

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2202503.00131WO1	FOR FURTHER ACTION		See Form PCT/IPEA/416
International application No. PCT/US15/36605	International filing date (day/month/year) 19 June 2015 (19.06.2015)	Priority date (day/month/year) 20 June 2014 (20.06.2014)	
International Patent Classification (IPC) or national classification and IPC IPC: A61K 9/20(2006.01),9/46(2006.01),31/133(2006.01),31/4709(2006.01) USPC: 424/466;514/210.21			
Applicant MELINTA THERAPEUTICS, INC.			
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u>16</u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☐ (sent to the applicant and to the International Bureau) a total of <u>0</u> sheets, as follows: ☐ sheets of the description, claims and/or drawings which have been amended and/or sheets containing rectifications authorized by this Authority, unless those sheets were superseded or cancelled, and any accompanying letters (see Rules 46.5, 66.8, 70.16, 91.2, and Section 607 of the Administrative Instructions). ☐ sheets containing rectifications, where the decision was made by this Authority not to take them into account because they were not authorized by or notified to this Authority at the time when this Authority began to draw up this report, and any accompanying letters (Rules 66.4bis, 70.2(e), 70.16 and 91.2). ☐ superseded sheets and any accompanying letters, where this Authority either considers that the superseding sheets contain an amendment that goes beyond the disclosure in the international application as filed, or the superseding sheets were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in item 4 of Box No.I and the Supplemental Box (see Rule 70.16(b)). b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____ containing a sequence listing, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see paragraph 3bis of Annex C of the Administrative Instructions).			
4. This report contains indications relating to the following items: ☒ Box No. I Basis of the report ☐ Box No. II Priority ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement ☐ Box No. VI Certain documents cited ☐ Box No. VII Certain defects in the international application ☒ Box No. VIII Certain observations on the international application			
Date of submission of the demand 14 January 2016 (14.01.2016)		Date of completion of this report 01 March 2016 (01.03.2016)	
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Bethany Barham Telephone No. (571)272-0700	

Form PCT/IPEA/409 (cover sheet) (July 2014)

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Box No. I Basis of the report1. With regard to the **language**, this report is based on:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into English which is the language of a translation furnished for the purposes of:
- ☐ international search (Rules 12.3(a) and 23.1(b)).
 - ☐ publication of the international application (Rule 12.4(a)).
 - ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a) and (b)).

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

- ☒ the international application as originally filed/furnished
- ☒ the description:
 pages 1-52 as originally filed/furnished
 pages* NONE received by this Authority on _____
 pages* NONE received by this Authority on _____
- ☒ the claims:
 pages 53-61 as originally filed/furnished
 pages* NONE as amended (together with any statement) under Article 19
 pages* NONE received by this Authority on _____
- ☒ the drawings:
 pages 1/4-4/4 as originally filed/furnished
 pages* NONE received by this Authority on _____
 pages* NONE received by this Authority on _____

☐ a sequence listing - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since either they are considered to go beyond the disclosure as filed, or they were not accompanied by a letter indicating the basis for the amendments in the application as filed, as indicated in the Supplemental Box (Rules 70.2(c) and (c-bis)):

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____

5. ☐ This report has been established:

- ☐ taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rules 66.1(d-bis) and 70.2(e)).
- ☐ without taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rules 66.4bis) and 70.2(e)).

6. ☒ With regard to top-up searches (Rules 66.1ter and 70.2(f)):

- ☒ A top-up search was carried out by this Authority on 29 February 2016 (29.02.2016)
- ☐ Additional relevant documents have been discovered during the top-up search.
- ☐ No top-up search was carried out by this Authority because it would serve no useful purpose.

7. ☐ Supplementary international search report(s) from Authority(ies) _____ has/have been received and taken into account in establishing this report (Rule 45bis.8(b) and (c)).

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 14-16 and 29-49

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 14-16 and 29-49 are so unclear that no meaningful opinion could be formed (*specify*):

Claims 14-16, 29-49 are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ See Supplemental Box for further details

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PCT/US15/36605**Box No. V** Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims Please See Continuation Sheet YESClaims Please See Continuation Sheet NO

Inventive Step (IS)

Claims Please See Continuation Sheet YESClaims Please See Continuation Sheet NO

Industrial Applicability (IA)

Claims Please See Continuation Sheet YESClaims Please See Continuation Sheet NO

2. Citations and Explanations (Rule 70.7)

Please See Continuation Sheet

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 7-9 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 7-9 are indefinite for the following reason(s): Claims 7-9 refer to "the crystalline form of claim 5". There is a lack of antecedent basis for this limitation in these claims.

Claims 10 and 11 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claims 10 and 11 are indefinite for the following reason(s): the trihydrate for of the quinoline carboxylic acid in claims 10 and 11 is not furnished by the preceding claim 5, which renders the claim indefinite. For examination purposes, the quinolone carboxylic acid in claim 5 will be considered as quinolone carboxylic acid in dehydrated form or as trihydrate.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of a sequence listing filed or furnished:

a. (means)

- ☐ on paper
☐ in electronic form

b. (time)

- ☐ in the international application as filed
☐ together with the international application in electronic form
☐ subsequently to this Authority for the purposes of search and/or examination
☐ to this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the sequence listing, which forms part of the basis of the report, may be marked "superseded."*

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

V.1. Reasoned Statements:

The opinion as to Novelty was positive (Yes) with respect to claims 3, 6-9, 11, 12/3, 12/6-9, 12/11, 13/12/1-11, 17-28

The opinion as to Novelty was negative (No) with respect to claims 1-2, 4-5, 10, 12/1-2, 12/4-5, 12/10, 50

The opinion as to Inventive Step was positive (Yes) with respect to claims 8-9, 12/8-9, 13/12/8-9

The opinion as to Inventive Step was negative (NO) with respect to claims 1-7, 10-11, 12/1-7, 12/10-11, 13/12/1-7, 13/12/10-11, 17-28, 50

The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-11, 12/1-11, 13/12/1-11, 17-28, 50

The opinion as to Industrial Applicability was negative (NO) with respect to claims NONE

V. 2. Citations and Explanations:

Claims 1-2, 4-5, 10, 12/1-2, 12/4-5, 12/10 and 50 lack novelty under PCT Article 33(2) as being anticipated by US 2012/0065186 A1 to Li, et al. (hereinafter "Li").

As per claim 1, Li discloses a pharmaceutical composition comprising (a) a quinolone carboxylic acid derivative or a pharmaceutically acceptable salt (the pharmaceutical composition comprising delafloxacin meglumine; i.e., meglumine salt of delafloxacin, which is the quinolone carboxylic acid derivative 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate; paragraph [0136]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]).

As per claim 2, Li discloses the pharmaceutical composition of claim 1, and Li further discloses wherein said quinolone carboxylic acid derivative corresponds to the following structure of Formula 1, as shown (delafloxacin; paragraphs [0126], [0136]) wherein R1 represents a hydrogen atom (the hydrogen atom is attached to the carboxy group linked to the C3 carbon atom of the quinoline moiety in delafloxacin; paragraphs [0126], [0136]); R2 represents unsubstituted amino group (amino group is attached to the C6 carbon atom of the pyridinyl moiety of the delafloxacin; paragraphs [0126], [0136]); R3 represents a halogen atom (fluorine atom is attached to the C5 carbon atom of the pyridinyl moiety of the delafloxacin; paragraphs [0126], [0136]); R4 represents a halogen atom (fluorine atom is attached to the C6 carbon atom of the quinoline moiety of the delafloxacin; paragraphs [0126], [0136]); R5 represents a substituted saturated cyclic amino group (four membered cyclic

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azetidiny moiety substituted with hydroxy group is attached to the C7 carbon atom of the quinoline moiety of the delafoxacin; paragraphs [0126], [0136]); R6 represents a hydrogen atom (the hydrogen atom is attached to the C5 carbon atom of the quinoline moiety of the delafoxacin; paragraphs [0126], [0136]); X is a nitrogen atom (the N1 nitrogen atom is in the pyridinyl ring of the delafoxacin; paragraphs [0126], [0136]), Y is -CR7=, R7 is a halogen atom (the fluorine atom is attached to the C3 carbon atom is in the pyridinyl ring of the delafoxacin; paragraphs [0126], [0136]), Z is -CH= (the C4 carbon atom in the pyridinyl ring of the delafoxacin; paragraphs [0126], [0136]), with the proviso that at least one of X, Y and Z represent a nitrogen atom (X is the N1 nitrogen atom in the pyridinyl ring of the delafoxacin; paragraphs [0126], [0136]), and W represents -CR8= (the C8 carbon atom is in the quinoline moiety in delafoxacin; paragraphs [0126], [0136]); wherein R8 represents a halogen atom (the chlorine atom is attached to the C8 carbon atom of the quinoline moiety in delafoxacin; paragraphs [0126], [0136]), or a pharmaceutically acceptable salt (delafoxacin is in the form of a salt with meglumine, where the salt is a pharmaceutically acceptable salt; paragraphs [0013], [0136]).

As per claim 4, Li discloses the pharmaceutical composition of claim 1, and Li further discloses wherein said quinolone carboxylic acid derivative corresponds to the following compound (A), as shown (delafoxacin; paragraphs [0126], [0136]) or a pharmaceutically acceptable salt thereof (delafoxacin is in the form of a salt with meglumine, where the salt is a pharmaceutically acceptable salt; paragraphs [0013], [0136]).

As per claim 5, Li discloses the pharmaceutical composition of claim 1, and Li further discloses wherein said quinolone carboxylic acid derivative is a D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate (the quinolone carboxylic acid derivative is a crystalline D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate salt; paragraph [0035]).

As per claim 10, Li discloses the pharmaceutical composition of claim 5, and Li further discloses wherein said quinolone carboxylic acid derivative is D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate trihydrate (a composition wherein said quinolone carboxylic acid derivative is D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate trihydrate; paragraph [0127]).

As per claims 12/1-2, 12/4-5 and 12/10, Li discloses the pharmaceutical composition of claims 1-2, 4-5 and 10, and Li further discloses wherein the effervescent agent comprises sodium carbonate (the composition comprises sodium carbonate; paragraph [0260]).

As per claim 50, Li discloses a pharmaceutical composition for use in the manufacture of a medicament for treating, preventing or reducing the risk of infection in a patient in need thereof (compositions for manufacture of a medicament for treating, preventing or reducing the risk of infection in a patient in need thereof; paragraph [0277]), said composition comprising: (a) a quinolone carboxylic acid derivative (antimicrobial compositions of quinolone carboxylic acid derivatives; abstract); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]).

Claims 3 and 12/3 lack an inventive step under PCT Article 33(3) as being obvious over Li.

As per claim 3, Li discloses the pharmaceutical composition of claim 2, and Li further discloses wherein when R1 represents a hydrogen atom (the hydrogen atom is attached to the carboxy group linked to the C3 carbon atom of the quinoline moiety in delafoxacin; paragraphs [0126], [0136]), R2 represents an amino group (amino group is attached to the C6 carbon atom of the pyridinyl moiety of the delafoxacin; paragraphs [0126], [0136]), R3 represents a fluorine atom (fluorine atom is attached to the C5 carbon atom of the pyridinyl moiety of the delafoxacin; paragraphs [0126], [0136]), R4 represents a fluorine atom (fluorine atom is attached to the C6 carbon atom of the quinoline moiety of the delafoxacin; paragraphs [0126], [0136]), R6 represents a hydrogen atom (the hydrogen atom is attached to the C5 carbon atom of the quinoline moiety of the delafoxacin; paragraphs [0126], [0136]), X represents a nitrogen atom (the N1 nitrogen atom is in the pyridinyl ring of the delafoxacin; paragraphs [0126], [0136]), Y represents -CR7= wherein R7 represents a fluorine atom (the

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fluorine atom is attached to the C3 carbon atom in the pyridinyl ring of the delafloxacin; paragraphs [0126], [0136]), Z represents -CH= (the C4 carbon atom is in the pyridinyl ring of the delafloxacin; paragraphs [0126], [0136]), and W is -CR8= (the C8 carbon atom is in the quinoline moiety in delafloxacin; paragraphs [0126], [0136]) wherein R8 represents a chlorine atom (the chlorine atom is attached to the C8 carbon atom of the quinoline moiety in delafloxacin; paragraphs [0126], [0136]), or a pharmaceutically acceptable salt (delafloxacin is in the form of a salt with meglumine, where the salt is a pharmaceutically acceptable salt; paragraphs [0013], [0136]), and in a separate embodiment Li further discloses wherein R5 is not a 3-hydroxyazetidine-1-yl group (general formula 2, where R5 is a halogen; paragraph [0032]). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for wherein R5 is not a 3-hydroxyazetidine-1-yl group, as previously disclosed by Li in a separate embodiment (paragraph [0032]), for adjusting biopharmaceutical properties and toxicity of the compound. Further, provided that in both embodiments Li discloses quinolone carboxylic acid derivative (paragraphs [0032], [0126], [0136]), the modification to Li's composition, of providing for wherein R5 is not a 3-hydroxyazetidine-1-yl group, would have required only routine skill in the art.

As per claim 12/3, Li discloses the pharmaceutical composition of claim 3, and Li further discloses wherein the effervescent agent comprises sodium carbonate (the composition comprises sodium carbonate; paragraph [0260]).

Claims 6-7, 11, 12/6-7 and 12/11 lack an inventive step under PCT Article 33(3) as being obvious Li in view of the publication entitled "A Point-Focusing Camera for Single-Crystal Diffraction" (HARRISON).

As per claim 6, Li discloses the pharmaceutical composition of claim 1, and Li further discloses wherein said quinolone carboxylic acid derivative is a crystalline D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidinyl)-4-oxo-3-quinolinecarboxylate (the quinolone carboxylic acid derivative is a crystalline D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidinyl)-4-oxo-3-quinolinecarboxylate salt; paragraph [0035]) characterized by an X-ray powder diffraction pattern substantially in accordance with that shown in FIG. 1 (the powder diffraction pattern shown in figure 1 is substantially in accordance with the pattern shown in figure 1 of the instant application, where the location of the peaks are the same, and the intensity of the intensities of the peaks should be adjusted on the amount of the compound used for analysis; figure 1; paragraphs [0035], [0126]), wherein the pattern is obtained from a copper radiation source (Cu-Ka) (the powder diffraction pattern was measured with Cu-Ka radiation; paragraphs [0035], [0126]). Li does not disclose 40 kV, 4 mA. However, Harrison discloses 40 kV, 4 mA (X-ray tube operated at 40 kV and 4 mA; page 87, column 1, paragraph 2). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for 40 kV, 4 mA, as previously disclosed by Harrison (Harrison; page 87, column 1, paragraph 2), for providing a reproducible results in measuring of X-ray powder diffraction pattern using standardized power of the X-ray tube. Further, provided that Li and Harrison both disclose the procedure of producing the X-ray diffraction patterns (Li; paragraphs [0035], [0126]) (Harrison; abstract) using copper radiation (Li; paragraphs [0035], [0126]) (Harrison; page 87, column 1, paragraph 3), the modification to Li's composition, of providing for 40 kV, 4 mA, would have required only routine skill in the art.

As per claim 7, Li discloses the crystalline form of claim 5 (quinolone carboxylic acid derivative is in a crystalline form; paragraphs [0126]-[0127]), and Li further discloses characterized by an X-ray powder diffraction pattern having peaks (quinolone carboxylic acid derivative is in a crystalline form and characterized by the powder diffraction pattern; figures 1-2; paragraphs [0126]-[0127]) at about 6.35, 12.70, 19.10 and 20.50 degrees 2 theta (the powder diffraction pattern has peaks at about 6.35, 12.70, 19.10 and 20.50 degrees 2 theta, as shown in figures 1-2; paragraphs [0126]-[0127]), wherein the pattern is obtained from a copper radiation source (Cu-Ka) (the powder diffraction pattern was measured with Cu-Ka radiation; paragraphs [0035], [0126]-[0127]). Li does not disclose 40 kV, 4 mA. However, Harrison discloses 40 kV, 4 mA (X-ray tube operated at 40 kV and 4 mA; page 87, column 1, paragraph 2). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for 40 kV, 4 mA, as previously disclosed by Harrison (Harrison; page 87, column 1, paragraph 2), for providing a reproducible results in measuring of X-ray powder diffraction pattern using standardized power of the X-ray tube.

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As per claim 11, Li and Harrison, in combination, disclose the pharmaceutical composition of claim 7, and Li further discloses wherein said quinolone carboxylic acid derivative is crystalline D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate trihydrate (a composition wherein said quinolone carboxylic acid derivative is D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate trihydrate; paragraph [0127]), characterized, when measured at about 25 degrees C with Cu-Ka radiation (the powder diffraction pattern was measured with Cu-Ka radiation at 25 degrees C; paragraphs [0035], [0126]-[0127]), by the x-ray powder diffraction pattern shown in FIGURE 2 (x-ray powder diffraction of D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate trihydrate is shown on figure 2; paragraph [0127]).

As per claims 12/6-7 and 12/11, Li and Harrison, in combination, disclose the pharmaceutical composition of claims 6-7 and 11, and Li further discloses wherein the effervescent agent comprises sodium carbonate (the composition comprises sodium carbonate; paragraph [0260]).

Claims 13/12/1-5 and 13/12/10 lack an inventive step under PCT Article 33(3) as being obvious over Li in view of US 5,223,264 A to Wehling, et al (Hereinafter "Wehling").

As per claims 13/12/1-5 and 13/12/10, Li discloses the pharmaceutical composition of claims 12/1-5 and 12/10, and Li further discloses comprising citric acid, maleic acid, tartaric acid or fumaric acid (compounds include citric acid, maleic acid, tartaric acid, fumaric acid; paragraph [0147]). Li does not disclose a motivation to select citric acid, maleic acid, tartaric acid or fumaric acid from the list of other useful acids. However, Wehling discloses the motivation to select citric acid, maleic acid, tartaric acid or fumaric acid from the list of other useful acids (the effervescent disintegration agent may include citric acid, tartaric acid, malic acid, fumaric acid, and at least one base consisting of carbonate salts; column 3, lines 10-18). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for the motivation to select citric acid, maleic acid, tartaric acid or fumaric acid from the list of other useful acids, as previously disclosed by Wehling (Wehling; column 3, lines 10-18), for producing effervescent composition. Further, provided that Li and Wehling both disclose the compositions comprising effervescent agents (Li; paragraph [0260]) (Wehling; abstract) and pharmaceutically active ingredients (Li; paragraphs [0136], [0144]-[0145]) (Wehling; column 4, lines 5-10), where the composition comprises base and acid as additional ingredients (Li; paragraphs [0147], [0260]) (Wehling; column 3, lines 10-18), the modification to Li's composition, of providing for the motivation to select citric acid, maleic acid, tartaric acid or fumaric acid from the list of other useful acids, would have required only routine skill in the art.

Claims 17-20 lack an inventive step under PCT Article 33(3) as being obvious over Li in view of WO 2013/090891 A1 to CELANESE EVA PERFORMANCE POLYMERS, .INC (hereinafter "Celanese").

As per claim 17; Li discloses a pharmaceutical composition comprising: (a) from about 0.01% to about 80% by weight of a quinolone carboxylic acid derivative, as compared to the total weight of the composition on an acid basis (the pharmaceutical composition comprises from about 0.01 percent to about 50 percent of the quinolone carboxylic acid antimicrobial agent delafloxacin, as compared to the total weight of the composition, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0049]-[0050], [0189]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]). Li does not disclose from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition. However, Celanese discloses from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition (additional effervescent materials may be included in composition, additional ingredients may be included from 0.01 to 70 percent by weight of the controlled release vehicle; paragraphs [0086], [0090]; claim 7). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, as previously disclosed by Celanese (Celanese; paragraphs [0086], [0090]; claim 7), for providing a detailed protocol for producing effervescent composition. Further,

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provided that Li and Celanese both disclose the compositions comprising effervescent agents (Li; paragraph [0260]) (Celanese; paragraph [0086]) and an active agent for infection treatment (Li; abstract) (Celanese; paragraph [00104]), the modification to Li's composition, of providing for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, would have required only routine skill in the art.

As per claim 18, Li discloses a pharmaceutical composition comprising: (a) from about 0.01 percent to about 80 percent by weight of a quinolone carboxylic acid derivative, as compared to the total weight of the composition on an acid basis (the pharmaceutical composition comprises from about 0.01 percent to about 50 percent of the quinolone carboxylic acid antimicrobial agent delafloxacin, as compared to the total weight of the composition, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0049]-[0050], [0189]); (b) from about 0.1 percent to about 50 percent by weight of meglumine, as compared to the total weight of the composition (the pharmaceutical composition comprising comprises from about 0.1 percent to about 50 percent of the meglumine, as compared to the total weight of the composition; paragraph [0049], [0051]); and (c) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in claim 12 of the instant application; paragraph [0260]). Li does not disclose from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition. However, Celanese discloses from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition (additional effervescent materials may be included in composition, additional ingredients may be included from 0.01 to 70 percent by weight of the controlled release vehicle; paragraphs [0086], [0090]; claim 7). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, as previously disclosed by Celanese (Celanese; paragraphs [0086], [0090]; claim 7), for providing a detailed protocol for producing effervescent composition.

As per claim 19, Li discloses a pharmaceutical composition comprising: (a) from about 0.01 percent to about 50 percent by weight of delafloxacin, as compared to the total weight of the composition on an acid basis (the pharmaceutical composition comprising comprises from about 0.01 percent to about 50 percent of delafloxacin, as compared to the total weight of the composition, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0049]-[0050], [0189]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]). Li does not disclose from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition. However, Celanese discloses from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition (additional effervescent materials may be included in composition, additional ingredients may be included from 0.01 to 70 percent by weight of the controlled release vehicle; paragraphs [0086], [0090]; claim 7). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, as previously disclosed by Celanese (Celanese; paragraphs [0086], [0090]; claim 7), for providing a detailed protocol for producing effervescent composition.

As per claim 20, Li discloses a pharmaceutical composition comprising: (a) from about 0.01 percent to about 50 percent by weight of delafloxacin, as compared to the total weight of the composition on an acid basis (the pharmaceutical composition comprising comprises from about 0.01 percent to about 50 percent of delafloxacin, as compared to the total weight of the composition, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0049]-[0050], [0189]); (b) from about 0.1 percent to about 50 percent by weight of meglumine, as compared to the total weight of the composition (the pharmaceutical composition comprises from about 0.1 percent to about 50 percent of the meglumine, as compared to the total weight of the composition; paragraph [0049], [0051]); and (c) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]). Li does not disclose from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition. However, Celanese discloses from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition (additional effervescent materials may be included in composition, additional ingredients may be included from

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0.01 to 70 percent by weight of the controlled release vehicle; paragraphs [0086], [0090]; claim 7). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition as previously disclosed by Li, in order to have provided for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, as previously disclosed by Celanese (Celanese; paragraphs [0086], [0090]; claim 7), for providing a detailed protocol for producing effervescent composition.

Claims 21-22 lack an inventive step under PCT Article 33(3) as being obvious over Li in view of US 6,350,470 B1 to Pather, et al (hereinafter "Pather").

As per claim 21, Li discloses a pharmaceutical composition comprising: (a) from about 0.01 percent to about 50 percent by weight of delafloxacin, as compared to the total weight of the composition on an acid basis (the pharmaceutical composition comprises from about 0.01 percent to about 50 percent of delafloxacin, as compared to the total weight of the composition, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0049]-[0050] [0189]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in claim 12 of the instant application; paragraph [0260]). Li does not disclose from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, said effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid. However, Pather discloses from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition (Pather; the effervescent is provided in an amount of between about 5 percent and about 95 percent by weight, based on the weight of the finished tablet; column 2, lines 55-60), said effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid (Pather; effervescent enhancers evolve gas by means of a chemical reaction upon exposure to water, and include acid and carbonate, which are citric acid and sodium bicarbonate, and also, include required for effervescence a pH adjusting substance sodium dihydrogen phosphate; column 2, lines 60-67; column 3, lines 1-10, 15-20, 55-60). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, said effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, as previously disclosed by Pather (Pather; column 2, lines 55-67; column 3, lines 1-10, 15-20, 55-60), for providing a detailed protocol for producing effervescent composition. Further, provided that Li and Pather both disclose the compositions comprising effervescent agents (Li; paragraph [0260]) (Pather; column 2, lines 55-67; column 3, lines 1-10, 15-20, 55-60) and an active agent for infection treatment (Li; abstract) (Pather; the composition comprises acyclovir; column 3, lines 60-64; column 4; lines 1-5), the modification to Li's composition, of providing for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, said effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, would have required only routine skill in the art.

As per claim 22, Li discloses a pharmaceutical composition comprising: (a) from about 0.01 percent to about 50 percent by weight of delafloxacin, as compared to the total weight of the composition on an acid basis (the pharmaceutical composition comprising comprises from about 0.01 percent to about 50 percent of delafloxacin, as compared to the total weight of the composition, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0049]-[0050] [0189]); (b) from about 0.1 percent to about 50 percent by weight of meglumine, as compared to the total weight of the composition (the pharmaceutical composition comprising comprises from about 0.1 percent to about 50 percent of the meglumine, as compared to the total weight of the composition; paragraph [0049], [0051]); and (c) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, a disclosed in claim 12 of the instant application; paragraph [0260]). Li does not disclose from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, said effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid. However, Pather discloses from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition (Pather; the effervescent is provided in an amount of between about 5 percent and about 95 percent by weight, based on the weight of the finished tablet; column 2, lines 55-60), said effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid (Pather; effervescent

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enhancers evolve gas by means of a chemical reaction upon exposure to water, and include acid and carbonate, which are citric acid and sodium bicarbonate, and also, include required for effervescence a pH adjusting substance sodium dihydrogen phosphate; column 2, lines 60-67; column 3, lines 1-10, 15-20, 55-60). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for from about 0.1 percent to about 50 percent by weight of an effervescent agent, as compared to the total weight of the composition, said effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, as previously disclosed by Pather (Pathar; column 2, lines 55-67; column 3, lines 1-10, 15-20, 55-60), for providing a detailed protocol for producing effervescent composition.

Claims 23-28 lack an inventive step under PCT Article 33(3) as being obvious over Li in view of US 2012/0149690 A1 to Dang, et al (hereinafter "Dang").

As per claim 23, Li discloses a pharmaceutical composition comprising: (a) from about 100 mg to about 750 mg of delafloxacin, on an acid active basis (the pharmaceutical composition comprising from about 100 mg to about 500 mg of delafloxacin, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0062]-[0063], [0189]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]). Li does not disclose from about 100 mg to about 500 mg of an effervescent agent. However, Dang discloses from about 100 mg to about 500 mg of an effervescent agent (tablets comprise from 50 to 5000 mg of an effervescent base, the effervescent base comprises an organic edible acid, a salt thereof, and at least one alkali metal bicarbonate; paragraphs [1110], [1114]). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li in order to have provided for from about 100 mg to about 500 mg of an effervescent agent, and citric acid, as previously disclosed by Dang (Dang; paragraphs [1110], [1114]), for providing a detailed protocol for producing effervescent composition. Further, provided that Li and Dang both disclose the compositions comprising effervescent agents (Li; paragraph [0260]) (Dang; paragraph [1115]) and an active agent for infection treatment (Li; abstract) (Dang; paragraph [0097]), the modification to Li's composition, of providing for from about 100 mg to about 500 mg of an effervescent agent, would have required only routine skill in the art.

As per claim 24, Li discloses a pharmaceutical composition comprising: (a) from about 100 mg to about 750 mg of delafloxacin, on an acid active basis (the pharmaceutical composition comprising from about 100 mg to about 500 mg of delafloxacin, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0062]-[0063], [0189]); and (b) an effervescent agent (the effervescent base comprises from about 50 mg to about 2000 mg sodium bicarbonate and from about 20 mg to about 1500 mg citric acid; paragraph [1115]). Li does not disclose from about 100 mg to about 500 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid. However, Dang discloses from about 100 mg to about 500 mg of an effervescent agent (tablets comprise from 50 to 5000 mg of an effervescent base, the effervescent base comprises an organic edible acid a salt thereof, and at least one alkali metal bicarbonate; paragraphs [1110], [1114]) comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid (the effervescent base comprises from about 50 mg to about 2000 mg sodium bicarbonate and from about 20 mg to about 1500 mg citric acid, it is also suitable to add buffer substances such as phosphates to adjust the pH value to 6 to 7.5 pharmaceutically acceptable acidic salts include sodium dihydrogen phosphate; paragraphs [1112], [1115], [1201]). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for from about 100 mg to about 500 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, as previously disclosed by Dang (Dang; paragraphs [1110], [1112], [1114]-[1115], [1201]), for providing a detailed protocol for producing effervescent composition.

As per claim 25, Li discloses a pharmaceutical composition comprising: (a) about 400 mg of delafloxacin meglumine, on an acid active basis (the pharmaceutical composition comprising from about 100 mg to about 500 mg of delafloxacin and 15 mg to about 125 mg of meglumine, the weight of the compound should be adjusted if a salt is used, i.e., weight on an acid basis; paragraphs [0062]-[0064], [0189]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]). Li does not disclose about 150 mg of an

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effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid. However, Dang discloses about 150 mg of an effervescent agent (tablets comprise from 50 to 5000 mg of an effervescent base, the effervescent base comprises an organic edible acid, a salt thereof, and at least one alkali metal bicarbonate; paragraphs [1110], [1114]) comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid (the effervescent base comprises from about 50 mg to about 2000 mg sodium bicarbonate and from about 20 mg to about 1500 mg citric acid, it is also suitable to add buffer substances such as phosphates to adjust the pH value to 6 to 7.5, pharmaceutically acceptable acidic salts include sodium dihydrogen phosphate; paragraphs [1112], [1115], [1201]). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for about 150 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, as previously disclosed by Dang (Dang; paragraphs [1110], [1112], [1114]-[1115], [1201]), for providing a detailed protocol for producing effervescent composition.

As per claim 26, Li discloses a pharmaceutical composition comprising: (a) about 400 mg of delafloxacin (the pharmaceutical composition comprising from about 100 mg to about 500 mg of delafloxacin; paragraphs [0062]-[0063]), (b) about 177 mg of meglumine (active compound comprises from about 0.1 to about 1500 mg per dose, the composition comprises from about 0.1 percent to about 50 percent by weight of meglumine; paragraphs [0049], [0051], [0275]); and (c) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]). Li does not disclose about 150 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid. However, Dang discloses about 150 mg of an effervescent agent (tablets comprise from 50 to 5000 mg of an effervescent base, the effervescent base comprises an organic edible acid, a salt thereof, and at least one alkali metal bicarbonate; paragraphs [1110], [1114]) comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid (the effervescent base comprises from about 50 mg to about 2000 mg sodium bicarbonate and from about 20 mg to about 1500 mg citric acid, it is also suitable to add buffer substances such as phosphate, to adjust the pH value to 6 to 7.5, pharmaceutically acceptable acidic salts include sodium dihydrogen phosphate; paragraphs [1112], [1115], [1201]). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for about 150 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, as previously disclosed by Dang (Dang; paragraphs [1110], [1112], [1114]-[1115], [1201]), for providing a detailed protocol for producing effervescent composition.

As per claim 27, Li discloses a pharmaceutical composition comprising: (a) about 450 mg of delafloxacin (the pharmaceutical composition comprising from about 100 mg to about 500 mg of delafloxacin; paragraphs [0062]-[0063]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the instant application; paragraph [0260]). Li does not disclose about 150 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid. However, Dang discloses about 150 mg of an effervescent agent (tablets comprise from 50 to 5000 mg of an effervescent base, the effervescent base comprises an organic edible acid, a salt thereof, and at least one alkali metal bicarbonate; paragraphs [1110], [1114]) comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid (the effervescent base comprises from about 51 mg to about 2000 mg sodium bicarbonate and from about 20 mg to about 1500 mg citric acid, it is also suitable to add buffer substances such as phosphates to adjust the pH value to 6 to 7.5, pharmaceutically acceptable acidic salts include sodium dihydrogen phosphate; paragraphs [1112], [1115], [1201]). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for about 150 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, as previously disclosed by Dang (Dang; paragraphs [1110], [1112], [1114]-[1115], [1201]), for providing a detailed protocol for producing effervescent composition.

As per claim 28, Li discloses a pharmaceutical composition comprising: (a) about 650 mg of delafloxacin meglumine (active compound comprises from about 0.1 to about 1500 mg per dose, the composition comprises from about 0.01 percent to about 50 percent by weight of delafloxacin and from about 0.1 percent to about 50 percent by weight of meglumine; paragraphs [0049]-[0051], [0275]); and (b) an effervescent agent (the composition comprises sodium carbonate, which is the effervescent agent, as disclosed in the claim 12 of the

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instant application; paragraph [0260]). Li does not disclose about 150 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid. However, Dang discloses about 150 mg of an effervescent agent (tablets comprise from 50 to 5000 mg of an effervescent base, the effervescent base comprises an organic edible acid, a salt thereof, and at least one alkali metal bicarbonate; paragraphs [1110], [1114]) comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid (the effervescent base comprises from about 50 mg to about 2000 mg sodium bicarbonate and from about 20 mg to about 1500 mg citric acid, it is also suitable to add buffer substances such as phosphates to adjust the pH value to 6 to 7.5, pharmaceutically acceptable acidic salts include sodium dihydrogen phosphate; paragraphs [1112], [1115], [1201]). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for about 150 mg of an effervescent agent comprising a mixture of sodium bicarbonate, sodium dihydrogen phosphate, and citric acid, as previously disclosed by Dang (Dang; paragraphs [1110], [1112], [1114]-[1115], [1201]), for providing a detailed protocol for producing effervescent composition.

Claims 13/12/6-7 and 13/12/11 lack an inventive step under PCT Article 33(3) as being obvious over Li in view of Harrison, and further in view of Wehling.

As per claims 13/12/6-7 and 13/12/11, Li and Harrison, in combination, disclose the pharmaceutical composition of claims 12/6-7 and 12/11, and Li further discloses comprising citric acid, maleic acid, tartaric acid or fumaric acid (compounds include citric acid, maleic acid, tartaric acid, fumaric acid; paragraph [0147]). Li does not disclose a motivation to select citric acid, maleic acid, tartaric acid or fumaric acid from the list of other useful acids. However, Wehling discloses the motivation to select citric acid, maleic acid, tartaric acid or fumaric acid from the list of other useful acids (the effervescent disintegration agent may include citric acid, tartaric acid, malic acid, fumaric acid, and at least one base consisting of carbonate salts; column 3, lines 10-18). Thus, it would have been obvious to a person of ordinary skill in the art, at the time of the invention, to have modified the composition, as previously disclosed by Li, in order to have provided for the motivation to select citric acid, maleic acid, tartaric acid or fumaric acid from the list of other useful acids, as previously disclosed by Wehling (Wehling; column 3, lines 10-18), for producing effervescent composition.

Claims 8-9, 12/8-9, and 13/12/8-9 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the claimed matter.

Claim 8 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the crystalline form of claim 5, characterized by a melting point of about 168-171 degrees C.

Li discloses the crystalline form of claim 5 (quinolone carboxylic acid derivative is in a crystalline form; paragraphs [0126]-[0127]). However, Li does not disclose the crystalline form characterized by a melting point of about 168-171 degrees C.

US 5,194,617 A to Minowa, et al (hereinafter "Minowa") discloses the crystalline form characterized by a melting point of about 168-171 degrees C (compound 4, which is 2-(cis-1-nonenyl)-3-methyl-4-quinolone, has a melting point 170-171 degrees C; column 7, lines 1-15). However, Minowa does not disclose the crystalline form of D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-6-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidyl)-4-oxo-3-quinolinecarboxylate characterized by a melting point of about 168-171 degrees C.

WO 2012/069856 A1 to LIVERPOOL SCHOOL OF TROPICAL MEDICINE (hereinafter "Liverpool") discloses the crystalline form characterized by a melting point of about 168-171 degrees C (compound 41a, which is 7-methoxy-3-methyl-2-(1-(4-(trifluoromethoxy) benzyl)-1H-pyrazol-4-yl)quinolin-4(1H)-one has a melting point 171-173 degrees C; paragraphs [00388]-[00389]). However, Liverpool does not disclose the crystalline form of D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidyl)-4-oxo-3-quinolinecarboxylate characterized by a melting point of about 168-171 degrees C.

Claim 9 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the crystalline form of claim 5, characterized by the differential scanning calorimetry thermogram shown in FIG. 3.

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Li discloses the crystalline form of claim 5 (quinolone carboxylic acid derivative is in a crystalline form; paragraphs [0126]-[0127]). However, Li does not disclose the crystalline form characterized by the differential scanning calorimetry thermogram shown in FIG. 3.

WO 2012/097273 A1 to VERTEX PHARMACEUTICALS INCORPORATED (hereinafter "Vertex") discloses the crystalline form characterized by the differential scanning calorimetry thermogram (figure 2 shows a DSC Differential Scanning Calorimetry thermogram of solid Form I of the 6-fluoro benzimidazolyl urea; paragraph [0020]). However, Vertex does not disclose the crystalline form of D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate characterized by the differential scanning calorimetry thermogram shown in FIG. 3.

CA 2 824 197 A to INFINITY PHARMACEUTICALS, INC (hereinafter "Infinity") discloses the crystalline form characterized by the differential scanning calorimetry thermogram (figure 12 shows a differential scanning calorimetry DSC thermogram for Polymorph Form A; paragraph [0040]). However, Infinity does not disclose the crystalline form of D-glucitol, 1-deoxy-1-(methylamino)-, 1-(6-amino-3,5-difluoro-2-pyridinyl)-8-chloro-6-fluoro-1,4-dihydro-7-(3-hydroxy-1-azetidiny)-4-oxo-3-quinolinecarboxylate characterized by the differential scanning calorimetry thermogram shown in FIG. 3.

Claims 12/8-9 and 13/12/8-9 meet the criteria set out in PCT Article 33(2)-(3), because they depend on claims 8-9.

Claims 1-11, 12/1-11, 13/12/1-11, 17-28 and 50 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.