition comprising the crystal form of claim 28, and one or more pharmaceutically acceptable excipients or carriers, each independently selected from carboxymethyl cellulose, cellulose, lactose, magnesium stearate, starch, and stearic acid.
33. (New) A crystal form of Compound 1, or a tautomer thereof:



Compound 1

- which has an X-ray powder diffraction pattern comprising peaks at approximately 9.3, 15.3 and 18.6 °2θ.
34. (New) The crystal form of claim 33 which has an X-ray powder diffraction pattern further comprising peaks at approximately 7.0, 10.5 and 23.2 °2θ.
35. (New) The crystal form of claim 33 which has a differential scanning calorimetry thermogram comprising an endotherm with a maximum at approximately 269.7 °C when heated from about 25 °C to about 300 °C.
36. (New) The crystal form of claim 33 which has a differential scanning calorimetry thermogram comprising an exotherm with a maximum at approximately 180.4 °C when heated from about 25 °C to about 300 °C.
37. (New) The crystal form of claim 33 which is substantially pure.

38. (New) A pharmaceutical composition comprising the crystal form of claim 33, and one or more pharmaceutically acceptable excipients or carriers, each independently selected from carboxymethyl cellulose, cellulose, lactose, magnesium stearate, starch, and stearic acid.

REMARKS

Upon entry of the presently made amendments, claims 10 and 12-38 will be pending.

Claims 1-9 and 11 have been canceled, without prejudice.

Claim 10 has been amended, without prejudice, to recite a crystal form of Compound 1 having an X-ray powder diffraction pattern comprising peaks at approximately 9.8, 12.0 and 17.9 °2 θ . Support for such an amendment can be found throughout the specification as filed, at least at paragraphs [00104] and [00247].

Claim 12 has been amended, without prejudice, to depend from claim 10. Support for such an amendment can be found throughout the specification as filed, at least at paragraph [00173].

New claims 13-38 have been added. Support for new claims 13-38 can be found at least in the below listed paragraphs of the application as filed as follows:

Claim No.	Support
13	Paragraphs [00104] and [00247]
14	Paragraphs [00106], [00244] and [00246]
15	Paragraph [00109]
16	Paragraphs [00110] and [00250]
17	Paragraphs [00110] and [00250]
18	Paragraphs [00112], [00244] and [00249] and FIG. 9
19	Paragraph [00244] and FIG. 9
20	Paragraph [00115]
21	Paragraph [00173]
22	Paragraphs [00116] and [00253]
23	Paragraphs [00116] and [00253]
24	Paragraphs [00252] and [00244] and FIG. 14
25	Paragraph [00244] and FIG. 14
26	Paragraph [00121]
27	Paragraph [00173]
28	Paragraphs [00122] and [00256]

29	Paragraphs [00122] and [00256]
30	Paragraphs [00124] and [00244] and FIG. 19
31	Paragraph [00126]
32	Paragraph [00173]
33	Paragraphs [00127] and [00259]
34	Paragraphs [00127] and [00259]
35	Paragraphs [00129] and [00244] and FIG. 23
36	Paragraph [00244] and FIG. 23
37	Paragraph [00132]
38	Paragraph [00173]

No new matter has been added.

Applicants reserve their right to prosecute the subject matter of any canceled claim, any amended claim, any withdrawn claim or any unclaimed subject matter in one or more related applications.

I. Claim Objection

Claim 12 is objected for allegedly not explicitly defining “Compound 1” by name or structure.

Without acquiescing in the rejection, and solely to expedite prosecution of the present application, claim 12 has been amended, without prejudice, to depend from claim 10.

Applicants respectfully submit that the objection of claim 12 has been overcome and should be withdrawn.

II. Rejection Under 35 U.S.C. § 112, Indefiniteness

Claim 11 is rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite.

Without acquiescing in the rejection, and solely to expedite prosecution of the present application, claim 11 has been canceled, without prejudice.

Applicants respectfully submit that the rejection of claim 11 under 35 U.S.C. § 112, second paragraph, is moot and should be withdrawn because of the cancellation of claim 11.

III. Rejection Under 35 U.S.C. § 102, Novelty

Claim 10 is rejected under 35 U.S.C. 102(a)(1) as allegedly being anticipated by U.S. Pat. App. Pub. No. 2011/0137028 to Harris *et al.* (hereinafter “Harris”). Applicants respectfully traverse this rejection.

Without acquiescing in the rejection, and solely to expedite prosecution of the present application, claim 10 has been amended, without prejudice, to recite a crystal form of Compound 1 having an X-ray powder diffraction pattern comprising peaks at approximately 9.8, 12.0 and 17.9 °2θ.

The Federal Circuit held that anticipation is established only when a single prior art reference discloses, either expressly or under the principles of inherency, each and every element of the claimed invention. *In re Spada*, 911 F.2d 705, 707, (Fed. Cir. 1990); *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444 (Fed. Cir. 1984); *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants respectfully submit that at least because Harris does not provide any teaching regarding a crystal form of Compound 1 having an X-ray powder diffraction pattern comprising peaks at approximately 9.8, 12.0 and 17.9 °2θ, Harris does not anticipate claim 10.

Accordingly, Applicants respectfully submit that the rejection to claim 10 under 35 U.S.C. § 102(a)(1) has been overcome and should be withdrawn.

IV. Rejection Under 35 U.S.C. § 103, Obviousness

Claim 12 is rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Pat. App. Pub. No. 2010/0216781 to Perrin-Ninkovic *et al.* (hereafter “Perrin-Ninkovic”). Applicants respectfully traverse this rejection.

Without acquiescing in the rejection, and solely to expedite prosecution of the present application, claim 12 has been amended, without prejudice, to depend from claim 10.

A. Perrin-Ninkovic does not teach or suggest every element of claim 12.

To reject a claim based on obviousness, an Examiner must resolve the *Graham* factual inquiries. Then, an Examiner must articulate a finding that the prior art included each element claimed, although not necessarily in a single prior art reference, with the only difference between the claimed invention and the prior art being the lack of actual combination of the elements in a

single prior art reference. *KSR Int'l Co. v. Teleflex Inc.*, 82 U.S.P.Q.2d 1385, 1395 (2007); *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 U.S.P.Q. 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163 U.S.P.Q. 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 U.S.P.Q. 303, 306 (1950); MPEP § 2143.A.

Applicants respectfully submit that because Perrin-Ninkovic does not provide any teaching or suggestion regarding a crystal form of Compound 1 having an X-ray powder diffraction pattern comprising peaks at approximately 9.8, 12.0 and 17.9 °2 θ as recited in claim 10, and because claim 12 depends from claim 10, Perrin-Ninkovic does not teach or suggest each and every element of claim 12.

Without the required finding that the prior art teaches or suggests each element claimed, Applicants respectfully submit that a proper *prima facie* case of obviousness cannot be made. MPEP § 2143.A.

B. Polymorph production is unpredictable.

The Examiner has noted that Perrin-Ninkovic teaches Compound 1. *See* page 7, the Office Action mailed on October 14, 2015.

Applicants respectfully submit that claim 12 recites a novel crystal form not disclosed, inherently or otherwise, by Perrin-Ninkovic.

Applicants respectfully submit that it is well established that crystal forms, even of known compounds, can be patented. *Glaxo, Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047 (Fed. Cir. 1995).

Applicants respectfully submit that Perrin-Ninkovic does not teach or suggest any method for producing the claimed crystal forms of Compound 1. Accordingly, Applicants respectfully submit that Perrin-Ninkovic cannot support a proper *prima facie* case of obviousness of claim 12.

Specifically, while Perrin-Ninkovic enables the preparation of Compound 1 itself, it does not provide the requisite guidance to enable a person having ordinary skill in the art (hereinafter "PHOSITA") to prepare the claimed crystal forms of Compound 1 with a reasonable expectation of success.

Applicants respectfully submit that it is not possible to predict *a priori* if crystalline forms of a compound even exist, let alone how to successfully prepare them. *See* (i) Braga and

Grepioni, 2005, "Making crystals from crystals: a green route to crystal engineering and polymorphism," *Chem. Commun.*:3635-3645; (ii) Jones *et al.*, 2006, Pharmaceutical Cocrystals: An Emerging Approach to Physical Property Enhancement," *MRS Bulletin* 31:875-879; (iii) Price, 2004, "The computational prediction of pharmaceutical crystal structures and polymorphism," *Advanced Drug Delivery Reviews* 56:301-319; and (iv) Bernstein, 2004, "Crystal Structure Prediction and Polymorphism," *ACA Transactions* 39:14-23 (a copy of each enclosed herewith).

Applicants respectfully submit that these references teach the high degree of unpredictability in the field of crystalline form production, such that a PHOSITA would have no reasonable expectation of success with respect to preparing the claimed crystal forms of Compound 1. Without the required reasonable expectation of success, Applicants respectfully submit that a proper *prima facie* case of obviousness cannot be made. *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988); MPEP § 2143.02.

Accordingly, Applicants respectfully submit that the rejection of claim 12 under 35 U.S.C. 103(a) has been overcome and should be withdrawn.

V. Claim Rejections – Obviousness-type Double Patenting

(1) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 14-28 of U.S. Patent No. 8,110,578 (hereafter "'578") in view of Harris and in further view of Perrin-Ninkovic.

(2) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4, 6, 8, 9, 16, 19 and 20 of U.S. Patent No. 8,507,492 (hereafter "'492") in view of Harris and in further view of Perrin-Ninkovic.

(3) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-27 of U.S. Patent No. 9,079,900 (hereafter "'900") in view of Harris and in further view of Perrin-Ninkovic.

(4) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-21 of U.S. Patent No. 8,686,135 (hereafter "'135") in view of Harris and in further view of Perrin-Ninkovic.

(5) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-7 of U.S. Patent App. No. 13/192,792 (hereafter “792”) in view of Harris and in further view of Perrin-Ninkovic.

(6) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-22 of U.S. Patent App. No. 13/803,323 (hereafter “323”) in view of Harris and in further view of Perrin-Ninkovic.

(7) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-22 of U.S. Patent App. No. 13/803,317 (hereafter “317”) in view of Harris and in further view of Perrin-Ninkovic.

(8) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-22 of U.S. Patent App. No. 13/803,061 (hereafter “061”) in view of Harris and in further view of Perrin-Ninkovic.

(9) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-22 of U.S. Patent App. No. 13/803,305 (hereafter “305”) in view of Harris and in further view of Perrin-Ninkovic.

(10) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-3, 6 and 10-34 of U.S. Patent App. No. 14/055,985 (hereafter “985”) in view of Harris and in further view of Perrin-Ninkovic.

(11) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-19 of U.S. Patent App. No. 14/254,010 (hereafter “010”) in view of Harris and in further view of Perrin-Ninkovic.

(12) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-19 of U.S.

Patent App. No. 14/254,020 (hereafter "'020") in view of Harris and in further view of Perrin-Ninkovic.

(13) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-17 of U.S. Patent App. No. 14/254,009 (hereafter "'009") in view of Harris and in further view of Perrin-Ninkovic.

(14) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-7 of U.S. Patent App. No. 14/254,017 (hereafter "'017") in view of Harris and in further view of Perrin-Ninkovic.

(15) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-34 of U.S. Patent App. No. 14/254,004 (hereafter "'004") in view of Harris and in further view of Perrin-Ninkovic.

(16) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-24 of U.S. Patent App. No. 14/254,001 (hereafter "'001") in view of Harris and in further view of Perrin-Ninkovic.

(17) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-33 of U.S. Patent App. No. 14/254,015 (hereafter "'015") in view of Harris and in further view of Perrin-Ninkovic.

(18) Claims 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-20 of U.S. Patent App. No. 14/137,700 (hereafter "'700") in view of Harris and in further view of Perrin-Ninkovic.

Without acquiescing in the rejection, and solely to expedite prosecution of the present application, claim 10 has been amended, without prejudice, to recite a crystal form of Compound 1 having an X-ray powder diffraction pattern comprising peaks at approximately 9.8, 12.0 and 17.9 °2 θ .

Without acquiescing in the rejection, and solely to expedite prosecution of the present application, claim 12 has been amended, without prejudice, to depend from claim 10.

Applicants respectfully submit that none of the above references, *i.e.*, '578, '492, '900, '135, '792, '323, '317, '061, '305, '985, '010, '020, '009, '017, '004, '001, '015, '700, Harris and Perrin-Ninkovic, teach or suggest each and every element of claims 10 and 12. In particular, none of the above references teach or suggest a crystal form of Compound 1 having an X-ray powder diffraction pattern comprising peaks at approximately 9.8, 12.0 and 17.9 °2θ as recited in claims 10 and 12. Without the required finding that the prior art teaches or suggests each element claimed, Applicants respectfully submit that a proper *prima facie* case of obviousness cannot be made. *KSR*, 82 U.S.P.Q.2d at 1395; *Sakraida*, 189 U.S.P.Q. at 453; *Anderson's-Black Rock, Inc.*, 163 U.S.P.Q. at 675; *Great Atlantic & P. Tea Co.*, 87 U.S.P.Q. at 306; MPEP § 2143.A.

Applicants respectfully submit that a PHOSITA would have no reasonable expectation of success with respect to preparing the crystal form of Compound 1 recited in claims 10 and 12 for the reasons set forth above. Without the required reasonable expectation of success, Applicants respectfully submit that a proper *prima facie* case of obviousness cannot be made. *In re Dow Chem. Co.*, 837 F.2d at 473; MPEP § 2143.02.

Accordingly, Applicants respectfully submit that the rejection of claims 10 and 12 under the judicially created doctrine of obviousness-type double patenting has been overcome and should be withdrawn.

CONCLUSION

Applicants have made an earnest and *bona fide* effort to clarify the issues before the Examiner and to place this case in condition for allowance. Reconsideration and allowance of all claims is believed to be in order, and a timely Notice of Allowance to this effect is respectfully requested.

It is estimated that no fee is due in connection with this Response other than that due in connection with the additional claims; however, in the event that any additional fee is due, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Date: January 14, 2016

/Michael J. Bruner/

By: Michael J. Bruner (Reg. No. 47,458)

JONES DAY

222 East 41st Street

New York, New York 10017

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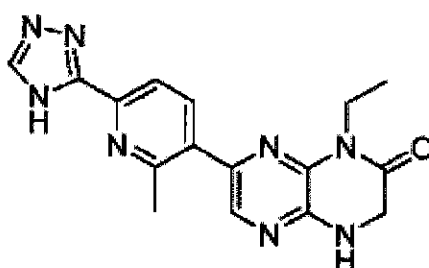
Modificaciones a las Reivindicaciones:

Este listado de reivindicaciones reemplazará todas las versiones anteriores, y los listados, de las reivindicaciones en la solicitud:

Listado de reivindicaciones:

1-9. (Canceladas)

10. (Actualmente modificada) Una forma de cristal del Compuesto 1, o un tautómero del mismo:



Compuesto I

que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ.

11. (Cancelada)

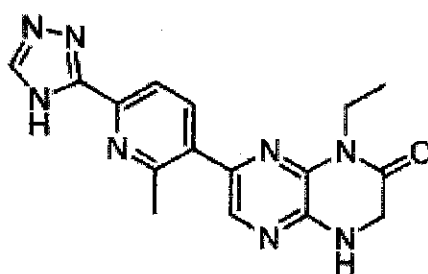
12. (Actualmente modificada) Una composición farmacéutica que comprende la forma de cristal de la reivindicación 10, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.

13. (Nueva) La forma de cristal de la reivindicación 10 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 15.9, 25.2 y 27.1 °2θ.

14. (Nueva) La forma de cristal de la reivindicación 10 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.6° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

15. (Nueva) La forma de cristal de la reivindicación 10 que es sustancialmente pura.

16. (Nueva) Una forma de cristal del Compuesto 1, o un tautómero del mismo:



Compuesto 1

que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 7.5, 10.4 y 11.7 °2 θ .

17. (Nueva) La forma de cristal de la reivindicación 16 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 4.9, 8.6 y 17.9 °2 θ .

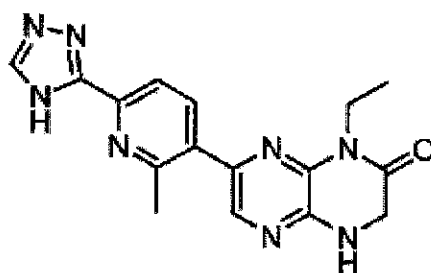
18. (Nueva) La forma de cristal de la reivindicación 16 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 267.8° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

19. (Nueva) La forma de cristal de la reivindicación 16 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 158.8° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

20. (Nueva) La forma de cristal de la reivindicación 16 que es sustancialmente pura.

21. (Nueva) Una composición farmacéutica que comprende la forma de cristal de la reivindicación 16, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.

22. (Nueva) Una forma de cristal del Compuesto 1, o un tautómero del mismo:



Compuesto 1

que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.3, 11.7 y 19.9 °2θ.

23. (Nueva) La forma de cristal de la reivindicación 22 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 7.4, 17.3 y 23.7 °2θ.

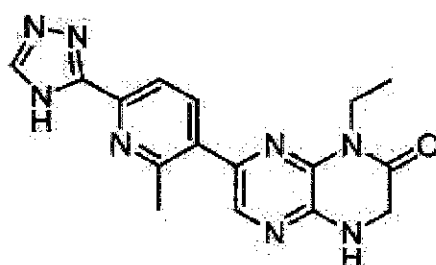
24. (Nueva) La forma de cristal de la reivindicación 22 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 270.3° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

25. (Nueva) La forma de cristal de la reivindicación 22 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 135.9° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

26. (Nueva) La forma de cristal de la reivindicación 22 que es sustancialmente pura.

27. (Nueva) Una composición farmacéutica que comprende la forma de cristal de la reivindicación 22, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.

28. (Nueva) Una forma de cristal del Compuesto 1, o un tautómero del mismo:



Compuesto 1

que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 11.0, 20.2 y 21.9 °2θ.

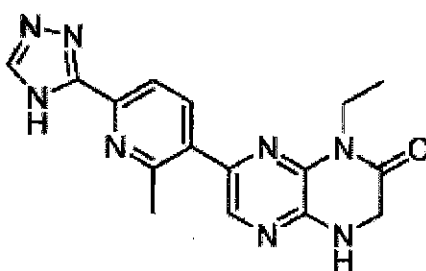
29. (Nueva) La forma de cristal de la reivindicación 28 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 18.2, 19.6 y 23.4 °2θ.

30. (Nueva) La forma de cristal de la reivindicación 28 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.0° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

31. (Nueva) La forma de cristal de la reivindicación 28 que es sustancialmente pura.

32. (Nueva) Una composición farmacéutica que comprende la forma de cristal de la reivindicación 28, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.

33. (Nueva) Una forma de cristal del Compuesto 1, o un tautómero del mismo:



Compuesto 1

que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.3, 15.3 y 18.6 °2θ.

34. (Nueva) La forma de cristal de la reivindicación 33 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 7.0, 10.5 y 23.2 °2θ.

35. (Nueva) La forma de cristal de la reivindicación 33 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo

en aproximadamente 269.7° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

36. (Nueva) La forma de cristal de la reivindicación 33 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 180.4° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

37. (Nueva) La forma de cristal de la reivindicación 33 que es sustancialmente pura.

38. (Nueva) Una composición farmacéutica que comprende la forma de cristal de la reivindicación 33, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.

OBSERVACIONES

A la entrada de las modificaciones hechas actualmente, las reivindicaciones 10 y 12 a 38 estarán en trámite. Se han cancelado las Reivindicaciones 1 a 9 y 11, sin perjuicio.

Se ha modificado la Reivindicación 10, sin perjuicio, para describir una forma de cristal del Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ. Se puede encontrar el soporte para dicha modificación a través de la especificación como se presentó, por lo menos en los párrafos [00104] y [00247].

Se han modificado las Reivindicación 12, sin perjuicio, para depender de la reivindicación 10. Se puede encontrar el soporte para dicha modificación a través de la especificación como se presentó, por lo menos en el párrafo [00173].

Se han agregado las nuevas reivindicaciones 13 a 38. Se puede encontrar el soporte para las nuevas reivindicaciones 13 a 38 por lo menos en los párrafos enumerados adelante de la solicitud según se presentó como sigue:

Reivindicación No.	Soporte
13	Párrafos [00104] y [00247]
14	Párrafos [00106], [00244] y [00246]
15	Párrafo [00109]
16	Párrafos [00110] y [00250]
17	Párrafos [00110] y [00250]
18	Párrafos [00112], [00244] y [00249] y figura 9
19	Párrafo [00244] y figura 9
20	Párrafo [00115]
21	Párrafo [00173]
22	Párrafos [00116] y [00253]
23	Párrafos [00116] y [00253]
24	Párrafos [00252] y [00244] y figura 14
25	Párrafo [00244] y figura 14
26	Párrafo [00121]
27	Párrafo [00173]
28	Párrafos [00122] y [00256]
29	Párrafos [00122] y [00256]

30	Párrafos [00124] y [00244] y figura 19
31	Párrafos [00126]
32	Párrafo [00173]
33	Párrafos [00127] y [00259]
34	Párrafos [00127] y [00259]
35	Párrafos [00129] y [00244] y figura 23
36	Párrafo [00244] y figura 23
37	Párrafo [00132]
38	Párrafo [00173]

No se ha agregado nueva materia.

Los solicitantes se reservan su derecho a enjuiciar la materia objeto de cualquier reivindicación cancelada, cualquier reivindicación modificada, cualquier reivindicación retirada o cualquier materia objeto reivindicada no reivindicada en una o más solicitudes adicionales.

I. Objeción a la Reivindicación

Se objeta la Reivindicación 12 por supuestamente no definir de forma explícita el “Compuesto 1” por nombre y estructura.

Sin estar conforme con en el rechazo, y exclusivamente para agilizar el procesamiento de la presente solicitud, se ha modificado la reivindicación 12, sin perjuicio, para depender de reivindicación 10.

Los solicitantes afirman respetuosamente que se ha superado la objeción de la reivindicación 12 y se debe retirar.

II. Rechazo En Virtud de 35 U.S.C. § 112, Indefinición

Se rechaza la Reivindicación 11 en virtud de 35 U.S.C. § 112, segundo párrafo, por supuestamente se indefinida.

Sin estar conforme con el rechazo, y exclusivamente para agilizar el procesamiento de la presente solicitud, se ha cancelado la reivindicación 11, sin perjuicio.

Los Solicitantes respetuosamente afirman que el rechazo de la reivindicación 11 en virtud de 35 U.S.C. § 112, segundo párrafo, es discutible y se debe retirar debido a la cancelación de la reivindicación 11.

III. Rechazo En virtud de 35 U.S.C. § 102, Novedad

Se rechaza la Reivindicación 10 en virtud de 35 U.S.C. 102(a)(1) ya que supuestamente se anticipó por Publicación Solicitud de Patente Estadounidense No. 2011/0137028 otorgada a Harris et al. (en adelante "Harris"). Los Solicitantes respetuosamente contradicen este rechazo.

Sin estar conforme con el rechazo, y exclusivamente para agilizar el procesamiento de la presente solicitud, se ha modificado la reivindicación 10, sin perjuicio, para describir una forma de cristal del Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ.

El Circuito Federal sostuvo que la anticipación solo se establece cuando una única referencia de la técnica anterior divulga, expresamente o en virtud de los principios de coherencia, todos y cada elemento de la invención reivindicada. En relación con *Spada*, 911 F.2d 705, 707, (Cir. Fed. 1990); *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444 (Cir. Fed. 1984); *Verdegaal Bros. vs. Union Oil Co. de California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Cir. Fed. 1987).

Los solicitantes respetuosamente afirman que por lo menos debido a que Harris no proporciona ninguna enseñanza con respecto una forma de cristal del Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ, Harris no anticipa la reivindicación 10.

De acuerdo con lo anterior, los Solicitantes respetuosamente afirman que se ha superado el rechazo a la reivindicación 10 en virtud de 35 U.S.C. § 102(a)(1) y se debe retirar.

IV. Rechazo En virtud de 35 U.S.C. § 103, Obviedad

Se rechaza la Reivindicación 12 en virtud de 35 U.S.C. 103(a) ya que supuestamente es no patentable sobre la La Publicación de Solicitud de Patente

Estadounidense No. 2010/0216781 otorgada a Perrin-Ninkovic et al. (en adelante "Perrin-Ninkovic"). Los Solicitantes respetuosamente contradicen este rechazo.

Sin estar conforme con el rechazo, y exclusivamente para agilizar el procesamiento de la presente solicitud, se ha modificado la reivindicación 12, sin perjuicio, para depender de reivindicación 10.

A. Perrin-Ninkovic no enseña ni sugiere cada elemento de la reivindicación 12.

Para rechazar una reivindicación con base en obviedad, un Examinador debe resolver las preguntas factuales de *Graham*. Luego, un Examinador debe articular una conclusión de que la técnica anterior incluyó cada elemento reivindicado, aunque no necesariamente en una única referencia de técnica anterior, siendo la única diferencia entre la invención reivindicada y la técnica anterior la falta de combinación real de los elementos en una única referencia de la técnica anterior. *KSR Int'l Co. v. Teleflex Inc.*, 82 U.S.P.Q.2d 1385, 1395 (2007); *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 U.S.P.Q. 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57,62-63, 163 U.S.P.Q. 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 U.S.P.Q. 303, 306 (1950); MPEP § 2143.A.

Los Solicitantes respetuosamente afirman que debido a que Perrin-Ninkovic no proporciona ninguna enseñanza o sugerencia con respecto a una forma de cristal del Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ como se menciona en la reivindicación 10, y debido a que la reivindicación 12 depende de la reivindicación 10, Perrin-Ninkovic no enseña ni sugiere todos y cada elemento de la reivindicación 12.

Sin la conclusión requerida de que la técnica anterior enseñe o sugiera cada elemento reivindicado, los Solicitantes respetuosamente afirman que no se puede hacer un caso *prima facie* de obviedad adecuado. MPEP § 2143.A.

B. La producción de polimorfo es impredecible.

El Examinador ha notado que Perrin-Ninkovic enseña el Compuesto 1. Véase página 7, Acción Oficial enviada por correo el 14 de octubre de 2015.

Los Solicitantes respetuosamente afirman que la reivindicación 12 describe una forma de cristal novedosa no divulgada, de forma inherente o de otra forma, en Perrin-Ninkovic.

Los Solicitantes respetuosamente afirman que está bien establecido que se pueden patentar las formas de cristal, incluso de compuestos conocidos. *Glaxo, Inc. v. Novopharm Ltd*, 52 F.3d 1043, 1047 (Cir. Fed. 1995).

Los Solicitantes respetuosamente afirman que Perrin-Ninkovic no enseña ni sugiere ningún método para producir las formas de cristal reivindicadas del Compuesto 1. De acuerdo con lo anterior, los Solicitantes respetuosamente afirman que Perrin-Ninkovic no respalda un caso de obviedad *prima facie* adecuado de la reivindicación 12.

Específicamente, aunque Perrin-Ninkovic permite la preparación del Compuesto 1 en sí mismo, no proporciona la orientación necesaria para permitir que una persona que tiene experticia común en la técnica (en adelante "PHOSITA") prepare las formas de cristal reivindicadas del Compuesto 1 con una expectativa razonable de éxito.

Los Solicitantes respetuosamente afirman que no es posible predecir *a priori* si incluso existen las formas cristalinas de un compuesto, mucho menos como prepararlas con éxito. Véase (i) Braga y Grepioni, 2005, "Making crystals from crystals: a green route to crystal engineering and polymorphism," *Chem. Commun.*: 3635-3645; (ii) Jones *et al.*, 2006, Pharmaceutical Cocrystals: An Emerging Approach to Physical Property Enhancement," *MRS Bulletin* 31:875-879; (iii) Price, 2004, "The computational prediction of pharmaceutical crystal structures and polymorphism," *Advanced Drug Delivery Reviews* 56:301-319; y (iv) Bernstein, 2004, "Crystal Structure Prediction and Polymorphism," *ACA Transactions* 39:14-23 (se adjunta una copia de cada una).

Los Solicitantes respetuosamente afirman que estas referencias enseñan el alto grado de impredecibilidad en el campo de la producción de la forma cristalina, de tal manera que un PHOSITA no tendría expectativas razonables de éxito con respecto a la preparación de las formas de cristal reivindicadas del Compuesto 1. Sin la expectativa razonable de éxito requerida, los Solicitantes respetuosamente afirman que no se puede hacer un caso de obviedad *prima facie* adecuado. Con respecto a *Dow Chem. Co.*, 837 F.2d 469,473 (Cir. Fed. 1988); MPEP § 2143.02.

De acuerdo con lo anterior, los Solicitantes respetuosamente afirman que se ha superado el rechazo de la reivindicación 12 en virtud de 35 U.S.C. 103(a) y se debe retirar.

V. Rechazos a la Reivindicación – Obviedad – Doble Patentamiento

(1) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 14 a 28 de la Patente Estadounidense No. 8,110,578 (en adelante “578”) en vista de Harris y en vista adicionalmente de Perrin-Ninkovic.

(2) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 4, 6, 8, 9, 16, 19 y 20 de la Patente Estadounidense No. 8,507,492 (en adelante “492”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(3) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 27 de la Patente Estadounidense No. 9,079,900 (en adelante “900”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(4) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 21 de la Patente Estadounidense No. 8,686,135 (en adelante “135”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(5) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 7 de la Solicitud de Patente Estadounidense No. 13/192,792 (en adelante “792”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(6) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 22 de Solicitud de Patente Estadounidense No. 13/803,323 (en adelante “323”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(7) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 22 de la Solicitud de Patente Estadounidense No. 13/803,317 (en adelante “317”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(8) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 22 de la Solicitud de Patente Estadounidense No. 13/803,061 (en adelante “061”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(9) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 22 de la Solicitud de Patente Estadounidense No. 13/803,305 (en adelante “305”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(10) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 3,6 y 1034 de la Solicitud de Patente Estadounidense No. 14/055,985 (en adelante “985”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(11) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 19 de la Solicitud de Patente Estadounidense No. 14/254,010 (en adelante “010”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(12) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que

supuestamente no son patentables sobre las reivindicaciones 1 a 19 de la Solicitud de Patente Estadounidense No. 14/254,020 (en adelante “020”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(13) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 17 de la Solicitud de Patente Estadounidense No. 14/254,009 (en adelante “009”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(14) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 7 de la Solicitud de Patente Estadounidense No. 14/254,017 (en adelante “017”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(15) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 34 de la Solicitud de Patente Estadounidense No. 14/254,004 (en adelante “004”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(16) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 24 de la Solicitud de Patente Estadounidense No. 14/254,001 (en adelante “001”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(17) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 33 de la Solicitud de Patente Estadounidense No. 14/254,015 (en adelante “015”) en vista de Harris y en vista adicional de Perrin-Ninkovic.

(18) Las Reivindicaciones 10 y 12 se rechazan provisionalmente en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento ya que supuestamente no son patentables sobre las reivindicaciones 1 a 20 de la Solicitud

de Patente Estadounidense No. 14/137,700 (en adelante "700") en vista de Harris y en vista adicional de Perrin-Ninkovic.

Sin estar conforme con el rechazo, y exclusivamente para agilizar el procesamiento de la presente solicitud, se ha modificado la reivindicación 10, sin perjuicio, para describir una forma de cristal del Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ.

Sin estar conforme con el rechazo, y exclusivamente para agilizar el procesamiento de la presente solicitud, se ha modificado la reivindicación 12, sin perjuicio, para depender de reivindicación 10.

Los Solicitantes respetuosamente afirman que ninguna de las anteriores referencias, es decir, '578, '492, '900, '135, '792, '323, '317, '061, '305, '985, '010, '020, '009, '017, '004, '001, '015, '700, Harris y Perrin-Ninkovic, enseñan o sugieren todos y cada elemento de las reivindicaciones 10 y 12. En particular, ninguna de las referencias anteriores enseña o sugiera una forma de cristal del Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ como se menciona en las reivindicaciones 10 y 12. Sin la conclusión requerida de que la técnica anterior enseñe o sugiera cada elemento reivindicado, los Solicitantes respetuosamente afirman que no se puede hacer un caso de obviedad *prima facie* adecuado. *KSR*, 82 U.S.P.Q.2d en 1395; *Sakraida*, 189 U.S.P.Q. en 453; *Anderson's-Black Rock, Inc.*, 163 U.S.P.Q. en 675; *Great Atlantic & P. Tea Co.*, 87 U.S.P.Q. en 306; MPEP § 2143.A.

Los Solicitantes respetuosamente afirman que PHOSITA no tendría expectativas razonables de éxito con respecto a la preparación de la forma de cristal del Compuesto 1 mencionado en la reivindicaciones 10 y 12 por las razones establecidas anteriormente. Sin la expectativa razonable de éxito requerida, los Solicitantes respetuosamente afirman que no se puede hacer un caso de obviedad *prima facie* adecuado. *Con respecto a Dow Chem. Co.*, 837 F.2d en 473; MPEP § 2143.02.

De acuerdo con lo anterior, los Solicitantes respetuosamente afirman que se ha superado el rechazo de las reivindicaciones 10 y 12 en virtud de la doctrina creada judicialmente de obviedad - doble patentamiento y se debe retirar.

CONCLUSIÓN

Los solicitantes han hecho un esfuerzo serio y de buena fe para aclarar las cuestiones ante el Examinador y para poner este caso en condiciones de aprobación. Se considera que la reconsideración y aprobación de todas las reivindicaciones están en orden, y se solicita respetuosamente un Aviso de Aprobación para este efecto.

Se estima que no se debe ninguna tarifa en relación con esta Respuesta que no sea la debida en relación con las reivindicaciones adicionales; sin embargo, en caso de que se adeude cualquier tarifa adicional, por favor cargue la tarifa requerida a la Cuenta de Depósito de Jones Day No. 50-3013.

Respetuosamente,

Fecha: Enero 14 de 2016 /Michael J. Bruner/

Por: Michael J. Bruner

(Reg. No. 47.458)

JONES DAY

222 East 41st Street

Nueva York, Nueva York 10017

(404) 581-8614

Office Action Summary	Application No. 14/254,023	Applicant(s) MENON ET AL.	
	Examiner MATTHEW COUGHLIN	Art Unit 1626	AIA (First Inventor to File) Status Yes

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 29 September 2015.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☒ Claim(s) 1-12 is/are pending in the application.
5a) Of the above claim(s) 1-9 is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☒ Claim(s) 10-12 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10) ☐ The specification is objected to by the Examiner.

11) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some** c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)
Paper No(s)/Mail Date 10/06/2014, 08/13/2014 and 05/25/2014.

3) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____

4) ☐ Other: _____

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The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

DETAILED ACTION

Claims 1-12 are pending in the application. Claims 10-12 are rejected. Claims 1-9 are withdrawn from further consideration.

Election/Restrictions

Applicant's election of Group II, claims 10-12, in the reply filed on September 29th, 2015 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was treated **without** traverse in the reply filed on September 29th, 2015.

Information Disclosure Statement

The Examiner has considered the Information Disclosure Statement(s) filed on October 6th, 2014, August 13th, 2014 and May 25th, 2014.

Claim Objections

(1) It is suggested that Applicant define "Compound 1" in claim 12 since claim 12 is independent and does not explicitly define the compound by name or structure.

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Claim Rejections - 35 USC § 112 - 2nd paragraph

The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Claims 11 is rejected as indefinite based on the limitations "Forms A-E". It is noted that that instant specification does not provide a clear definition of what properties must be observed for a particular form to qualify as A, B, C, D or E. For instance, Applicant presents the following on page 31:

[00101] The solid forms provided herein (e.g., Form A, Form B, Form C, Form D and Form E of Compound 1) may be characterized using a number of methods known to a person skilled in the art, including, but not limited to, single crystal X-ray diffraction, X-ray powder diffraction (XRPD), microscopy (e.g., scanning electron microscopy (SEM)), thermal analysis (e.g., differential scanning calorimetry (DSC), thermal gravimetric analysis (TGA), and hot-stage microscopy), and spectroscopy (e.g., infrared, Raman, and solid-state nuclear magnetic resonance). The particle size and size distribution of the solid form provided herein may be determined by conventional methods, such as laser light scattering technique.

The specification provides no clear description of what properties must be observed in order to conclude that a particular form is one of the five

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instantly claimed. As an example regarding Form A, Applicant provides the following paragraph on pages 31 and 32:

[00104] In one embodiment, provided herein is Form A of Compound 1. In one embodiment, Form A of Compound 1 is anhydrous. In another embodiment, Form A of Compound 1 is non-hygroscopic. In another embodiment, Form A of Compound 1 is crystalline. In one embodiment, Form A of Compound 1 has an X-ray powder diffraction pattern substantially as shown in FIG. 2. In one embodiment, Form A of Compound 1 has one or more

characteristic X-ray powder diffraction peaks at a two-theta angle of approximately 8.0, 9.8, 12.0, 15.9, 17.4, 17.9, 18.3, 19.5, 21.6, 21.9, 22.3, 24.0, 25.2, 26.4, 26.5, 27.1, 28.0, 29.4, 30.1, 31.3, 32.1, 36.4, 38.6 or 39.4 degrees. In a specific embodiment, Form A of Compound 1 has one, two, three, four, five, six, seven or eight characteristic X-ray powder diffraction peaks at a two-theta angle of approximately 9.8, 12.0, 15.9, 17.4, 17.9, 21.9, 25.2 or 27.1 degrees. In another embodiment, Form A of Compound 1 has one, two, three or four characteristic X-ray powder diffraction peaks at a two-theta angle of approximately 9.8, 12.0, 17.9 or 25.2 degrees. In another embodiment, Form A of Compound one has one, two, three, four, five, six, seven or eight characteristic X-ray powder diffraction peaks as set forth in Table 2.

It could be the case that a given form must possess each of the properties cited above or some but not all or even none and need only have one of the many additional properties disclosed in paragraphs [00105]-[00109]. For these reasons, the scope encompassed by "Forms A-E" is unclear. It is suggested that Applicant amend the claims to require at least defining property of the individual crystalline forms such as certain X-ray powder diffraction peaks along with a corresponding variation such as ± 0.2 degrees 2 theta (as defined in paragraph [00103]).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless -

(a) (1) the claimed invention was patented, described in a printed publication, or in public use, on sale or otherwise available to the public before the effective filing date of the claimed invention.

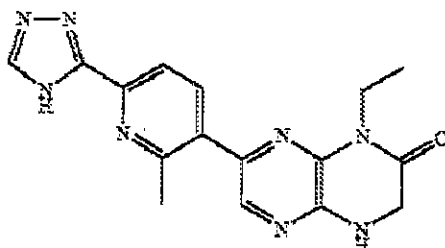
Claim 10 is rejected under 35 U.S.C. 102(a) (1) as being anticipated by U.S. PGPub No. 2011/0137028 A1 by Harris et al.

Harris et al. teach the following example on page 37:

Example 12

1-Ethyl-7-(2-methyl-6-(4H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one

[0559]



Harris et al. further teach the following on page 38 (paragraph [0562]):

cooled to room temperature and held overnight. The solids were collected by vacuum filtration and dried to obtain 1-ethyl-7-(2-methyl-6-(4H-1,2,4-triazol-3-yl)pyridin-3-yl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one as an off-white solid.

Accordingly, Harris et al. teach a solid form of the compound instantly depicted in claim 10. Applicant provides the following definition on page 7 of the specification:

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[0051] The term "solid form" refers to a physical form which is not predominantly in a liquid or a gaseous state. As used herein and unless otherwise specified, the term "solid form," when used herein to refer to Compound 1, refers to a physical form comprising Compound 1 which is not predominantly in a liquid or a gaseous state. A solid form may be a crystalline form, an amorphous form, or a mixture thereof. In certain embodiments, a solid form may be a liquid crystal. In certain embodiments, the term "solid forms comprising Compound 1" includes crystal forms comprising Compound 1, amorphous forms comprising Compound 1, and mixtures thereof. In certain embodiments, the solid form of Compound 1 is Form A, Form B, Form C, Form D or Form E.

Since the prior art teaches that the compound was obtained as a solid, the prior art teaches the limitation of a "solid form" as recited in claim 10.

Claim Rejections - 35 USC § 103

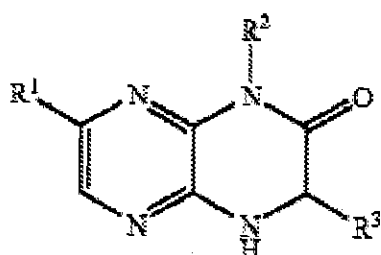
The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102 of this title, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 12 is rejected under 35 U.S.C. 103 as being unpatentable over U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al.

Determining the scope and contents of the prior art. (See MPEP § 2141.01)

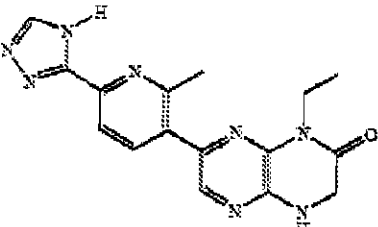
Perrin-Ninkovic et al. teach compounds of the following general formula for use in the treatment of, for instance, cancer (abstract):



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As an example, Perrin-Ninkovic et al. teach the following compound on page 109:

TABLE 1-continued

Compd No.	Compd Structure	Compd Name	MS (ESI) m/z	Act. Level
23i		1-ethyl-7-(2-methyl-6-(4H-1,2,4-triazol-3-yl)pyridin-3-yl)-1,4-dihydropyridine(2,3-b)pyridine-3(1H)-one	397.6 [M+1] ⁺	D

Ascertainment of the differences between the prior art and the claims. (See MPEP § 2141.02)

The prior art does not teach an explicit composition comprising the compound above with one of the carriers or excipients recited by claim 12.

Finding of prima facie obviousness --- rationale and motivation (See MPEP § 2141.02)

Perrin-Ninkovic et al. teach the following on page 2:

[0016] Further provided herein are compositions comprising an effective amount of a Heteroaryl Compound and compositions comprising an effective amount of a Heteroaryl Compound and a pharmaceutically acceptable carrier or vehicle. The compositions are useful for treating or preventing cancer, inflammatory conditions, immunological conditions, neurodegenerative diseases, diabetes, obesity, neurological disorders, age-related diseases, or cardiovascular conditions and conditions treatable or preventable by inhibition of a kinase pathway, in one embodiment, the mTOR/PI3K/Akt pathway.

The prior art provides further detailed information beginning on page 31 including the following teachings of excipients, etc. (paragraph [0461], underline added):

The Heteroaryl Compounds can be administered to a patient orally or parenterally in the conventional form of preparations, such as capsules, microcapsules, tablets, granules, powder, troches, pills, suppositories, injections, suspensions and syrups. Suitable formulations can be prepared by methods commonly

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employed using conventional, organic or inorganic additives, such as an excipient (e.g., sucrose, starch, mannitol, sorbitol, lactose, glucose, cellulose, talc, calcium phosphate or calcium carbonate), a binder (e.g., cellulose, methylcellulose, hydroxymethylcellulose, polypropylpyrrolidone, polyvinylpyrrolidone, gelatin, gum arabic, polyethyleneglycol, sucrose or starch), a disintegrator (e.g., starch, carboxymethylcellulose, hydroxypropylstarch, low substituted hydroxypropylcellulose, sodium bicarbonate, calcium phosphate or calcium citrate), a lubricant (e.g., magnesium stearate, light anhydrous silicic acid, talc or sodium lauryl sulfate), a flavoring agent (e.g., citric acid, menthol, glycine or orange powder), a preservative (e.g., sodium benzoate, sodium bisulfite, methylparaben or propylparaben), a stabilizer (e.g., citric acid, sodium citrate or acetic acid), a suspending agent (e.g., methylcellulose, polyvinyl pyrrolidone or aluminum stearate), a dispersing agent (e.g., hydroxypropylmethylcellulose), a diluent (e.g., water), and base wax (e.g., cocoa butter, white petrolatum or polyethylene glycol). [...]

Accordingly, the prior art generally teaches pharmaceutical compositions along with examples of known excipients and formulation agents including five of the six recited in instant claim 12. It is noted, however, that the prior art provides the additional guidance regarding lubricants in paragraph [0475] (page 32):

A lubricant might be necessary in a tablet formulation to prevent the tablet and punches from sticking in the die. The lubricant can be chosen from such slippery solids as talc, magnesium and calcium stearate, stearic acid and hydrogenated vegetable oils.

Accordingly, the prior art teaches each of the instantly claimed excipients and carriers as examples. In the interest of developing appropriate compositions for administration in the therapeutic methods of the prior art, a person having ordinary skill in the art would have been motivated to screen the formulating agents taught by the prior art. It is obvious to add a carrier to an obvious compound. *Ex parte Douros*, 163 USPQ 667 (PTO Bd. App. 1968). If Applicant intends to rely on unexpected results as a means of overcoming the instant rejection, Applicant is directed to MPEP 716.02(d), which states the following:

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Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)

In the instant situation, the claim merely requires compound 1 (or any pharmaceutically acceptable salt thereof) in any physical form and the presence of at least one of the excipients or carriers listed in claim 12. The claim places no limitation on relative amounts. The specification contains various tables comparing compositions, however, these are limited to particular compositions with defined amounts and cannot be reasonably asserted to stand for the proposition that any unexpected results are commensurate with the scope instantly claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In*

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re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit <http://www.uspto.gov/forms/>. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to <http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp>.

Introduction to rejections below: The rejections below follow the same basic fact pattern and in the interest of clarity of the instant Office Action and the record as a whole the Examiner notes that the cited patents and copending applications are directed to compounds, compositions, methods of using or methods of making thereof where the instant compound "Compound 1" is embraced by the generic structures of the conflicting claims. Each of the rejections below is based on the fact that many different patents and copending applications recite compounds, compositions and methods that are generic to the instantly claimed salts where the motivation to arrive at the

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instant claimed solid form is the same as discussed above either in that the prior art teaches an explicit solid form that would be amenable to further use (under 35 USC 102) or the prior art would have led a person having ordinary skill in the art to make the instantly claimed compositions thereof (35 USC 103). Since the references cited above are available as prior art, these references are relied upon in the rejections and provisional rejections below and the explanation of the art or rationale regarding obviousness is incorporated by reference in the rejections below when referring to U.S. PGPub No. 2011/0137028 A1 by Harris et al. and U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al.

(1) Claims 10 and 12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 14-28 of U.S. Patent No. 8,110,578 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the patent are generic to compounds, compositions and/or methods embracing the solid form or composition.

(2) Claims 10 and 12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-4, 6, 8, 9, 16, 19 and 20 of U.S. Patent No. 8,507,492 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the patent are generic to

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compounds, compositions and/or methods embracing the solid form or composition.

(3) Claims 10 and 12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 9,079,900 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the patent are generic to compounds, compositions and/or methods embracing the solid form or composition.

(4) Claims 10 and 12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 8,686,135 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the patent are generic to compounds, compositions and/or methods embracing the solid form or composition.

(5) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-7 of copending Application No. 13/192,792 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having

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ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(6) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of copending Application No. 13/803,323 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(7) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of copending Application No. 13/803,317 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

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(8) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of copending Application No. 13/803,061 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(9) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-22 of copending Application No. 13/803,305 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(10) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-3, 6 and 10-34 of copending Application No. 14/055,985 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of

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claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(11) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-19 of copending Application No. 14/254,010 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(12) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-19 of copending Application No. 14/254,020 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

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(13) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-17 of copending Application No. 14/254,009 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(14) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-7 of copending Application No. 14/254,017 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(15) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-34 of copending Application No. 14/254,004 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by

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Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(16) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-24 of copending Application No. 14/254,001 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

(17) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-33 of copending Application No. 14/254,015 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

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This is a provisional nonstatutory double patenting rejection.

(18) Claims 10 and 12 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-20 of copending Application No. 14/137,700 in view of U.S. PGPub No. 2011/0137028 A1 by Harris et al. and in further view of U.S. PGPub No. 2010/0216781 A1 by Perrin-Ninkovic et al. where a solid form of compound 1 of claim 10 is known and where compositions thereof would have been obvious to a person having ordinary skill in the art where the claims of the copending case are generic to compounds, compositions and/or methods embracing the solid form or composition.

This is a provisional nonstatutory double patenting rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MATTHEW COUGHLIN whose telephone number is (571)270-1311. The examiner can normally be reached on Monday through Friday from 12:00 pm - 8:00 pm.

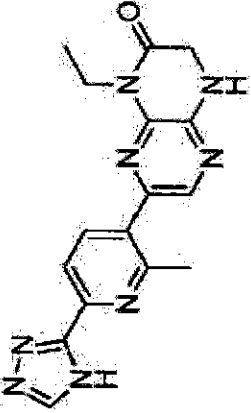
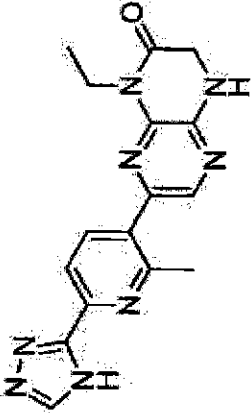
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

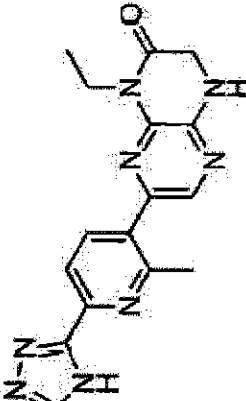
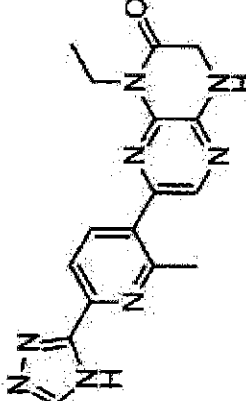
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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

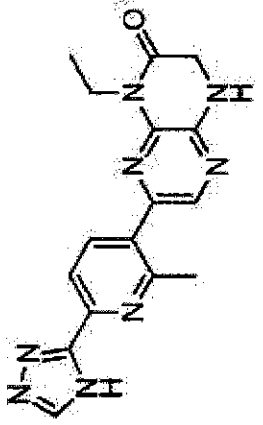
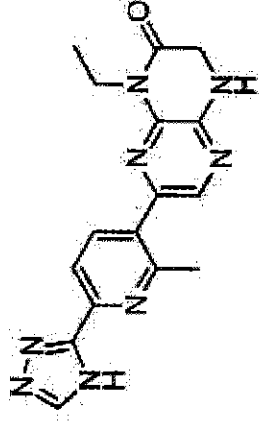
/MATTHEW COUGHLIN/
Primary Examiner, Art Unit 1626

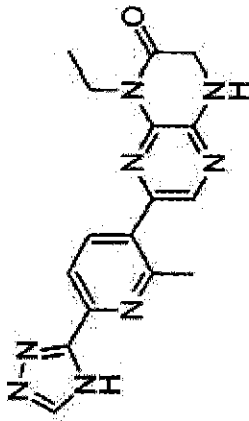
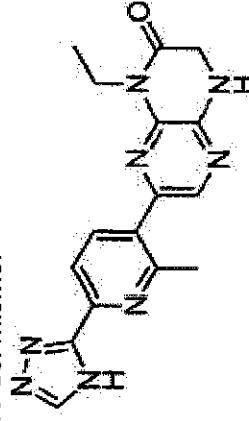
TABLA DE CORRESPONDENCIA ENTRE LAS REIVINDICACIONES CONCEDIDAS POR LA USPTO Y LAS REIVINDICACIONES PENDIENTES ANTE LA SIC

Reivindicaciones patentadas USPTO	Reivindicaciones modificadas y pendientes en COLOMBIA	Explicación de la correspondencia
1. Una forma de cristal del Compuesto 1, o un tautómero del mismo:  Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ. 2. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 10, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.	1. Una forma de cristal del Compuesto 1, o un tautómero del mismo:  Compuesto I que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.8, 12.0 y 17.9 °2θ. 2. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 10, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.	Las reivindicaciones actualmente pendientes ante la SIC son exactamente iguales a las concedidas por la USPTO

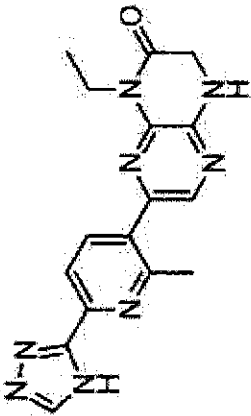
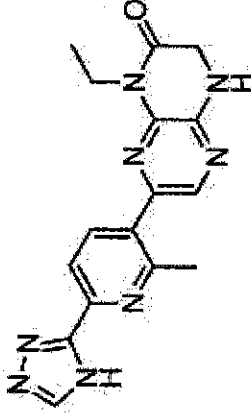
3. La forma de cristal de la reivindicación 1 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 15.9, 25.2 y 27.1 °2θ. 4. La forma de cristal de la reivindicación 1 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.6° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 5. La forma de cristal de la reivindicación 1 que es sustancialmente pura. 6. Una forma de cristal del Compuesto 1, o un tautómero del mismo:	3. La forma de cristal de la reivindicación 1 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 15.9, 25.2 y 27.1 °2θ. 4. La forma de cristal de la reivindicación 1 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.6° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 5. La forma de cristal de la reivindicación 1 que es sustancialmente pura. 6. Una forma de cristal del Compuesto 1, o un tautómero del mismo:	
 Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 7.5, 10.4 y 11.7 °2θ.	 Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 7.5, 10.4 y 11.7 °2θ.	

7. La forma de cristal de la reivindicación 6 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 4.9, 8.6 y 17.9 °2θ. 8. La forma de cristal de la reivindicación 6 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 267.8° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 9. La forma de cristal de la reivindicación 6 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 158.8° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 10. La forma de cristal de la reivindicación 6 que es sustancialmente pura. 11. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 6, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.	7. La forma de cristal de la reivindicación 6 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 4.9, 8.6 y 17.9 °2θ. 8. La forma de cristal de la reivindicación 6 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 267.8° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 9. La forma de cristal de la reivindicación 6 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 158.8° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 10. La forma de cristal de la reivindicación 6 que es sustancialmente pura. 11. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 6, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.
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12. Una forma de cristal del Compuesto 1, o un tautómero del mismo:  Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.3, 11.7 y 19.9 °2θ.	12. Una forma de cristal del Compuesto 1, o un tautómero del mismo:  Compuesto 1 que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.3, 11.7 y 19.9 °2θ.
13. La forma de cristal de la reivindicación 12 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 7.4, 17.3 y 23.7 °2θ.	13. La forma de cristal de la reivindicación 12 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 7.4, 17.3 y 23.7 °2θ.
14. La forma de cristal de la reivindicación 12 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 270.3° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.	14. La forma de cristal de la reivindicación 12 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 270.3° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.

15. La forma de cristal de la reivindicación 12 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 135.9° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 16. La forma de cristal de la reivindicación 12 que es sustancialmente pura. 17. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 12, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico. 18. Una forma de cristal del Compuesto 1, o un tautómero del mismo:	15. La forma de cristal de la reivindicación 12 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 135.9° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 16. La forma de cristal de la reivindicación 12 que es sustancialmente pura. 17. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 12, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico. 18. Una forma de cristal del Compuesto 1, o un tautómero del mismo:	 Compuesto 1	 Compuesto 1
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que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 11.0, 20.2 y 21.9 °2θ.	que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 11.0, 20.2 y 21.9 °2θ.
19. La forma de cristal de la reivindicación 18 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 18.2, 19.6 y 23.4 °2θ.	19. La forma de cristal de la reivindicación 18 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 18.2, 19.6 y 23.4 °2θ.
20. La forma de cristal de la reivindicación 18 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.0° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.	20. La forma de cristal de la reivindicación 18 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.0° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.
21. La forma de cristal de la reivindicación 18 que es sustancialmente pura.	21. La forma de cristal de la reivindicación 18 que es sustancialmente pura.
22. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 18, y uno o más excipientes o portadores farmacéuticamente seleccionados de carboximetil celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.	22. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 18, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.

23. Una forma de cristal del Compuesto 1, o un tautómero del mismo:  Compuesto 1	23. Una forma de cristal del Compuesto 1, o un tautómero del mismo:  Compuesto 1	
que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.3, 15.3 y 18.6 °2θ.	que tiene un patrón de difracción de rayos X que comprende picos en aproximadamente 9.3, 15.3 y 18.6 °2θ.	
24. La forma de cristal de la reivindicación 23 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 7.0, 10.5 y 23.2 °2θ.	24. La forma de cristal de la reivindicación 23 que tiene un patrón de difracción de rayos X que comprende adicionalmente picos en aproximadamente 7.0, 10.5 y 23.2 °2θ.	
25. La forma de cristal de la reivindicación 23 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.7° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.	25. La forma de cristal de la reivindicación 23 que tiene un termograma de calorimetría de escaneo diferencial que comprende un endoterma con un máximo en aproximadamente 269.7° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C.	

26. La forma de cristal de la reivindicación 23 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 180.4° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 27. La forma de cristal de la reivindicación 23 que es sustancialmente pura. 28. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 23, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.	26. La forma de cristal de la reivindicación 23 que tiene un termograma de calorimetría de escaneo diferencial que comprende un exoterma con un máximo en aproximadamente 180.4° C cuando se calienta desde aproximadamente 25° C hasta aproximadamente 300° C. 27. La forma de cristal de la reivindicación 23 que es sustancialmente pura. 28. Una composición farmacéutica que comprende la forma de cristal de la reivindicación 23, y uno o más excipientes o portadores farmacéuticamente aceptables, cada uno independientemente seleccionado de carboximetil celulosa, celulosa, lactosa, estearato de magnesio, almidón, y ácido esteárico.
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