PTO/AIA/15 (03-13)
Approved for use through 01/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995 no persons are required to respond to a collection of information unless it displays a valid OMB control number

UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	U0157.70023US03
First Named Inventor	Michael J. Zaworotko
Title	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Express Mail Label No.	

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

1. [ ] **Fee Transmittal Form** (PTO/SB/17 or equivalent)
2. [X] **Applicant asserts small entity status.** See 37 CFR 1.27
3. [ ] **Applicant certifies micro entity status.** See 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent.
4. [X] **Specification** [*Total Pages* 42]
   Both the claims and abstract must start on a new page.
   (See MPEP § 608.01(a) for information on the preferred arrangement)
5. [X] **Drawing(s)** (35 U.S.C. 113) [*Total Sheets* 22]
6. **Inventor's Oath or Declaration** [*Total Pages* 3]
   (including substitute statements under 37 CFR 1.64 and assignments serving as an oath or declaration under 37 CFR 1.63(e))
   a. [ ] Newly executed (original or copy)
   b. [X] A copy from a prior application (37 CFR 1.63(d))
7. [X] **Application Data Sheet** * *See note below.*
   See 37 CFR 1.76 (PTO/AIA/14 or equivalent)
8. **CD-ROM or CD-R** in duplicate, large table, or Computer Program (*Appendix*)
   [ ] Landscape Table on CD
9. **Nucleotide and/or Amino Acid Sequence Submission** (*if applicable, items a. – c. are required*)
   a. [ ] Computer Readable Form (CRF)
   b. [ ] Specification Sequence Listing on:
      i. [ ] CD-ROM or CD-R (2 copies); or
      ii. [ ] Paper
   c. [ ] Statements verifying identity of above copies

ADDRESS TO: **Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450**

ACCOMPANYING APPLICATION PAPERS

10. [ ] **Assignment Papers** (cover sheet & document(s))
    Name of Assignee
11. [ ] **37 CFR 3.73(c) Statement** (*when there is an assignee*) [ ] **Power of Attorney**
12. [ ] **English Translation Document** (*if applicable*)
13. [ ] **Information Disclosure Statement** (PTO/SB/08 or PTO-1449)
    [ ] Copies of citations attached
14. [X] **Preliminary Amendment**
15. [ ] **Return Receipt Postcard** (*MPEP § 503*) (*Should be specifically itemized*)
16. [ ] **Certified Copy of Priority Document(s)** (*if foreign priority is claimed*)
17. [ ] **Nonpublication Request** Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent.
18. [ ] **Other:**

***Note:** (1) Benefit claims under 37 CFR 1.78 and foreign priority claims under 1.55 **must** be included in an Application Data Sheet (ADS).
(2) For applications filed under 35 U.S.C. 111, the application must contain an ADS specifying the applicant if the applicant is an assignee, person to whom the inventor is under an obligation to assign, or person who otherwise shows sufficient proprietary interest in the matter. See 37 CFR 1.46(b).

19. CORRESPONDENCE ADDRESS

[X] The address associated with Customer Number: 23628 **OR** [ ] Correspondence address below

Name					
Address					
City		State		Zip Code	
Country		Telephone		Email	

Signature	/Edward R. Gates/	Date	June 30, 2017
Name (Print/Type)	Edward R. Gates	Registration No. (Attorney/Agent)	31,616

5572568.1

Application Data Sheet

Inventor Information

Inventor Number::	1
Name Prefix::	Mr.
Given Name::	Michael
Middle Name::	J.
Family Name::	Zaworotko
City of Residence::	Tampa
State or Province of Residence::	FL
Country of Residence::	US
Street of mailing address::	4202 E. Fowler Avenue
City of mailing address::	Tampa
State or Province of mailing address::	FL
Country of mailing address::	US
Postal or Zip Code of mailing address::	33620

Inventor Number::	2
Given Name::	Nair
Family Name::	Rodriguez-Hornedo
City of Residence::	Ann Arbor
State or Province of Residence::	MI
Country of Residence::	US
Street of mailing address::	1690 Northbrook Drive

City of mailing address::	Ann Arbor
State or Province of mailing address::	MI
Country of mailing address::	US
Postal or Zip Code of mailing address::	48103

Inventor Number::	3
Given Name::	Brian
Family Name::	Moulton
City of Residence::	Temple Terrace
State or Province of Residence::	FL
Country of Residence::	US
Street of mailing address::	13455 Century Cove Drive #325
City of mailing address::	Temple Terrace
State or Province of mailing address::	FL
Country of mailing address::	US
Postal or Zip Code of mailing address::	33637

Correspondence Information

Correspondence Customer Number::	23628

Application Information

Application Type::	Regular
Subject Matter::	Utility
CD-ROM or CD-R?::	None

Sequence submission?::	None
Computer Readable Form (CRF)?::	No
Title::	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Attorney Docket Number::	U0157.70023US03
Request for Early Publication?::	No
Request for Non-Publication?::	No
Total Drawing Sheets::	22
Small Entity?::	Yes
Petition included?::	No
Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2::	No
This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013::	No

Representative Information

Representative Customer Number::	23628

Domestic Priority Information

Application::	Continuity Type::	Parent Application::	Parent Filing Date::	Prior Appl Status::
This Application	Continuation of	10/378956	03/03/03	Pending
10/378956	An application claiming the benefit under 35 USC 119(e)	60/360768	03/01/02	Expired

Foreign Priority Information

Applicant Information

Applicant Number::	1
Applicant Type::	Assignee
Organization Name::	University of South Florida
Street of mailing address::	3802 Spectrum Boulevard
	Suite 100
City of mailing address::	Tampa
State or Province of mailing address::	FL
Country of mailing address::	US
Postal or Zip Code of mailing address::	33612

Applicant Number::	2
Applicant Type::	Assignee
Organization Name::	The Regents of the University of Michigan

Street of mailing address::	Wolverine Tower
	Room 2071; 3003 S. State Street
City of mailing address::	Ann Arbor
State or Province of mailing address::	MI
Country of mailing address::	US
Postal or Zip Code of mailing address::	48109-1280

Assignee Information Including Non-Applicant Assignee Information

Authorization or Opt-Out of Authorization to Permit Access

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Signature:

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). **However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).**

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Edward R. Gates/	Date (YYYY-MM-DD)	2017-06-30
Name	Edward R. Gates	Registration Number	31,616

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 8 of 415

DECLARATION (37 C.F.R. § 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 C.F.R. § 1.76)

Title of Invention	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

As the below named inventor, I declare that:

This declaration is directed to:

[x] The attached application, or

[ ] United States application or PCT international application number _____ filed on _____

[ ] As amended on _____ (if applicable):

The above-identified application was made or authorized to be made by me.

I believe the inventor(s) named below to be the original and first inventor(s) of the subject matter which is claimed and for which a patent is sought.

I believe I am the original inventor or an original joint inventor of a claimed invention in the application.

I have reviewed and understand the contents of the above-identified application, including the claims, as amended by any amendment specifically referred to above.

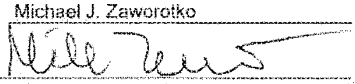
I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in 37 C.F.R. § 1.56.

All statements made herein of my own knowledge are true, and all statements made herein on information and belief are believed to be true.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. § 1001 by fine or imprisonment of not more than five (5) years, or both.

LEGAL NAME OF SOLE OR FIRST INVENTOR

Inventor one: Michael J. Zaworotko Date: Feb 4th 2014

Signature:  Citizen of: United Kingdom and Canada

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor two: Nair Rodriguez-Hornedo Date: _____

Signature: _____ Citizen of: United States

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor three: Brian Moulton Date: _____

Signature: _____ Citizen of: Canada

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor four: _____ Date: _____

Signature: _____ Citizen of: _____

[ ] Additional inventors are being named on _____ additional form(s) attached hereto.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 9 of 415

DECLARATION (37 C.F.R. § 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 C.F.R. § 1.76)

Title of Invention	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

As the below named inventor, I declare that:

This declaration is directed to:

[x] The attached application, or

[ ] United States application or PCT international application number _____ filed on _____

[ ] As amended on _____ (if applicable);

The above-identified application was made or authorized to be made by me.

I believe the inventor(s) named below to be the original and first inventor(s) of the subject matter which is claimed and for which a patent is sought.

I believe I am the original inventor or an original joint inventor of a claimed invention in the application.

I have reviewed and understand the contents of the above-identified application, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in 37 C.F.R. § 1.56.

All statements made herein of my own knowledge are true, and all statements made herein on information and belief are believed to be true.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. § 1001 by fine or imprisonment of not more than five (5) years, or both.

LEGAL NAME OF SOLE OR FIRST INVENTOR

Inventor one: Michael J. Zaworotko Date: _____

Signature: _____ Citizen of: United Kingdom and Canada

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor two: Nair Rodriguez-Hornedo Date: Jan. 07, 2014

Signature: Nair Rodriguez-Hornedo Citizen of: United States

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor three: Brian Moulton Date: _____

Signature: _____ Citizen of: Canada

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor four: _____ Date: _____

Signature: _____ Citizen of: _____

[ ] Additional inventors are being named on _____ additional form(s) attached hereto.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 10 of 415

DECLARATION (37 C.F.R. § 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 C.F.R. § 1.76)

Title of Invention	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

As the below named inventor, I declare that:

This declaration is directed to:

[x] The attached application, or

[ ] United States application or PCT international application number _____ filed on _____

[ ] As amended on _____ (if applicable);

The above-identified application was made or authorized to be made by me.

I believe the inventor(s) named below to be the original and first inventor(s) of the subject matter which is claimed and for which a patent is sought.

I believe I am the original inventor or an original joint inventor of a claimed invention in the application.

I have reviewed and understand the contents of the above-identified application, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in 37 C.F.R. § 1.56.

All statements made herein of my own knowledge are true, and all statements made herein on information and belief are believed to be true.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. § 1001 by fine or imprisonment of not more than five (5) years, or both.

LEGAL NAME OF SOLE OR FIRST INVENTOR

Inventor one: Michael J. Zaworotko Date: _____

Signature: _____ Citizen of: United Kingdom and Canada

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor two: Nair Rodriguez-Hornedo Date: _____

Signature: _____ Citizen of: United States

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor three: Brian Moulton Date: 01.28.14

Signature: _____ Citizen of: Canada

LEGAL NAME OF ADDITIONAL JOINT INVENTOR, if any

Inventor four: _____ Date: _____

Signature: _____ Citizen of: _____

[ ] Additional inventors are being named on _____ additional form(s) attached hereto.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 11 of 415

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	Not Yet Assigned
Confirmation No.:	N/A
Filed:	Concurrently Herewith
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	Not Yet Assigned
Art Unit:	N/A

Certificate of Electronic Filing under 37 CFR §1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: June 30, 2017 Electronic Signature for Nicole M. Forgrave: /Nicole M. Forgrave/

FIRST PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.115

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

Prior to examination on the merits, please amend the above-identified U.S. patent application as follows:

Amendments to the Specification begin on page 2 of this paper.

Remarks/Arguments begin on page 3 of this paper.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 12 of 415

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph under "CROSS-REFERENCE TO RELATED APPLICATION" on page 1 with the following paragraph:

The present application is a continuation of U.S. Application Serial No. 10/378,956, filed March 2, 2003, which is hereby incorporated by reference herein in its entirety, including any figures, tables, or drawings. U.S. Application Serial No. 10/378,956 claims the benefit of priority of U.S. Provisional Application Serial No. 60/360,768, filed March 1, 2002, which is hereby incorporated by reference herein in its entirety, including any figures, tables, or drawings.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 13 of 415

REMARKS

Applicant has amended the specification to update the section under "CROSS-REFERENCE TO RELATED APPLICATION".

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge Deposit Account No. 23/2825 under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Dated: June 30, 2017

Respectfully submitted,

By: /Edward R. Gates/
Edward R. Gates
Registration No.: 31,616
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 14 of 415

DESCRIPTION

MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

CROSS-REFERENCE TO RELATED APPLICATION

The present application claims the benefit of priority of U.S. Provisional Application Serial No. 60/360,768, filed March 1, 2002, which is hereby incorporated by reference herein in its entirety, including any figures, tables, or drawings.

BACKGROUND OF THE INVENTION

[0001] The last decade has witnessed tremendous advances in the understanding of, and the ability to manipulate, molecular and supramolecular assemblies (Moulton, B. *et al.*, *Chem. Rev.*, 2001, 101:1629-1658). There are new paradigms concerning the design and synthesis of a new generation of functional materials and molecules. Such advances are a consequence of the fundamental importance of intermolecular interactions, structure and cooperativity in many aspects of molecular science, from environmental science to molecular biology, to pharmacology, to materials science. Thus, the prospects for control and manipulation of materials at the molecular level, particularly in areas related to non-covalent bonding and nanotechnology, are now truly exceptional. However, whereas crystal structure determination has been a tool used by scientists since the 1920's, crystal structure prediction remains a largely unmet goal (Ball, P. *Nature*, 1996, 381:648-650; Gavezzotti, A. *Acc. Chem. Res.*, 1994, 27:309-314). Furthermore, the existence of more than one crystalline form of a given molecular compound, typically in the form of polymorphs or solvates, represents both a problem and an opportunity (Desiraju, G.R. *Science*, 1997, 278:404-405; Bernstein, J. *et al.*, *Angew. Chem., Int. Ed. Engl.*, 1999, 38:3441-3461). This is particularly true for the pharmaceutical industry.

[0002] Crystal engineering (Schmidt, G.M.J. *Pure Appl. Chem.*, 1971, 27:647-678; Desiraju, G.R. *Crystal Engineering: the Design of Organic Solids*, 1989, Elsevier: Amsterdam) is predicated on the assumption that crystals are *de facto* examples of self-assembly, *i.e.* crystals are comprised from a series of molecular recognition events or *supramolecular synthons*

(Desiraju, G.R. *Angew. Chem., Int. Ed. Engl.*, 1995, 34:2311-2327). It also offers a more realizable goal than crystal structure prediction since it relies on design and allows for careful selection of substrates, *i.e.* substrates that are predisposed to form predictable self-assembled superstructures can be targeted for study. Furthermore, the prototypal molecules used in crystal engineering contain exofunctional molecular recognition sites and they can be complementary with themselves (self-assembly) (Boucher, E. *et al.*, *J. Org. Chem.*, 1995, 60:1408-1412) or with other molecules (modular self-assembly) (Zaworotko, M.J. *Chem. Soc. Rev.*, 1994, 23:283-288; Sharma, C.V.K. and M.J. Zaworotko *Chem. Commun.*, 1996, 2655-2656). Coincidentally, most pharmaceutical molecules also contain exterior molecular recognition sites and, although this makes them susceptible to polymorphism and solvate formation, it also makes them attractive candidates for crystal engineering studies.

[0003] The ability of crystalline self-assemblies to be built from a bottom-up approach (Feynman, R. *Engineering and Science*, 1960, 22-36) could provide an exceptional control of the design of new phases at a molecular level. This contrasts with the current state-of-the-art: "The number of forms known for a given compound is proportional to the time and money spent in research on that compound" (McCrone, W.C. *Polymorphism in Physics and Chemistry of the Organic Solid-State*, pp. 726, Fox *et al.* Eds., Interscience: New York, 1965). This statement summarizes the predicaments and opportunities that one faces when dealing with a need to assert control over the composition and structure of pharmaceutical compounds in the solid state. Specifically, physical properties of crystalline solids are critically dependent on the internal arrangement of molecules or ions, making prediction of composition, crystal structure and morphology from knowledge of molecular structure a scientific challenge of the highest order. However, crystal structure prediction and even prediction of composition remains a largely unmet goal. Nonetheless, crystal engineering offers the intriguing possibility of using molecular components for their ability to impart functional characteristics (such as solubility, dissolution rate and stability) for the development of new delivery systems.

[0004] Undesirable physicochemical properties, physiological barriers, or issues of toxicity often limit the therapeutic benefit of drugs. This has motivated research in drug delivery systems for poorly soluble, poorly absorbed and labile substances. Crystalline self-assemblies represent a promising delivery modality for improving drug solubility, dissolution rate, stability and bioavailability. In addition, enhancement of drug activity can be achieved by means of

inclusion complexation or molecular encapsulation. These systems offer various advantages over amorphous polymeric delivery systems both from design and stability perspectives. In this context, the existence of more than one crystalline form of a given compound, typically in the form of polymorphs or solvates, represents both a problem and an opportunity. Several factors further complicate the situation. For example, the Food and Drug Administration's (FDA's) strict purity requirements effectively mean that a particular crystalline phase of a drug must be selected and that its composition must be established. This has typically meant that a consistent X-ray powder diffraction (XPD) pattern is required (Federal Drug Administration *Fed. Regist.*, 1997, 62:62893-62894). The need to ensure that processing produces both purity and ease of processing is problematic because many drug molecules are prone to form multiple phases, and crystal size and morphology can vary for a given phase. The commercial and public image costs of not ensuring that processing is reliable and reproducible is at best very high, as demonstrated by the recent pull back and reformulation of NORVIR by ABBOTT LABORATORIES).

[0005] That XPD patterns have been relied on for quality control is convenient but is in many ways unfortunate since XPD is not as foolproof as single crystal X-ray crystallography (*e.g.* similar patterns can be obtained for different phases, composition is not unambiguously determined), and XPD does not determine crystal packing. Knowledge of crystal packing is important because it helps explain the solubility and composition of a particular phase and provides other valuable information. However, the materials properties of pharmaceuticals and the existence of polymorphs are generally investigated at the tail end of the drug development process.

[0006] Accordingly, it would be advantageous to provide a wide range of novel solid phases having properties, such as melting point, solubility, dissolution rate, chemical stability, thermodynamic stability, and/or bioavailability, which are different from existing solid forms of the pharmaceutical molecule upon which they are based.

BRIEF SUMMARY OF THE INVENTION

[0007] The subject invention relates to the application of the concepts of crystal engineering towards the design of new pharmaceutical phases that contain more than one molecular component.

[0008] The subject invention concerns multiple-component solids having at least one active pharmaceutical ingredient. Examples of pharmaceutical molecules that may be utilized as active pharmaceutical ingredients in the multiple-component solids of the subject invention include, but are not limited to, aspirin, one or more members of the profen series (*e.g.*, ibuprofen and flurbiprofen), carbamazepine, phenytoin, and acetaminophen. Multiple-component solids, such as multiple-component crystals, containing these pharmaceutical ingredients and complementary molecules (hereafter referred to as "cocrystal formers") have been characterized by various techniques and can exhibit physical and/or chemical properties that are the same or different from the parent pharmaceutical ingredient as a direct result of alternative molecular recognition patterns. These novel crystalline assemblies can afford improved drug solubility, dissolution rate, stability and bioavailability.

[0009] The subject invention relates to the application of the concepts of crystal engineering towards the design of new pharmaceutical solid phases, such as multiple-component phases, using cocrystal formers that are complementary in the sense of supramolecular chemistry, *i.e.* they form supramolecular synthons with pharmaceutical molecules or ions. The cocrystal formers can be, but are not limited to, solvent molecules, other drug molecules, GRAS compounds, or approved food additives. Pharmaceutical molecules or ions are inherently predisposed for such crystal engineering studies since they already contain molecular recognition sites that bind selectively to biomolecules, and they are prone to supramolecular self-assembly. Examples of the groups commonly found in active pharmaceutical ingredients, and which are capable of forming supramolecular synthons include, but are not limited to, acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases (*e.g.* pyridines, imidazoles), amines, alcohols, halogens, sulfones, nitro groups, S-heterocycles, N-heterocycles (saturated or unsaturated), and O-heterocycles. Other examples include ethers, thioethers, thiols, esters, thioesters, thioketones, epoxides, acetonates, nitrils, oximes, and organohalides. Some of these groups can form supramolecular synthons with identical groups in similar or different molecules and are termed homosynthons, *e.g.* acids and amides. Other groups can form supramolecular synthons with different groups and are termed heterosynthons, *e.g.* acid/amide; pyridine/amide; alcohol/amine. Heterosynthons are particularly suitable for formation of multiple-component crystals whereas homosynthons can sometimes form multiple-component crystals.

[0010] In one aspect, the subject invention concerns methods for identifying complementary chemical functionalities to form a desired supramolecular synthon, wherein the method comprises the steps of evaluating the structure of an active pharmaceutical ingredient (API), which can include determining its crystal structure; determining whether the API contains chemical functionalities capable of forming supramolecular synthons with itself; identifying from a plurality of chemical functionalities that are known to form a supramolecular synthon at least one chemical functionality that will form a further supramolecular synthon to the supramolecular synthon formed by the API, wherein the identified chemical functionality is not capable of disrupting non-covalent bonding within the supramolecular synthon formed by the supramolecular synthon formed by the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to the supramolecular synthon formed by the API; and identifying co-crystal formers having chemical functionalities that are complementary with the API.

[0011] In another aspect, the subject invention concerns methods for identifying complementary chemical functionalities to form a desired supramolecular synthon, wherein the method comprises the steps of evaluating the structure of an API, which can include determining its crystal structure; determining whether the API contains chemical functionalities capable of forming supramolecular synthons with itself; identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the API, wherein the identified chemical functionality is capable of disrupting non-covalent bonding within the supramolecular synthon formed by the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the API; and identifying co-crystal formers having chemical functionalities that are complementary with the API. Thus, according to this method, the formation of homosynthons for the purpose of disrupting the intermolecular interactions between pharmaceutical moieties can be carried out.

In still another aspect, the subject invention concerns methods for identifying complementary chemical functionalities to form a desired supramolecular synthon, wherein the method comprises the steps of evaluating the structure of an API, which can include determining its crystal structure; determining whether the API contains chemical functionalities capable of forming supramolecular synthons with different molecules; identifying from a plurality of

chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the API; and identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

[0012] As indicated above, certain aspects of the subject invention can involve selecting a chemical functionality that is capable of disrupting the non-covalent bonding between identical functionalities (homosynthon) and form a non-covalent bond between different, yet complementary, functionalities (heterosynthon); selecting a plurality of molecular entities that comprise the complementary functionality (preferably GRAS compounds or approved food additives); identifying additional chemical features on the molecular entities that will not interfere with the formation of the desired supramolecular synthon and that will impart the desired physical properties to the target phase; and, optionally, preparing a new solid phase that is composed of the pharmaceutical moiety and the complementary molecular entity (such as a multiple-component phase or two component phase) by crystallization techniques comprising reactions in solvent, and/or solventless reactions, that afford crystalline materials. Optionally, the methods can further include at least one of the subsequent steps of determining the structure of the new solid phase formed; and analyzing the physical properties of the new solid phase.

[0013] The subject invention further concerns new solid phases identified or produced using the methods identified herein. The subject invention further pertains to a multiple-component phase composition comprising a solid material (phase) that is sustained by intermolecular interactions between two or more independent molecular entities, in any stoichiometric ratio, wherein at least one of the independent molecular entities is a pharmaceutical entity. The multiple-component phase composition can be, for example, a discrete supramolecular entity or a polymeric structure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] **Figure 1** shows the chemical structure of ibuprofen. The external functionalities are an isopropyl group (encircled on the left, in cyan) and a carboxylic acid (encircled on the right, in magenta).

[0015] Figure 2 shows a scheme with the synthon of pure ibuprofen on the left and the supramolecular entity containing the synthon on the right, demonstrating that pure phases of ibuprofen are sustained by carboxylic acid-carboxylic acid interactions. The standard chemical color correlation appears in all the figures where color is utilized (*e.g.*, red = oxygen; white = oxygen; dark blue = nitrogen; light blue = fluorene; yellow = sulfur).

[0016] Figure 3 shows a scheme wherein the carboxylic acid-carboxylic acid interactions of ibuprofen are disrupted by co-crystallization with an aromatic amine. Specifically, by using diamines, 2:1 multiple-component phases are produced.

[0017] Figures 4A–4B show an acetaminophen 1-D polymeric chain and an acetaminophen/4,4'-bipyridine/water crystal, respectively. Reported forms are monoclinic (*$P2_1/n$*) (Haisa, M. *et al.*, *Acta Crystallogr., Sect B*, 1974, 30:2510) and orthorhombic (*Pbca*) (Haisa, M. *et al.*, *Acta Crystallogr., Sect B*, 1976, 32:1283) polymorphs. The monoclinic polymorph forms pleated sheets with all hydrogen bonding donors and acceptors interacting. The orthorhombic polymorph forms form 1-D polymeric chains with all donors and acceptors interacting.

[0018] Figures 5A-5B show pure phenytoin and a phenytoin/pyridone co-crystal, respectively. Phenytoin has one known pure form (Carmerman, A. *et al.*, *Acta Crystallogr., Sect B*, 1971, 27:2207). The crystal structure reveals a two dimensional polymeric network formed by hydrogen bonds between both the carbonyl and 2° amine.

[0019] Figures 6A-6D show supramolecular entities containing synthons and corresponding crystal structures of pure aspirin and aspirin/4,4'-bipyridine. Figures 3A and 3B show the supramolecular entity containing the synthon of pure aspirin and corresponding crystal structure, respectively. Figures 6C and 6D show the supramolecular entity containing the synthon and corresponding co-crystal of aspirin/4,4'-bipyridine, respectively. The pure phase (Chiari, G. *et al.*, *Acta Crystallogr., Sect B*, 1981, 37:1623) of acetylsalicylic acid, has centrosymmetric carboxylic acid homodimers and crystallizes in the space group *$P2_1/c$*, packing in 2D polymeric sheets with hydrophobic planes.

[0020] Figures 7A-7D show supramolecular entities containing synthons and corresponding crystal structures of pure ibuprofen [2-(4-isobutylphenyl) propionic acid] and ibuprofen/4,4'-bipyridine. Figures 7A and 7B show the supramolecular entity containing the synthon of pure ibuprofen and corresponding crystal structure, respectively. Figures 7C and 7D

show the supramolecular entity containing the synthon of ibuprofen/4,4'-bipyridine and corresponding co-crystal, respectively. The reported crystal structures of ibuprofen are racemic (McConnell, J.F. *Cryst. Strucut. Commun.*, 1974, 3:73) and S (+) forms (Freer, A.A. *et al.*, *Acta Crystallogr., Sect C (Cr. Str. Comm)*, 1993, 49:1378). Both contain hydrogen bonded carboxylic acid homodimers. Racemic dimers have centers of inversion across the dimer, which crystallize in the space group $P2_1/c$. The S (+) form contains asymmetric dimers, which crystallize in the space group $P2_1$. Both crystals pack in 2-D polymeric sheets sustained by π-π stacking and hydrophobic in-layer interactions.

[0021] Figures 8A-8D show supramolecular entities containing synthons and corresponding crystal structures of pure flurbiprofen [2-(2-fluror-4-biphenyl) propionic acid] and flurbiprofen/4,4'-bipyridine. Figures 8A and 8B show the supramolecular entity containing the synthon of pure flurbiprofen and corresponding crystal structure, respectively. Figures 5C and 5D show the supramolecular synthon of flurbiprofen/4,4'-bipyridine and corresponding co-crystal, respectively. Flurbiprofen has one reported pure form (Flippen, J.L. *et al.*, *Acta Crystallogr., Sect. B*, 1975, 31:926) and contain hydrogen bonded carboxylic acid homodimers with a center of inversion and crystallizes in the *P-1* space group. 2-D polymeric sheets are formed through π-π and hydrophobic interactions from the phenyl rings.

[0022] Figures 9A and 9B show the supramolecular entity containing the synthon of flurbiprofen/trans-1,2-bis(4-pyridyl)ethylene and the corresponding crystal structure, respectively.

[0023] Figures 10A and 10B show the crystal structures of pure carbamazepine and carbamazepine/*p*-phthalaldehyde, respectively. Carbamazepine [5H-Dibenz(b, f) azepine-5-carboxamide] (CBZ) has been shown to exist in at least three anhydrous forms and two solvated forms (a dihydrate and an acetonate) (Himes, V.L. *et al.*, *Acta Crystallogr.*, 1981, 37:2242-2245; Lowes, M.M.J. *et al.*, *J. Pharm. Sci.*, 1987, 76:744-752; Reck, G. *et al.*, *Cryst. Res. Technol.*, 1986, 21:1463-1468). The primary intermolecular interaction in these crystal forms is the dimer formed between the carboxamide moieties of each CBZ molecule forming centrosymmetric dimers. The anhydrous polymorphs are monoclinic, trigonal, and triclinic. The polymorphs are enantiotropically related with the monoclinic form being the most thermodynamically stable at room temperature.

[0024] Figure 11 shows the crystal structure of carbamazepine/nicotinamide (vitamin B3).

[0025] Figure 12 shows the crystal structure of carbamazepine/saccharin, engineered using the carbamazepine/nicotinamide co-crystal as a model.

[0026] Figures 13A-13C show the chemical structures of ibuprofen, flurbiprofen, and aspirin, respectively.

[0027] Figures 14A and **14B** show the crystal structures of carbamazepine and carbamazepine/2,6-pyridinedicarboxylic acid, respectively.

[0028] Figures 15A and 15B show the crystal structures of carbamazepine and carbamazepine/5-nitroisophthalic acid, respectively.

[0029] Figures 16A and **16B** show the crystal structures of carbamazepine and carbamazepine/acetic acid.

[0030] Figures 17A and **17B** show the crystal structure of carbamazepine and carbamazepine/adamantanetetracarboxylic acid.

[0031] Figures 18A and **18B** show the crystal structure of carbamazepine and carbamazepine/benzoquinone.

[0032] Figures 19A and **19B** show the crystal structure of carbamazepine and carbamazepine/butyric acid.

[0033] Figures 20A and **20B** show the crystal structure of carbamazepine and carbamazepine/DMSO.

[0034] Figures 21A and **21B** show the crystal structure of carbamazepine and carbamazepine/formamide.

[0035] Figures 22A and **22B** show the crystal structure of carbamazepine and carbamazepine/formic acid.

[0036] Figures 23A and **23B** show the crystal structure of carbamazepine and carbamazepine/trimesic acid.

[0037] Figure 24 shows an exemplified scheme for preparing multiple-component phase compositions of the subject invention.

DETAILED DISCLOSURE OF THE INVENTION

[0038] The subject invention relates to the application of the concepts of crystal engineering towards the design of new multiple-component solid phases, such as multiple-component crystals, having at least one active pharmaceutical component. Examples of multiple-component crystals of the subject invention include, but are not limited to, acetominophen/4,4'-bipyridine/water, phenytoin/pyridone, aspirin/4,4'-bipyridine, ibuprofen/4,4'-bipyridine, flurbiprofen/4,4'-bipyridine, flurbiprofen/trans-1,2-bis (4-pyridyl) ethylene, carbamazepine/*p*-phthalaldehyde, carbamazepine/nicotinamide (GRAs), carbamazepine/saccharin (GRAs), carbamazepine/2,6-pyridinedicarboxylic acid, carbamazepine/5-nitroisophthalic acid, carbamazepine/acetic acid, carbamazepine/1,3,5,7-adamantanetetracarboxylic acid, carbamazepine/benzoquinone, carbamazepine/butyric acid, carbamazepine/dimethyl sulfoxide (DMSO), carbamazepine/formamide, carbamazepine/formic acid, and carbamazepine/trimesic acid, which have been characterized by various techniques and exhibit physical properties different from the parent pharmaceutical ingredient as a direct result of hydrogen bonding interaction. These crystalline assemblies can afford improved drug solubility, dissolution rate, stability and bioavailability, for example.

[0039] In one aspect, the subject invention concerns methods for identifying complementary chemical functionalities to form a desired supramolecular synthon, wherein the method comprises the steps of evaluating the structure of an active pharmaceutical ingredient (API), which can include determining its crystal structure; determining whether the API contains chemical functionalities capable of forming supramolecular synthons with itself; identifying from a plurality of chemical functionalities that are known to form a supramolecular synthon at least one chemical functionality that will form a further supramolecular synthon to the supramolecular synthon formed by the API, wherein the identified chemical functionality is not capable of disrupting non-covalent bonding within the supramolecular synthon formed by the supramolecular synthon formed by the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to the supramolecular synthon formed by the API; and identifying co-crystal formers having chemical functionalities that are complementary with the API.

[0040] In another aspect, the subject invention concerns methods for identifying complementary chemical functionalities to form a desired supramolecular synthon, wherein the

method comprises the steps of evaluating the structure of an API, which can include determining its crystal structure; determining whether the API contains chemical functionalities capable of forming supramolecular synthons with itself; identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the API, wherein the identified chemical functionality is capable of disrupting non-covalent bonding within the supramolecular synthon formed by the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the API; and identifying co-crystal formers having chemical functionalities that are complementary with the API. Thus, according to this method, the formation of homosynthons for the purpose of disrupting the intermolecular interactions between pharmaceutical moieties can be carried out.

[0041] In still another aspect, the subject invention concerns methods for identifying complementary chemical functionalities to form a desired supramolecular synthon, wherein the method comprises the steps of evaluating the structure of an API, which can include determining its crystal structure; determining whether the API contains chemical functionalities capable of forming supramolecular synthons with different molecules; identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the API; and identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

[0042] In each of the three aspects of the methods described above, the methods can further comprise preparing a multiple-component solid phase composition composed of the API and at least one of the identified co-crystal formers. The identified co-crystal former can be, for example, a different API, a GRAS compound, a food additive, a low toxicity organic, or a metal-organic complex. Various methods can be utilized for preparing the multiple-component solid phase composition, such as crystallization from solution, cooling the melt, sublimation and grinding. In addition, the methods of the subject invention can further comprise either or both of the following steps: determining the structure of the new multiple-component solid phase composition, and analyzing the physical and/or chemical properties of the new multiple-component solid phase composition.

[0043] The subject invention further concerns new solid phases identified or produced using the methods identified herein. The subject invention further pertains to a multiple-component phase composition comprising a solid material (phase) that is sustained by intermolecular interactions between two or more independent molecular entities, in any stoichiometric ratio, wherein at least one of the independent molecular entities is a pharmaceutical entity. The multiple-component phase composition of the subject invention can be, for example, a discrete supramolecular entity or a polymeric structure. The multiple-component phase compositions of the subject invention can have properties, such as melting point, solubility, dissolution rate, stability, and/or bioavailability, which are different from the pharmaceutical compound, or compounds, upon which they are based.

[0044] By way of example, the external functionalities of ibuprofen are an isopropyl group and a carboxylic acid, as shown in Figure 1.

[0045] Using the methods of the subject invention, it has been determined that this interaction can be disrupted by co-crystallization with an aromatic amine, as shown in Figure 2. Specifically, by using diamines, 2:1 multiple-component phases of ibuprofen have been prepared, as shown in Figure 3, as well as other phases exemplified herein. Therefore, the methods of the subject invention can be used to identify complementary chemical functionalities and produce multiple-component phase compositions for a variety of pharmaceuticals, including those pharmaceutical compounds with structures very different those of ibuprofen, flurbiprofen, and aspirin, which are shown in Figures 13A-13C, respectively.

[0046] As used herein, the term "multiple-component phase" refers to any solid material (phase) that is sustained by intermolecular interactions between at least two independent molecular entities, in any stoichiometric ratio, wherein at least one of the independent molecular entities is a pharmaceutical entity. Examples of intermolecular interactions include, but are not limited to one or more of the following: hydrogen bonding (weak and/or strong), dipole interactions (induced and/or non-induced), stacking interactions, hydrophobic interactions, and other inter-static interactions. Each independent molecular entity can be a discrete supramolecular entity or polymeric structure, for example. Preferably, one or more of the independent molecular entities comprises a molecule of a "GRAS" compound, that is, a compound "Generally Regarded as Safe by the Food and Drug Administration (FDA)". More preferably, the GRAS compound is a non-pharmaceutical entity.

[0047] The terms "pharmaceutical entity", "pharmaceutical moiety", "pharmaceutical component", "pharmaceutical molecule", and "active pharmaceutical ingredient (API)", and grammatical variations thereof, are used interchangeably herein to refer to any biologically active moiety having a therapeutic effect on a human or animal suffering from a given pathological condition, when administered in a given concentration. Therefore, pharmaceutical entities useful as the active pharmaceutical ingredients in the multiple phase solids of the subject invention can be administered to a human or animal, which may or may not be suffering from a pathological condition, and the pharmaceutical entity can have a prophylactic effect, a palliative effect, and/or be a curative intervention. As used herein, these pharmaceutical entities are intended to include pharmaceutically acceptable salts of a given pharmaceutical entity that retain all or a portion of their pharmaceutical activity. Pharmaceutical molecules or ions are inherently predisposed for such crystal engineering studies since they already contain molecular recognition sites that bind selectively to biomolecules, and they are prone to supramolecular self-assembly. Examples of the groups commonly found in active pharmaceutical ingredients, and which are capable of forming supramolecular synthons include, but are not limited to, acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases (*e.g.* pyridines, imidazoles), amines, alcohols, halogens, sulfones, nitro groups, S-heterocycles, N-heterocycles (saturated or unsaturated), and O-heterocycles. Other examples include ethers, thioethers, thiols, esters, thioesters, thioketones, epoxides, acetonates, nitrils, oximes, and organohalides. Other examples include ethers, thioethers, thiols, esters, thioesters, thioketones, epoxides, acetonates, nitrils, oximes, and organohalides. Some of these groups can form supramolecular synthons with identical groups in similar or different molecules and are termed homosynthons, *e.g.*, acids and amides. Other groups can form supramolecular synthons with different groups and are termed heterosynthons, *e.g.*, acid/amide; pyridine/amide; alcohol/amine. Heterosynthons are particularly suitable for formation of multiple-component crystals whereas homosynthons can sometimes form multiple-component crystals.

[0048] As used herein, the term "supramolecular synthon" refers to the sum of the components of a multi-component non-covalent interaction, wherein the non-covalent interaction contributes to the formation of a discrete supramolecular entity or polymeric structure, wherein each component is a chemical functionality. A supramolecular synthon can be a dimer, trimer, or *n*-mer, for example.

[0049] The multiple-component phase compositions can be formulated according to known methods for preparing pharmaceutically useful compositions. Such pharmaceutical compositions can be adapted for various forms of administration, such as oral, parenteral, nasal, topical, transdermal, *etc.* The multiple-component phase solids of the subject invention can be made into solutions or amorphous compounds, as injections, pills, or inhalants, for example. Optionally, the pharmaceutical compositions can include a pharmaceutically acceptable carrier or diluent. Formulations are described in a number of sources which are well known and readily available to those skilled in the art. For example, *Remington's Pharmaceutical Science* (Martin EW [1995] Easton Pennsylvania, Mack Publishing Company, 19th ed.) describes formulations that can be used in connection with the subject invention. Formulations suitable for administration include, for example, aqueous sterile injection solutions, which may contain antioxidants, buffers, bacteriostats, and solutes which render the formulation isotonic with the blood of the intended recipient; and aqueous and nonaqueous sterile suspensions which may include suspending agents and thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example sealed ampoules and vials, and may be stored in a freeze dried (lyophilized) condition requiring only the condition of the sterile liquid carrier, for example, water for injections, prior to use. Extemporaneous injection solutions and suspensions may be prepared from sterile powder, granules, or tablets of the multiple-component phase compositions of the subject invention, for example. It should be understood that in addition to the ingredients particularly mentioned above, the formulations of the subject invention can include other agents conventional in the art having regard to the type of formulation in question.

[0050] In terms of superstructure, three general types of compounds generated by interaction of a pharmaceutical molecule with another molecule include: (1) multiple-component compounds, in which superstructure is generated by two or more molecules, both of which are integral components of the network and complementary; (2) clathrate inclusion compounds, in which the compounds' superstructure is generated by self-assembly of one or more molecules and a guest molecules is enclosed within the superstructure; and (3) porous inclusion compounds, in which the superstructure is open framework in nature.

[0051] The subject invention concerns multiple-component compositions, and it is demonstrated herein that the concepts of crystal engineering and supramolecular synthons can be applied to prepare a wide range of novel pharmaceutical materials that are based on rational

design. Therefore, the multiple-component compounds of the subject invention can be generated in such a fashion that they have desirable composition, structure and properties. More specifically, an issue that is particularly relevant to pharmaceutical compositions of matter and processing is addressed by the subject invention: the diversity of compositions, superstructures and solubilities that can be generated when drug molecules form multiple-component phases with complementary molecules. Multiple-component phases involving the following drugs are exemplified herein: aspirin, acetaminophen, ibuprofen (and related compounds), phenytoin and carbamazepine and appropriate molecular additives. These novel phases include both "model multiple-component phases" that illustrate the concept of crystal engineering and multiple-component phases that incorporate pharmaceuticals with "GRAS" compounds, that is, compounds "Generally Regarded as Safe by the FDA", and/or food additives.

[0052] In the context of organic and pharmaceutical solids, the subject invention addresses these issues by demonstrating that crystal engineering offers a paradigm for the supramolecular synthesis (Chang, Y.L. *et al.*, *J. Am. Chem. Soc.*, 1993, 115:5991-6000) of a wide range of new multiple-component phases that have predetermined compositions and, in some instances, predetermined topology. Such an ability to build hierarchical structures from molecular or supramolecular modules facilitates precise control of structure and function of solid phases. These multiple-component phases have the following advantages over single component phases and traditional multiple-component phases (solid dispersions): high thermodynamic stability (thereby reducing problems associated with solid phase transformations), modified bioavailability (finely tunable solubility and delivery), and enhanced processability (crystal morphology, mechanical properties, hygroscopicity).

[0053] The subject invention has the following implications from a scientific perspective: (a) protocols are now available for the rational design of a new generation of pharmaceutical phases that contain at least two components that are sustained by supramolecular synthons; (b) correlation of structure and function of the new pharmaceutical phases via characterization of structure, crystal energy, solubility, dissolution rate, and stability is now possible; and (c) a new range of novel phases for the treatment of pathological conditions in humans and animals are available.

[0054] The subject invention extends the state-of-the-art in at least three ways: (1) by generating a rational, supramolecular strategy for the design of novel, multiple-component

crystalline phases; (2) by extending this strategy to pharmaceutical phases; and (3) by using this strategy to control the delivery properties and stability of pharmaceutical compounds.

[0055] The following pages describe examples of multiple-component crystalline phases that have been characterized using single crystal X-ray crystallography and structure-sensitive analytical techniques: FT-IR, XRPD, DSC, TGA. They represent prototypal examples of the invention as they are all based upon pharmaceutical molecules that are inherently predisposed to form supramolecular synthons with other complementary functional groups. They were chosen for study because of well-known limitations in their solubility/bioavailibility. In each example, the nature of the pure phase is discussed and it is sustained by a supramolecular homosynthon (self-complementary functionalities). The multiple-component phases prepared confirm the ability to persistently and rationally disrupt the homosynthon by judicious choice of a second molecular component that is predisposed to form a supramolecular heterosynthon. That these new solid phases will have different solubility profiles than their pure phases is to be expected. Examples designated as GRAS are those in which second a component that is "Generally Regarded as Safe by the FDA" was used.

Example 1—Multi-Component Crystal of Acetaminophen: Acetominophen/4,4'-bipyridine/water (1:1:1 stoichiometry)

[0056] 50 mg (0.3307 mmol) acetaminophen and 52 mg (0.3329 mmol) 4,4'-bipyridine were dissolved in hot water and allowed to stand. Slow evaporation yielded colorless needles of a 1:1:1 acetaminophen/4,4'-bipyridine/water co-crystal, as shown in Figure 4B.

[0057] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{36}H_{44}N_2O_4$, M=339.84, triclinic, space group $P\bar{1}$; a = 7.0534(8), b = 9.5955(12), c = 19.3649(2) Å, α = 86.326(2), β = 80.291(2), γ = 88.880(2)°, U = 1308.1(3) Å^3, T = 200(2) K, Z = 2, μ(Mo-Kα) = 0.090 mm^{-1}, D_c = 1.294 Mg/m^3, λ = 0.71073 Å^3, F(000) = 537, $2\theta_{max}$ = 25.02°; 6289 reflections measured, 4481 unique (R_{int} = 0.0261). Final residuals for 344 parameters were R_1 = 0.0751, wR_2 = 0.2082 for I>2σ(I), and R_1 = 0.1119, wR_2 = 0.2377 for all 4481data.

[0058] Crystal packing: The co-crystals contain bilayered sheets in which water molecules act as a hydrogen bonded bridge between the network bipyridine moieties and the acetaminophen. Bipyridine guests are sustained by π-π stacking interactions between two

network bipyridines. The layers stack via π-π interactions between the phenyl groups of the acetaminophen moieties.

[0059] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 57.77° C (endotherm); m.p. = 58-60° C (MEL-TEMP); (acetaminophen m.p. = 169° C, 4,4'-bipyridine m.p. = 111-114° C).

Example 2—Multi-Component Crystal of Phenytoin: Phenytoin/Pyridone (1:1 stoichiometry)

[0060] 28 mg (0.1109 mmol) phenytoin and 11 mg (0.1156 mmol) 4-hydroxypyridone were dissolved in 2 mL acetone and 1 mL ethanol with heating and stirring. Slow evaporation yielded colorless needles of a 1:1 phenytoin/pyridone co-crystal, as shown in Figure 5B.

[0061] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{20}H_{17}N_3O_3$, M = 347.37, monoclinic $P2_1/c$; a = 16.6583(19), b = 8.8478(10), c = 11.9546(14) Å, β = 96.618(2)°, U = 1750.2(3) Å^3, T = 200(2) K, Z = 4, μ(Mo-Kα) = 0.091 mm^{-1}, D_c = 1.318 Mg/m^3, λ = 0.71073 Å^3, F(000) = 728, $2\theta_{max}$ = 56.60°; 10605 reflections measured, 4154 unique (R_{int} = 0.0313). Final residuals for 247 parameters were R_1 = 0.0560, wR_2 = 0.1356 for I>2σ(I), and R_1 = 0.0816, wR_2 = 0.1559 for all 4154 data.

[0062] Crystal packing: The co-crystal is sustained by hydrogen bonding of adjacent phentoin molecules between the carbonyl and the amine closest to the tetrahedral carbon, and by hydrogen bonding between pyridone carbonyl functionalities and the amine not involved in phenytoin-phenytoin interactions. The pyridone carbonyl also hydrogen bonds with adjacent pyridone molecules forming a one-dimensional network.

[0063] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR), characteristic peaks for the co-crystal were identified as: 2°amine found at 3311cm^{-1}, carbonyl (ketone) found at 1711cm^{-1}, olephin peak found at 1390cm^{-1}.

[0064] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 233.39° C (endotherm) and 271.33° C (endotherm); m.p. = 231-233° C (MEL-TEMP); (phenytoin m.p. = 295° C, pyridone m.p. = 148° C).

[0065] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), a 29.09% weight loss starting at 192.80° C, 48.72% weight loss starting at 238.27° C, and 18.38% loss starting at 260.17° C followed by complete decomposition.

[0066] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using Cu Kα (λ = 1.540562), 30kV, 15mA). The powder data were collected over an angular range of 3° to 40° 2θ in continuous scan mode using a step size of 0.02° 2θ and a scan speed of 2.0°/minute. XRPD: Showed analogous peaks to the simulated XRPD derived from the single crystal data. In all cases of recrystallization and solid state reaction, experimental (calculated): 5.2 (5.3); 11.1 (11.3); 15.1 (15.2); 16.2 (16.4); 16.7 (17.0); 17.8 (17.9); 19.4 (19.4); 19.8 (19.7); 20.3 (20.1); 21.2 (21.4); 23.3 (23.7); 26.1 (26.4); 26.4 (26.6); 27.3 (27.6); 29.5 (29.9).

Example 3—Multi-Component Crystal of Aspirin (acetylsalicylic acid): Aspirin/4,4'-bipyridine (2:1 stoichiometry)

[0067] 50 mg (0.2775 mmol) aspirin and 22 mg (0.1388 mmol) 4,4'-bipyridine were dissolved in 4 mL hexane. 8 mL ether was added to the solution and allowed to stand for one hour, yielding colorless needles of a 2:1 aspirin/4,4'-bipyridine co-crystal, as shown in Figure 6D. Alternatively, aspirin/4,4'-bipyridine (2:1 stoichiometry) can be made by grinding the solid ingredients in a pestle and mortar.

[0068] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{28}H_{24}N_2O_8$, M = 516.49, orthorhombic *Pbcn*; a = 28.831(3), b = 11.3861(12), c = 8.4144(9) Å, U = 2762.2(5) Å^3, T = 173(2) K, Z = 4, μ(Mo-Kα) = 0.092 mm^{-1}, D_c = 1.242 Mg/m^3, λ = 0.71073 Å^3, F(000) = 1080, $2\theta_{max}$ = 25.02°; 12431 reflections measured, 2433 unique (R_{int} = 0.0419). Final residuals for 202 parameters were R_1 = 0.0419, wR_2 = 0.1358 for I>2σ(I), and R_1 = 0.0541, wR_2 = 0.1482 for all 2433 data.

[0069] Crystal packing: The co-crystal contains the carboxylic acid-pyridine heterodimer that crystallizes in the *Pbcn* space group. The structure is an inclusion compound containing disordered solvent in the channels. In addition to the dominant hydrogen bonding interaction of the heterodimer, π-π stacking of the bipyridine and phenyl groups of the aspirin and hydrophobic interactions contribute to the overall packing interactions.

[0070] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR), characteristic (-COOH) peak at 1679 cm^{-1} was shifted up and less intense at 1694cm^{-1}, where as the lactone peak is shifted down slightly from 1750cm^{-1} to 1744cm^{-1}.

[0071] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 95.14° C (endotherm); m.p. = 91-96° C (MEL-TEMP); (aspirin m.p. = 1345° C, 4,4'-bipyridine m.p. = 111-114° C).

[0072] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), weight loss of 9% starting at 22.62° C, 49.06% weight loss starting at 102.97° C followed by complete decomposition starting at 209.37° C.

Example 4—Multi-Component Crystal of Ibuprofen: Ibuprofen/4,4'-Bipyridine (2:1 stoichiometry)

[0073] 50 mg (0.242 mmol) racemic ibuprofen and 18mg (0.0960 mmol) 4,4'-bipyridine were dissolved in 5 mL acetone. Slow evaporation of the solvent yielded colorless needles of a 2:1 ibuprofen/4,4'-bipyridine co-crystal, as shown in Figure 7D.

[0074] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{36}H_{44}N_2O_4$, M = 568.73, triclinic, space group *P-1*; a = 5.759(3), b = 11.683(6), c = 24.705(11) Å, α = 93.674(11), β = 90.880(10), γ = 104.045(7)°, *U* = 1608.3(13) Å^3, T= 200(2) K, Z = 2, μ(Mo-Kα) = 0.076 mm^{-1}, D_c = 1.174 Mg/m^3, λ = 0.71073 Å^3, F(000) = 612, $2\theta_{max}$ = 23.29°; 5208 reflections measured, 3362 unique (R_{int} = 0.0826). Final residuals for 399 parameters were R_1 = 0.0964, wR_2 = 0.2510 for I>2σ(I), and R_1 = 0.1775, wR_2 = 0.2987 for all 3362 data.

[0075] Crystal packing: The co-crystal contains ibuprofen/bipyridine heterodimers, sustained by two hydrogen bonded carboxylic acidpyridine supramolecular synthons, arranged in a herringbone motif that packs in the space group *P-1*. The heterodimer is an extended version of the homodimer and packs to form a two-dimensional network sustained by π-π stacking of the bipyridine and phenyl groups of the ibuprofen and hydrophobic interactions from the ibuprofen tails.

[0076] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). Analysis observed stretching of aromatic C-H at 2899 cm^{-1}; N--H bending and scissoring at 1886 cm.$_1$; C=O stretching at 1679 cm^{-1}; C-H out-of-plane bending for both 4,4'-bipyridine and ibuprofen at 808 cm^{-1} and 628 cm^{-1}.

[0077] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 64.85° C (endotherm) and 118.79° C (endotherm); m.p. = 113-120° C (MEL-TEMP); (ibuprofen m.p. = 75-77° C, 4,4'-bipyridine m.p. = 111-114° C).

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 33 of 415

[0078] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), 13.28% weight loss between room temperature and 100.02° C immediately followed by complete decomposition.

[0079] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using Cu Kα (λ = 1.540562), 30kV, 15mA). The powder data were collected over an angular range of 3° to 40° 2θ in continuous scan mode using a step size of 0.02° 2θ and a scan speed of 2.0°/minute. XRPD derived from the single crystal data, experimental (calculated): 3.4 (3.6); 6.9 (7.2); 10.4 (10.8); 17.3 (17.5); 19.1 (19.7).

Example 5—Multi-Component Crystal of Flurbiprofen: Flurbiprofen/4,4'-bipyridine (2:1 stoichiometry)

[0080] 50 mg (0.2046 mmol) flurbiprofen and 15 mg (0.0960 mmol) 4,4'-bipyridine were dissolved in 3 mL acetone. Slow evaporation of the solvent yielded colorless needles of a 2:1 flurbiprofen/4,4'-bipyridine co-crystal, as shown in Figure 8D.

[0081] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{40}H_{34}F_2N_2O_4$, M = 644.69, monoclinic $P2_1/n$; a = 5.860(4), b = 47.49(3), c = 5.928(4) Å, β = 107.382 (8)°, U = 1574.3(19) Å^3, T = 200(2) K, Z = 2, μ(Mo-Kα) = 0.096 mm^{-1}, D_c = 1.360 Mg/m^3, λ = 0.71073 Å^3, F(000) = 676, $2\theta_{max}$ = 21.69°; 4246 reflections measured, 1634 unique (R_{int} = 0.0677). Final residuals for 226 parameters were R_1 = 0.0908, wR_2 = 0.2065 for I>2σ(I), and R_1 = 0.1084, wR_2 = 0.2209 for all 1634 data.

[0082] Crystal packing: The co-crystal contains flurbiprofen/bipyridine heterodimers, sustained by two hydrogen bonded carboxylic acidpyridine supramolecular synthon, arranged in a herringbone motif that packs in the space group $P2_1/n$. The heterodimer is an extended version of the homodimer and packs to form a two-dimensional network sustained by π-π stacking and hydrophobic interactions of the bipyridine and phenyl groups of the flurbiprofen.

[0083] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR), aromatic C-H stretching at 3057 cm^{-1} and 2981 cm^{-1}; N--H bending and scissoring at 1886 cm^{-1}; C=O stretching at 1690 cm^{-1}; C=C and C=N ring stretching at 1418 cm^{-1}.

[0084] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 162.47° C (endotherm); m.p. = 155-160° C (MEL-TEMP); (flurbiprofen m.p. = 110-111° C, 4,4'-bipyridine m.p. = 111-114° C).

[0085] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), 30.93% weight loss starting at 31.13° C and a 46.26% weight loss starting at 168.74° C followed by complete decomposition.

[0086] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using Cu Kα (λ = 1.540562), 30kV, 15mA), the powder data were collected over an angular range of 3° to 40° 2θ in continuous scan mode using a step size of 0.02° 2θ and a scan speed of 2.0°/minute. XRPD derived from the single crystal data: experimental (calculated): 16.8 (16.8); 17.1 (17.5); 18.1 (18.4); 19.0 (19.0); 20.0 (20.4); 21.3 (21.7); 22.7 (23.0); 25.0 (25.6); 26.0 (26.1); 26.0 (26.6); 26.1 (27.5); 28.2 (28.7); 29.1 (29.7).

Example 6—Multi-Component Crystal of Flurbiprofen: Flurbiprofen/trans-1,2-bis (4-pyridyl) ethylene (2:1 stoichiometry)

[0087] 25 mg (0.1023 mmol) flurbiprofen and 10 mg (0.0548 mmol) trans-1, 2-bis (4-pyridyl) ethylene were dissolved in 3 mL acetone. Slow evaporation of the solvent yielded colorless needles of a 2:1 flurbiprofen/1,2-bis (4-pyridyl) ethylene co-crystal, as shown in Figure 9B.

[0088] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{42}H_{36}F_2N_2O_4$, M = 670.73, monoclinic $P2_1/n$; a = 5.8697(9), b = 47.357(7), c = 6.3587(10) Å, β = 109.492(3)°, U = 1666.2(4) Å^3, T = 200(2) K, Z = 2, μ(Mo-Kα) = 0.093 mm^{-1}, D_c = 1.337 Mg/m^3, λ = 0.71073 Å^3, F(000) = 704, $2\theta_{max}$ = 21.69°, 6977 reflections measured, 2383 unique (R_{int} = 0.0383). Final residuals for 238 parameters were R_1 = 0.0686, wR_2 = 0.1395 for I>2σ(I), and R_1 = 0.1403, wR_2 = 0.1709 for all 2383 data.

[0089] Crystal packing: The co-crystal contains flurbiprofen/1,2-bis (4-pyridyl) ethylene heterodimers, sustained by two hydrogen bonded carboxylic acid-pyridine supramolecular synthons, arranged in a herringbone motif that packs in the space group $P2_1/n$. The heterodimer from 1,2-bis (4-pyridyl) ethylene further extends the homodimer relative to example 5 and packs to form a two-dimensional network sustained by π-π stacking and hydrophobic interactions of the bipyridine and phenyl groups of the flurbiprofen.

[0090] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR), aromatic C-H stretching at 2927 cm^{-1} and 2850 cm^{-1}; N--H bending and scissoring at 1875 cm^{-1}; C=O stretching at 1707 cm^{-1}; C=C and C=N ring stretching at 1483 cm^{-1}.

[0091] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 100.01° C, 125.59° C and 163.54°C (endotherms); m.p. = 153-158° C (MEL-TEMP); (flurbiprofen m.p. = 110-111° C, trans-1, 2-bis (4-pyridyl) ethylene m.p. = 150-153° C).

[0092] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), 91.79% weight loss starting at 133.18° C followed by complete decomposition.

[0093] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using Cu Kα (λ = 1.540562), 30kV, 15mA), the powder data were collected over an angular range of 3° to 40° 2θ in continuous scan mode using a step size of 0.02° 2θ and a scan speed of 2.0°/minute. XRPD derived from the single crystal data, experimental (calculated): 3.6 (3.7); 17.3 (17.7); 18.1 (18.6); 18.4 (18.6); 19.1 (19.3); 22.3 (22.5); 23.8 (23.9); 25.9 (26.4); 28.1 (28.5).

Example 7—Multi-Component Crystal of Carbamazepine: Carbamazepine/*p*-Phthalaldehyde (1:1 stoichiometry)

[0094] 25 mg (0.1058 mmol) carbamazepine and 7 mg (0.0521 mmol) *p*-phthalaldehyde were dissolved in approximately 3 mL methanol. Slow evaporation of the solvent yielded colorless needles of a 1:1 carbamazepine/*p*-phthalaldehyde co-crystal, as shown in Figure 10B.

[0095] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{38}H_{30}N_4O_4$, M = 606.66, monoclinic *C2/c*; a = 29.191(16), b = 4.962(3), c = 20.316(11) Å, β = 92.105(8)°, *U* = 2941(3) Å^3, T= 200(2) K, Z = 4, μ(Mo-Kα) = 0.090 mm^{-1}, D_c = 1.370 Mg/m^3, λ = 0.71073 Å^3, F(000) = 1272, $2\theta_{max}$ = 43.66°, 3831 reflections measured, 1559 unique (R_{int} = 0.0510). Final residuals for 268 parameters were R_1 = 0.0332, wR_2 = 0.0801 for I>2σ(I), and R_1 = 0.0403, wR_2 = 0.0831 for all 1559 data.

[0096] Crystal packing: The co-crystals contain hydrogen bonded carboxamide homodimers that crystallize in the space group *C2/c*. The 1° amines of the homodimer are bifurcated to the carbonyl of the *p*-phthalaldehyde forming a chain with an adjacent homodimer. The chains pack in a crinkled tape motif sustained by π-π interactions between phenyl rings of the CBZ.

[0097] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). The 1° amine unsymmetrical and symmetrical stretching was shifted down to 3418 cm^{-1}; aliphatic aldehyde and 1° amide C=O stretching was shifted up to 1690 cm^{-1}; N-H in-plane bending at 1669 cm^{-1}; C-H aldehyde stretching at 2861 cm^{-1} and H-C=O bending at 1391 cm^{-1}.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 36 of 415

[0098] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 128.46° C (endotherm), m.p. = 121-124° C (MEL-TEMP), (carbamazepine m.p. = 190.2° C, *p*-phthalaldehyde m.p. = 116° C).

[0099] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), 17.66% weight loss starting at 30.33° C then a 17.57% weight loss starting at 100.14° C followed by complete decomposition.

[00100] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using Cu Kα (λ = 1.540562), 30kV, 15mA). The powder data were collected over an angular range of 3° to 40° 2θ in continuous scan mode using a step size of 0.02° 2θ and a scan speed of 2.0°/minute. XRPD derived from the single crystal data, experimental (calculated): 8.5 (8.7); 10.6 (10.8); 11.9 (12.1); 14.4 (14.7) 15.1 (15.2); 18.0 (18.1); 18.5 (18.2); 19.8 (18.7); 23.7 (24.0); 24.2 (24.2); 26.4 (26.7); 27.6 (27.9); 27.8 (28.2); 28.7 (29.1); 29.3 (29.6); 29.4 (29.8).

Example 8—Multi-Component Crystal of Carbamazepine: Carbamazepine/nicotinamide (GRAs) (1:1 stoichiometry)

[00101] 25 mg (0.1058 mmol) carbamazepine and 12 mg (0.0982 mmol) nicotinamide were dissolved in 4 mL of DMSO, methanol or ethanol. Slow evaporation of the solvent yielded colorless needles of a 1:1 carbamazepine/nicotinamide co-crystal, as shown in Figure 11.

[00102] Using a separate method, 25 mg (0.1058 mmol) carbamazepine and 12 mg (0.0982mmol) nicotinamide were ground together with mortar and pestle. The solid was determined to be 1:1 carbamazepine/nicotinamide microcrystals (XPD).

[00103] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{21}H_{18}N_4O_2$, M = 358.39, monoclinic *P2₁/n*; a = 5.0961(8), b = 17.595(3), c = 19.647(3) Å, β = 90.917(3)°, *U* = 1761.5(5) Å^3, T = 200(2) K, Z = 4, μ(Mo-Kα) = 0.090 mm^{-1}, D_c = 1.351 Mg/m^3, λ = 0.71073 Å^3, F(000) = 752, $2\theta_{max}$ = 56.60°, 10919 reflections measured, 4041 unique (R_{int} = 0.0514). Final residuals for 248 parameters were R_1 = 0.0732, wR_2 = 0.1268 for I>2σ(I), and R_1 = 0.1161, wR_2 = 0.1430 for all 4041 data.

[00104] Crystal packing: The co-crystals contain hydrogen bonded carboxamide homodimers. The 1° amines are bifurcated to the carbonyl of the nicotinamide on each side of the dimer. The 1° amines of each nicotinamide are hydrogen bonded to the carbonyl of the

adjoining dimer. The dimers form chains with π-π interactions from the phenyl groups of the CBZ.

[00105] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR), unsymmetrical and symmetrical stretching shifts down to 3443 cm^{-1} and 3388 cm^{-1} accounting for 1° amines; 1° amide C=O stretching at 1690 cm^{-1}; N-H in-plane bending at 1614 cm^{-1}; C=C stretching shifted down to 1579 cm^{-1}; aromatic H's from 800 cm^{-1} to 500 cm^{-1} are present.

[00106] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 74.49° C (endotherm) and 59.05° C (endotherm), m.p. = 153-158° C (MEL-TEMP), (carbamazepine m.p. = 190.2° C, nicotinamide m.p. = 150-160° C).

[00107] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), 57.94% weight loss starting at 205.43° C followed by complete decomposition.

[00108] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using Cu Kα (λ = 1.540562), 30kV, 15mA). The powder data were collected over an angular range of 3° to 40° 2θ in continuous scan mode using a step size of 0.02° 2θ and a scan speed of 2.0°/minute. XRPD: Showed analogous peaks to the simulated XRPD derived from the single crystal data. XRPD analysis experimental (calculated): 6.5 (6.7); 8.8 (9.0); 10.1 (10.3); 13.2 (13.5); 15.6 (15.8); 17.7 (17.9); 17.8 (18.1); 18.3 (18.6); 19.8 (20.1); 20.4 (20.7); 21.6 (22.); 22.6 (22.8); 22.9 (23.2); 26.4 (26.7); 26.7 (27.0); 28.0 (28.4).

Example 9—Multi-Component Crystal of Carbamazepine: Carbamazepine/saccharin (GRAs) (1:1 stoichiometry)

[00109] 25 mg (0.1058mmol) carbamazepine and 19 mg (0.1037 mmol) saccharin were dissolved in approximately 4 mL ethanol. Slow evaporation of the solvent yielded colorless needles of a 1:1 carbamazepine/saccharin cocrystal, as shown in Figure 12. Solubility measurements indicate that this multiple-component crystal of carbamazepine has improved solubility over previously known forms of carbamazepine (*e.g.*, increased molar solubility and longer solubility in aqueous solutions).

[00110] Crystal data: (Bruker SMART-APEX CCD Diffractometer), $C_{22}H_{17}N_3O_4S_1$, M = 419.45, triclinic *P-1*; a = 7.5140(11), b = 10.4538(15), c = 12.6826(18) Å, α = 83.642(2)°, β = 85.697(2) °, γ = 75.411(2) °, *U* = 957.0(2) $Å^3$, T = 200(2) K, Z = 2, μ(Mo-Kα) = 0.206 mm^{-1}, D_c = 1.456 Mg/m^3, λ = 0.71073 $Å^3$, F(000) = 436, $2\theta_{max}$ = 56.20°; 8426 reflections measured,

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 38 of 415

4372 unique (R_{int} = 0.0305). Final residuals for 283 parameters were R_1 = 0.0458, wR_2 = 0.1142 for I>2σ(I), and R_1 = 0.0562, wR_2 = 0.1204 for all 4372 data.

[00111] Crystal packing: The co-crystals contain hydrogen bonded carboxamide homodimers. The 2° amines of the saccharin are hydrogen bonded to the carbonyl of the CBZ on each side forming a tetramer. The crystal has a space group of *P-1* with π-π interactions between the phenyl groups of the CBZ and the saccharin phenyl groups.

[00112] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR), unsymmetrical and symmetrical stretching shifts up to 3495 cm^{-1} accounting for 1° amines; C=O aliphatic stretching was shifted up to 1726 cm^{-1}; N-H in-plane bending at 1649 cm^{-1}; C=C stretching shifted down to 1561 cm^{-1}; (O=S=O) sulfonyl peak at 1330 cm^{-1} C-N aliphatic stretching 1175 cm^{-1}.

[00113] Differential Scanning Calorimetry: (TA Instruments 2920 DSC), 75.31° C (endotherm) and 177.32° C (endotherm), m.p. = 148-155°C (MEL-TEMP); (carbamazepine m.p. = 190.2° C, saccharin m.p. = 228.8° C).

[00114] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA), 3.342% weight loss starting at 67.03° C and a 55.09% weight loss starting at 118.71° C followed by complete decomposition.

[00115] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using Cu Kα (λ = 1.540562), 30kV, 15mA). The powder data were collected over an angular range of 3° to 40° 2θ in continuous scan mode using a step size of 0.02° 2θ and a scan speed of 2.0°/minute. XRPD derived from the single crystal data, experimental (calculated): 6.9 (7.0); 12.2 (12.2); 13.6 (13.8); 14.0 (14.1); 14.1 (14.4); 15.3 (15.6); 15.9 (15.9); 18.1 (18.2); 18.7 (18.8); 20.2 (20.3); 21.3 (21.5); 23.7 (23.9); 26.3 (26.4); 28.3 (28.3).

Example 10—Multi-Component Crystal of Carbamazepine: Carbamazepine/2,6-pyridinedicarboxylic acid (2:3 stoichiometry)

[00116] 36 mg (0.1524 mmol) carbamazepine and 26 mg (0.1556 mmol) 2,6-pyridinedicarboxylic acid were dissolved in approximately 2 mL ethanol. Slow evaporation of the solvent yielded clear needles of a 1:1 carbamazepine/2,6-pyridinedicarboxylic acid co-crystal, as shown in Figure 14B.

[00117] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{22}H_{17}N_3O_5$, M=403.39, orthorhombic P2(1)2(1)2(1); a=7.2122, b=14.6491, c=17.5864 Å,α=90°, β=90°,

γ=90°, V=1858.0(2) Å^3, T=100 K, Z=4, μ(MO-Kα)=0.104 mm^{-1}, D_c=1.442 Mg/m^3, λ=0.71073Å^3 , F(000)840, $2\theta_{max}$=28.3. 16641 reflections measured, 4466 unique (R_{int}=0.093). Final residuals for 271 parameters were R_1=0.0425 and wR_2=0.0944 for I>2σ(I).

[00118] Crystal packing: Each hydrogen on the CBZ 1° amine is hydrogen bonded to a carbonyl group of a different 2,6-pyridinedicarboxylic acid moiety. The carbonyl of the CBZ carboxamide is hydrogen bonded to two hydroxide groups of one 2,6-pyridinedicarboxylic acid moitey.

[00119] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3439 cm^{-1}, (N-H stretch, 1° amine, CBZ); 1734 cm^{-1}, (C=O); 1649 cm^{-1}, (C=C).

[00120] Melting Point: 214-216°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, 2,6-pyridinedicarboxylic acid m.p. = 248-250°C).

[00121] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 69% weight loss starting at 215° C and a 17% weight loss starting at 392° followed by complete decomposition.

Example 11—Multi-Component Crystal of Carbamazepine: Carbamazepine/5-nitroisophthalic acid (1:1 stoichiometry)

[00122] 40 mg (0.1693 mmol) carbamazepine and 30 mg (0.1421 mmol) 5-nitroisophthalic acid were dissolved in approximately 3 mL methanol or ethanol. Slow evaporation of the solvent yielded yellow needles of a 1:1 carbamazepine/5-nitroisophthalic acid co-crystal, as shown in Figure 15B.

[00123] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{47}H_{40}N_6O_{16}$, M=944.85, monoclinic C2/c; a=34.355(8), b=5.3795(13), c=23.654(6) Å,α=90°, β=93.952(6)°, γ=90°, V=4361.2(18)Å^3, T=200(2) K, Z=4, μ(MO-Kα)=0.110 mm^{-1}, D_c=1.439 Mg/m^3, λ=0.71073Å^3 , F(000)1968, $2\theta_{max}$=26.43°. 11581 reflections measured, 4459 unique (R_{int}=0.0611). Final residuals for 311 parameters were R_1=0.0725, wR_2=0.1801 for I>2σ(I), and R_1=0.1441, wR_2=0.1204 for all 4459 data.

[00124] Crystal packing: The co-crystals are sustained by hydrogen bonded carboxylic acid homodimers between the two 5-nitroisophthalic acid moieties and hydrogen bonded

carboxy-amide heterodimers between the carbamazepine and 5-nitroisophthalic acid moiety. There is solvent hydrogen bonded to an additional N-H donor from the carbamazepine moiety.

[00125] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3470 cm^{-1}, (N-H stretch, 1° amine, CBZ); 3178 cm^{-1}, (C-H stretch, alkene); 1688 cm^{-1}, (C=O); 1602 cm^{-1}, (C=C).

[00126] Differential Scanning Calorimetry: (TA Instruments 2920 DSC). 190.51°C (endotherm). m.p. = NA (decomposes at 197-200°C) (MEL-TEMP). (carbamazepine m.p. = 191-192°C, 5-nitroisophthalic acid m.p. = 260-261°C).

[00127] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 32.02% weight loss starting at 202°, a 12.12% weight loss starting at 224° and a 17.94% weight loss starting at 285° followed by complete decomposition.

[00128] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using CuKα (λ=1.540562), 30kV, 15mA). The powder data were collected over an angular range of 3 to 40 2 in continuous scan mode using a step size of 0.02 2 and a scan speed of 2.0 /min. XRPD: Showed analogous peaks to the simulated XRPD derived from the single crystal data. XRPD analysis experimental (calculated): 10.138 (10.283), 15.291 (15.607), 17.438 (17.791), 21.166 (21.685), 31.407 (31.738), 32.650 (32.729).

Example 12—Multi-Component Crystal of Carbamazepine: Carbamazepine/acetic acid (1:1 stoichiometry)

[00129] 25 mg (0.1058 mmol) carbamazepine was dissolved in approximately 2 mL acetic acid. Slow evaporation of the solvent yielded yellow needles of a 1:1 carbamazepine/acetic acid co-crystal, as shown in Figure 16B.

[00130] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{17}H_{16}N_2O_3$, M=296.32, monoclinic P2(1)/c; a=5.1206(4), b=15.7136(13), c=18.4986(15) Å,α=90°, β=96.5460(10)°, γ=90°, V=1478.8(2)$Å^3$, T=100(2) K, Z=4, μ(MO-Kα)=0.093 mm^{-1}, D_c=1.331 Mg/m^3, λ=0.71073$Å^3$, F(000)624, $2\theta_{max}$=28.4°. 12951 reflections measured, 3529 unique (R_{int}=0.076). Final residuals for 203 parameters were R_1=0.0492, wR_2=0.1335 for I>2σ(I).

[00131] Crystal packing: The co-crystal is sustained by hydrogen bonded carboxamide-carboxylic heterodimers. The second 1° amine hydrogen from each CBZ joins 2 heterodimers side by side forming a tetramer.

[00132] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3462 cm^{-1}, (N-H stretch, 1° amine, CBZ); 1699 cm^{-1}, (C=O); 1629 cm^{-1}, (C=C, CBZ); 1419 cm^{-1}, (COOH, acetic acid).

[00133] Melting Point: 187°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, acetic acid m.p. = 16.6°C).

[00134] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 20.62% weight loss starting at 104° and a 77.05% weight loss starting at 200° followed by complete decomposition.

Example 13—Multi-Component Crystal of Carbamazepine: Carbamazepine/1,3,5,7-adamantanetetracarboxylic acid (1:1 stoichiometry)

[00135] 15 mg (0.1524 mmol) carbamazepine and 20 mg (0.1556 mmol) 1,3,5,7-adamantanetetracarboxylic acid were dissolved in approximately 1 mL methanol or 1 mL ethanol. Slow evaporation of the solvent yields clear plates of a 2:1 carbamazepine/1,3,5,7-adamantanetetracarboxylic acid co-crystal, as shown in Figure 17B.

[00136] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{44}H_{40}N_2O_{10}$, M=784.80, monoclinicC2/c; a=18.388(4), b=12.682(3), c=16.429(3) Å, β=100.491(6)°, V=3767.1(14) $Å^3$, T=100(2) K, Z=4, μ(MO-Kα)=0.099 mm^{-1}, D_c=1.384 Mg/m^3, λ=0.71073$Å^3$, F(000)1648, $2\theta_{max}$=28.20°. 16499 reflections measured, 4481 unique (R_{int}=0.052). Final residuals for 263 parameters were R_1=0.0433 and wR_2=0.0913 for I>2σ(I).

[00137] Crystal packing: The co-crystals form a single 3D network of four tetrahedron, linked by square planes similar to the *PtS* topology. The crystals are sustained by hydrogen bonding.

[00138] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3431 cm^{-1}, (N-H stretch, 1° amine, CBZ); 3123 cm^{-1}, (C-H stretch, alkene); 1723 cm^{-1}, (C=O); 1649 cm^{-1}, (C=C).

[00139] Melting Point: (MEL-TEMP). 258-260°C (carbamazepine m.p. = 191-192°C, adamantanetetracarboxylic acid m.p. = >390°C).

[00140] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 9% weight loss starting at 189°C, a 52% weight loss starting at 251°C and a 31% weight loss starting at 374°C followed by complete decomposition.

Example 14—Multi-Component Crystal of Carbamazepine: Carbamazepine/benzoquinone (1:1 stoichiometry)

[00141] 25 mg (0.1058 mmol) carbamazepine and 11 mg (0.1018 mmol) benzoquinone was dissolved in 2 mL methanol or THF. Slow evaporation of the solvent produced an average yield of yellow crystals of a 1:1 carbamazepine/benzoquinone co-crystal, as shown in Figure 18B.

[00142] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{21}H_{16}N_2O_3$, M=344.36, monoclinic P2(1)/c; a=10.3335(18), b=27.611(5), c=4.9960(9) Å, β=102.275(3)°, V=1392.9(4) $Å^3$, T=100(2) K, Z=3, D_c=1.232 Mg/m^3, μ(MO-Kα)=0.084 mm^{-1}, λ=0.71073$Å^3$, F(000)540, $2\theta_{max}$=28.24°. 8392 reflections measured, 3223 unique (R_{int}=0.1136). Final residuals for 199 parameters were R_1=0.0545 and wR_2=0.1358 for I>2σ(I), and R_1=0.0659 and wR_2=0.1427 for all 3223 data.

[00143] Crystal packing: The co-crystals contain hydrogen bonded carboxamide homodimers. Each 1° amine on the CBZ is bifurcated to a carbonyl group of a benzoquinone moiety. The dimers form infinite chains.

[00144] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3420 cm^{-1}, (N-H stretch, 1° amine, CBZ); 2750 cm^{-1}, (aldehyde stretch); 1672 cm^{-1}, (C=O); 1637 cm^{-1}, (C=C, CBZ).

[00145] Melting Point: 170°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, benzoquinone m.p. = 115.7°C).

[00146] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 20.62% weight loss starting at 168° and a 78% weight loss starting at 223° followed by complete decomposition.

Example 15—Multi-Component Crystal of Carbamazepine: Carbamazepine/butyric acid (1:1 stoichiometry)

[00147] 10 mg (0.0423 mmol) carbamazepine was dissolved in approximately 1 mL butyric acid. Slow evaporation of the solvent mixture produced an average yield of yellow/brown crystals of a 1:1 carbamazepine/butyric acid co-crystal, as shown in Figure 19B.

[00148] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{19}H_{20}N_2O_3$, M=324.37, triclinic P-1; a=9.1567, b=10.1745, c=10.5116 Å,α=72.850°, β=70.288°, γ=67.269°, V=832.17 Å^3, T=100° K, Z=2, μ(MO-Kα)=0.088 mm^{-1}, D_c=1.290 Mg/m^3, λ=0.71073Å^3 , F(000)344, $2\theta_{max}$=28.28°. 5315 reflections measured, 3686 unique (R_{int}=0.0552). Final residuals for 217 parameters were R_1=0.0499, wR_2=0.1137 for I>2σ(I), and R_1=0.0678, wR_2=0.1213 for all 3686 data.

[00149] Crystal packing: The co-crystals are sustained by hydrogen bonded carboxamide-carboxylic heterodimers between the carbamazepine moieties and the butyric acid moieties. The second 1° amine hydrogen from each CBZ joins 2 heterodimers side by side forming a tetramer.

[00150] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3486 cm^{-1}, (N-H stretch, 1° amine, CBZ); 3307 cm^{-1}, (C-H stretch, alkene); 1684 cm^{-1}, (C=O); 1540 cm^{-1}, (C=C).

[00151] Melting Point: 63-64°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, butyric acid m.p. = -94°C).

[00152] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA).16 % weight loss starting at 54°, a 16% weight loss starting at 134° and a 49% weight loss starting at 174° followed by complete decomposition.

Example 16—Multi-Component Crystal of Carbamazepine: Carbamazepine/DMSO (1:1 stoichiometry)

[00153] 25 mg (0.1058 mmol) carbamazepine was dissolved in approximately 1.5 mL DMSO. Slow evaporation of the solvent yielded colorless plates of a 1:1 carbamazepine/ DMSO co-crystal, as shown in Figure 20B.

[00154] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{34}H_{36}N_4O_4S_2$, M=628.79, triclinic P-1; a=7.3254(19), b=8.889(2), c=12.208(3) Å,α=94.840(5)°, β=94.926(5)°, γ=100.048(5)°, V=775.8(3)Å^3, T=200(2) K, Z=2, μ(MO-Kα)=0.216 mm^{-1}, D_c=1.320 Mg/m^3, λ=0.71073Å^3 , F(000)320, $2\theta_{max}$=28.3°. 4648 reflections measured, 3390 unique (R_{int}=0.0459). Final residuals for 209 parameters were R_1=0.0929, wR_2=0.3043 for I>2σ(I).

[00155] Crystal packing: The co-crystals are sustained by the hydrogen bonded carboxamide homosynthon. The 1° amines are hydrogen bonded to the sulfoxide of the DMSO

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 44 of 415

on each side of the homosynthon. The crystal is stabilized by π-π interactions from the tricyclic azepine ring system groups of the CBZ.

[00156] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3369 cm^{-1} (N-H stretch, 1° amine, CBZ); 1665 cm^{-1} (C=O stretching); 1481cm^{-1} (C=C).

[00157] Differential Scanning Calorimetry: (TA Instruments 2920 DSC). 100°C, 193°C (endotherms). m.p. = 189°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, DMSO m.p. = 18.45°C)

[00158] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 26% weight loss starting at 102°, a 64% weight loss starting at 212° followed by complete decomposition.

Example 17—Multi-Component Crystal of Carbamazepine: Carbamazepine/formamide (1:1 stoichiometry)

[00159] 10 mg (0.0423 mmol) carbamazepine was dissolved in a mixture of approximately 1 mL formamide/1 mL THF or 1 mL formamide/1 mL methanol. Slow evaporation of the solvent mixture produced an average yield of clear needles of a 1:1 carbamazepine/formamide co-crystal, as shown in Figure 21B.

[00160] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{16}H_{15}N_3O_2$, M=281.31, triclinic P-1; a=5.1077(11), b=16.057(3), c=17.752(4) Å,α=73.711(3)°, β=89.350(3)°, γ=88.636(3)°, V=1397.1(5) $Å^3$, T=100° K, Z=4, μ(MO-Kα)=0.091 mm^{-1}, D_c=1.337 Mg/m^3, λ=0.71073$Å^3$, F(000)592, $2\theta_{max}$=28.33°. 11132 reflections measured, 6272 unique (R_{int}=0.1916). Final residuals for 379 parameters were R_1=0.0766 and wR_2=0.1633 for I>2σ(I).

[00161] Crystal packing: The co-crystals are sustained by hydrogen bonded carboxamide homodimers between two carbamazepine moieties and carboxylic acid homodimers between two formamide moieties. Infinite chains are formed by the homodimers linked side by side, with every other set of CBZ molecules attached on the sides of the chain but not bonded to form a dimer.

[00162] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3392 cm^{-1}, (N-H stretch, 1° amine, CBZ); 2875 cm^{-1}, (C-H stretch, alkene); 1653 cm^{-1}, (C=O); 1590 cm^{-1} , (C=C).

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 45 of 415

[00163] Melting Point: 142-144°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, formamide m.p. = -94°C).

[00164] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 27% weight loss starting at 138°, a 67% weight loss starting at 195° followed by complete decomposition.

Example 18—Multi-Component Crystal of Carbamazepine: Carbamazepine/formic acid (1:1 stoichiometry)

[00165] 40 mg (0.1693 mmol) carbamazepine was dissolved in approximately 2 mL formic acid. Slow evaporation of the solvent yielded off-white starbursts of a 1:1 carbamazepine/formic acid co-crystal, as shown in Figure 22B.

[00166] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{16}H_{14}N_2O_3$, M=282.29, monoclinic P21/c; a=5.2031(9), b=14.741(2), c=17.882(3) Å,α=90°, β=98.132(3)°, γ=90°, V=1357.7(4)Å^3, T= 100 K, Z=4, μ(MO-Kα)=0.097 mm^{-1}, D_c=1.381 Mg/m^3, λ=0.71073Å^3 , F(000)592, $2\theta_{max}$=28.3. 9402 reflections measured, 3191 unique (R_{int}=0.111). Final residuals for 190 parameters were R_1=0.0533 and wR_2=0.1268 for I>2σ(I).

[00167] Crystal packing: The co-crystals are sustained by hydrogen bonded carboxylic acid-amine heterodimers arranged in centrosymmetric tetramers.

[00168] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3439 cm^{-1}, (1° amine stretch,CBZ); 3026 cm^{-1} (C-H stretch, CBZ); 1692 cm^{-1}, (1° amide, C=O stretch).

[00169] Melting Point: 187°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, formic acid m.p. = 8.4°C).

[00170] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 14.60% weight loss starting at 123° and a 68.91% weight loss starting at 196° followed by complete decomposition.

Example 19—Multi-Component Crystal of Carbamazepine: Carbamazepine/trimesic acid (1:1 stoichiometry)

[00171] 36 mg (0.1524 mmol) carbamazepine and 31 mg (0.1475 mmol) trimesic acid were dissolved in a solvent mixture of approximately 2 mL methanol and 2mL dichloromethane.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 46 of 415

Slow evaporation of the solvent mixture yielded white starbursts of a 1:1 carbamazepine/trimesic acid co-crystal, as shown in Figure 23B.

[00172] Crystal data: (Bruker SMART-APEX CCD Diffractometer). $C_{24}H_{18}N_2O_7$, M=446.26, monoclinic C2/c; a=32.5312(50), b=5.2697(8), c=24.1594(37) Å,α=90°, β=98.191(3)°, γ=90°, V=4099.39(37) Å^3, T=-173 K, Z=8, μ(MO-Kα)=0.110 mm^{-1}, D_c=1.439 Mg/m^3, λ=0.71073Å^3, F(000)1968, $2\theta_{max}$=26.43°. 11581 reflections measured, 4459 unique (R_{int}=0.0611). Final residuals for 2777 parameters were R_1=0.1563, wR_2=0.1887 for I>2σ(I), and R_1=0.1441, wR_2=0.1204 for all 3601 data.

[00173] Crystal packing: The co-crystals are sustained by hydrogen bonded carboxylic acid homodimers between carbamazepine and trimesic acid moieties and hydrogen bonded carboxylic acid-amine heterodimers between two trimesic acid moieties arranged in a stacked ladder formation.

[00174] Infrared Spectroscopy: (Nicolet Avatar 320 FTIR). 3486 cm^{-1}(N-H stretch, 1° amine, CBZ); 1688 cm^{-1} (C=O, 1° amide stretch, CBZ); 1602 cm^{-1} (C=C, CBZ).

[00175] Differential Scanning Calorimetry: (TA Instruments 2920 DSC). 273°C (endotherm). m.p. = NA, decomposes at 278°C (MEL-TEMP). (carbamazepine m.p. = 191-192°C, trimesic acid m.p. = 380°C)

[00176] Thermogravimetric Analysis: (TA Instruments 2950 Hi-Resolution TGA). 62.83% weight loss starting at 253° and a 30.20% weight loss starting at 278° followed by complete decomposition.

[00177] X-ray powder diffraction: (Rigaku Miniflex Diffractometer using CuKα (λ=1.540562), 30kV, 15mA). The powder data were collected over an angular range of 3 to 40 2 in continuous scan mode using a step size of 0.02 2 and a scan speed of 2.0 /min. XRPD analysis experimental: 10.736, 12.087, 16.857, 24.857, 27.857.

[00178] All patents, patent applications, provisional applications, and publications referred to or cited herein are incorporated by reference in their entirety, including all figures and tables, to the extent they are not inconsistent with the explicit teachings of this specification.

[00179] It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will

be suggested to persons skilled in the art and are to be included within the spirit and purview of this application.

Claims

1. A multiple-component phase composition comprising a solid phase that is sustained by intermolecular interactions between two or more independent molecular entities, wherein at least one of said two or more independent molecular entities is a pharmaceutical molecule.

2. The multiple-component phase composition of claim 1, wherein said multiple-component phase composition is a discrete supramolecular entity.

3. The multiple-component phase composition of claim 1, wherein said multiple-component phase composition is a polymeric structure.

4. The multiple-component phase composition of claim 1, wherein said pharmaceutical molecule is sustained by a supramolecular homosynthon when said pharmaceutical molecule is in its pure phase.

5. The multiple-component phase composition of claim 1, wherein said multiple-component phase composition has at least one physical property or chemical property that is different from that of said pharmaceutical when said pharmaceutical molecule is in its pure phase.

6. The multiple-component phase composition of claim 1, wherein said multiple-component phase composition has at least one physical or chemical property that is the same as that of said pharmaceutical molecule when said pharmaceutical molecule is in its pure phase.

7. The multiple-component phase composition of claim 5, wherein said at least one physical or chemical property is selected from the group consisting of chemical stability, thermodynamic stability, solubility, dissolution, bioavailability, crystal morphology, and hygroscopicity.

8. The multiple-component phase composition of claim 6, wherein said at least one physical or chemical property is selected from the group consisting of chemical stability, thermodynamic stability, solubility, dissolution, bioavailability, crystal morphology, and hygroscopicity.

9. The multiple-component phase composition of claim 1, wherein said pharmaceutical molecule is selected from the group consisting of aspirin, acetaminophen, profen, phenytoin, and carbamazepine.

10. The multiple-component phase composition of claim 1, wherein said two or more independent molecular entities are selected from the group consisting of: acetaminophen, 4,4'-bipyridine, and water; phenytoin and pyridine; aspirin and 4,4'-bipyridine; ibuprofen and 4,4'-bipyridine; flurbiprofen and 4,4'-bipyridine; flurbiprofen, trans-1,2-bis (4-pyridyl) ethylene; carbamazepine, *p*-phthalaldehyde; carbamazepine and nicotinamide; carbamazepine and saccharin; carbamazepine and 2,6-pyridinedicarboxylic acid; carbamazepine and 5-nitroisophthalic acid; carbamazepine and acetic acid; carbamazepine and 1,3,5,7,-adamantanetetracarboxylic acid; carbamazepine and benzoquinone; carbamazepine and butyric acid; carbamazepine and dimethyl sulfoxide; carbamazepine and formamide; carbamazepine and formic acid; and carbamazepine and trimesic acid.

11. The multiple-component phase composition of claim 1, wherein said intermolecular interactions are selected from the group consisting of hydrogen bonding (weak and/or strong), dipole interactions (induced and/or non-induced), stacking interactions, hydrophobic interactions, and other inter-static interactions.

12. The multiple-component phase composition of claim 1, wherein said intermolecular interactions are between complementary chemical functionalities on said two or more independent molecular entities.

13. The multiple-component phase composition of claim 15, wherein said complementary chemical functionalities include at least one chemical functionality selected from

the group consisting of acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases, amines, alcohols, halogens, sulfones, nitro groups, S-heterocycles, N-heterocycles, O-heterocycles, ethers thioethers, thiols, esters, thioesters, thioketones, epoxides, acetonates, nitrils, oximes, and organohalides.

14. The multiple-component phase composition of claim 12, wherein said complementary chemical functionalities on said two or more independent molecular entities are the same.

15. The multiple-component phase composition of claim 14, wherein said complementary chemical functionalities are acids.

16. The multiple-component phase composition of claim 14, wherein said complementary chemical functionalities are amides.

17. The multiple-component phase composition of claim 12, wherein said complementary chemical functionalities on said two or more independent molecular entities are not the same.

18. The multiple-component phase composition of claim 17, wherein said complementary chemical functionalities on said two or more independent molecular entities are selected from the group consisting of acids and amides; pyridines and amides; and alcohols and amines.

19. The multiple-component phase composition of claim 1, wherein two or more of said independent molecular entities is a pharmaceutical molecule.

20. A multiple-component phase composition comprising a solid phase that is sustained by intermolecular interactions between aspirin and at least one independent molecular entity.

21. A multiple-component phase composition comprising a solid phase that is sustained by intermolecular interactions between acetaminophen and at least one independent molecular entity.

22. A multiple-component phase composition comprising a solid phase that is sustained by intermolecular interactions between a profen and at least one independent molecular entity.

23. A multiple-component phase composition comprising a solid phase that is sustained by intermolecular interactions between phenytoin and at least one independent molecular entity.

24. A multiple-component phase composition comprising a solid phase that is sustained by intermolecular interactions between carbamazepine and at least one independent molecular entity.

25. A method for identifying complementary chemical functionalities in order to form a desired supramolecular synthon, said method comprising:

(a) evaluating the structure of an active pharmaceutical ingredient;

(b) determining whether the active pharmaceutical ingredient contains chemical functionalities capable of forming supramolecular synthons with itself;

(c) identifying from a plurality of chemical functionalities that are known to form a supramolecular synthon at least one functionality that will form a further supramolecular synthon to the supramolecular synthon formed by the active pharmaceutical ingredient, wherein the identified chemical functionality is not capable of disrupting non-covalent bonding within the supramolecular synthon formed by the supramolecular synthon formed by the active pharmaceutical ingredient, and wherein the selected chemical functionality is capable of forming a noncovalent bond to the supramolecular synthon formed by the active pharmaceutical ingredient; and

(d) identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

26. The method of claim 25, wherein said method further comprises preparing a multiple-component solid phase composition, wherein the multiple-component solid phase composition comprises the active pharmaceutical ingredient and at least one of the identified co-crystal formers.

27. The method of claim 26, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, a GRAS compound, a food additive, a low toxicity organic, and a metal-organic complex.

28. The method of claim 26, wherein the multiple-component solid phase composition is formed by one or more methods selected from the group consisting of crystallization from solution, cooling the melt, sublimation, and grinding.

29. A method for identifying complementary chemical functionalities in order to form a desired supramolecular synthon, said method comprising:

(a) evaluating the structure of an active pharmaceutical ingredient;

(b) determining whether the active pharmaceutical ingredient contains chemical functionalities capable of forming supramolecular synthons with itself;

(c) identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the active pharmaceutical ingredient, wherein the identified chemical functionality is capable of disrupting non-covalent bonding within the supramolecular synthon formed by the active pharmaceutical ingredient, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the active pharmaceutical ingredient; and

(d) identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

30. The method of claim 29, wherein said method further comprises preparing a multiple-component solid phase composition, wherein the multiple-component solid phase

composition comprises the active pharmaceutical ingredient and at least one of the identified co-crystal formers.

31. The method of claim 30, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, a GRAS compound, a food additive, a low toxicity organic, and a metal-organic complex.

32. The method of claim 30, wherein the multiple-component solid phase composition is formed by one or more methods selected from the group consisting of crystallization from solution, cooling the melt, sublimation, and grinding.

33. A method for identifying complementary chemical functionalities in order to form a desired supramolecular synthon, said method comprising:

(a) evaluating the structure of an active pharmaceutical ingredient;

(b) determining whether the active pharmaceutical ingredient contains chemical functionalities capable of forming supramolecular synthons with different molecules;

(c) identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the active pharmaceutical ingredient, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the active pharmaceutical ingredient; and

(d) identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

34. The method of claim 33, wherein said method further comprises preparing a multiple-component solid phase composition, wherein the multiple-component solid phase composition comprises the active pharmaceutical ingredient and at least one of the identified co-crystal formers.

35. The method of claim 34, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, a GRAS compound, a food additive, a low toxicity organic, and a metal-organic complex.

36. The method of claim 34, wherein the multiple-component solid phase composition is formed by one or more methods selected from the group consisting of crystallization from solution, cooling the melt, sublimation, and grinding.

Abstract

The subject invention concerns a method for identifying complementary chemical functionalities to form a desired supramolecular synthon. The subject invention also pertains to multiple-component phase compositions comprising one or more pharmaceutical entities and methods for producing such compositions.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 56 of 415

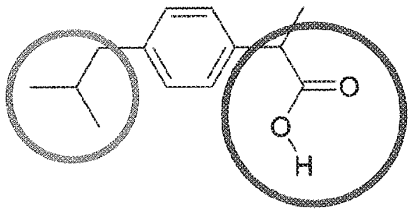


FIG. 1



FIG. 2

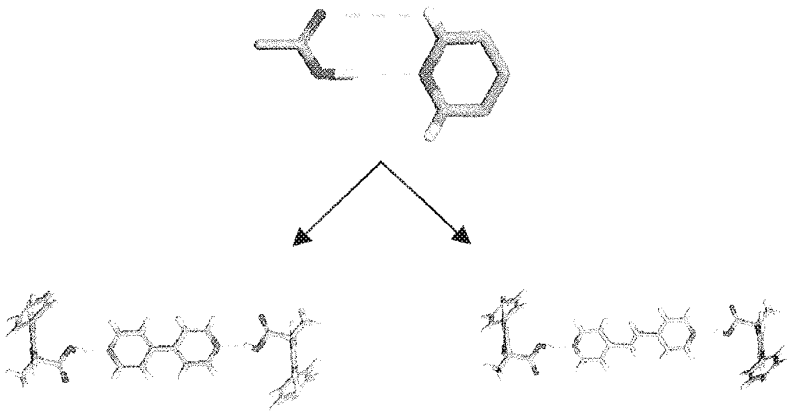


FIG. 3

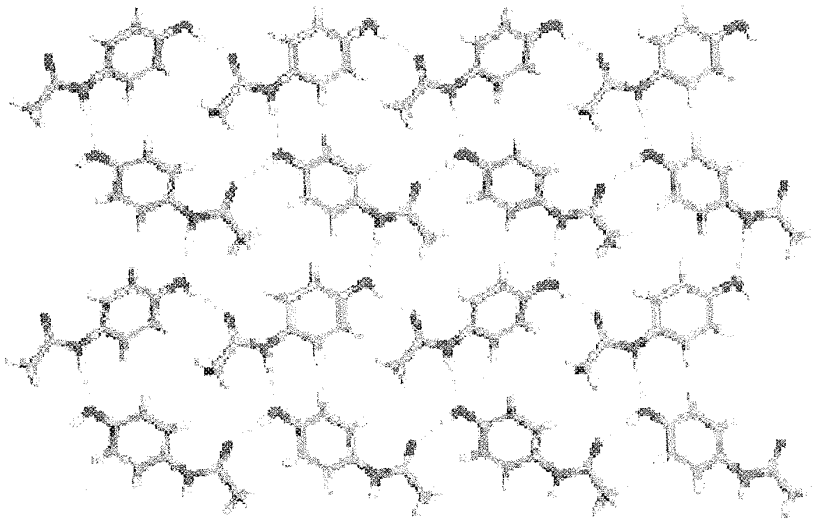


FIG. 4A

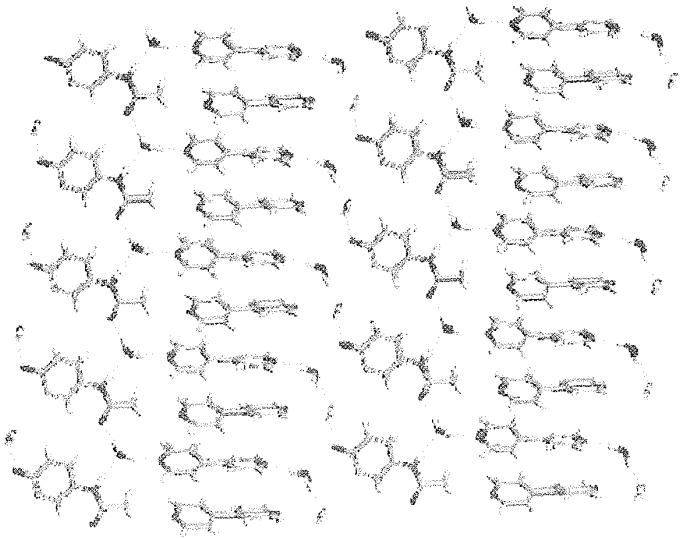


FIG. 4B

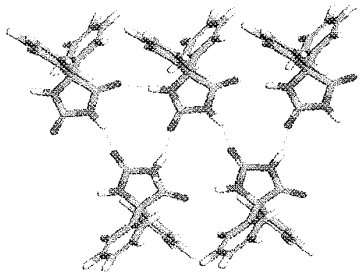


FIG. 5A

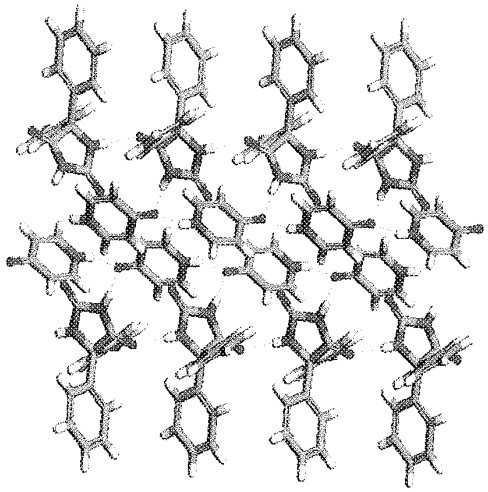


FIG. 5B

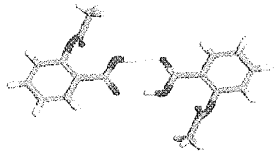


FIG. 6A

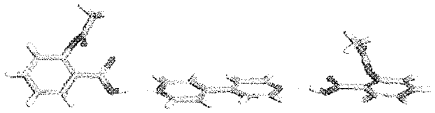


FIG. 6C

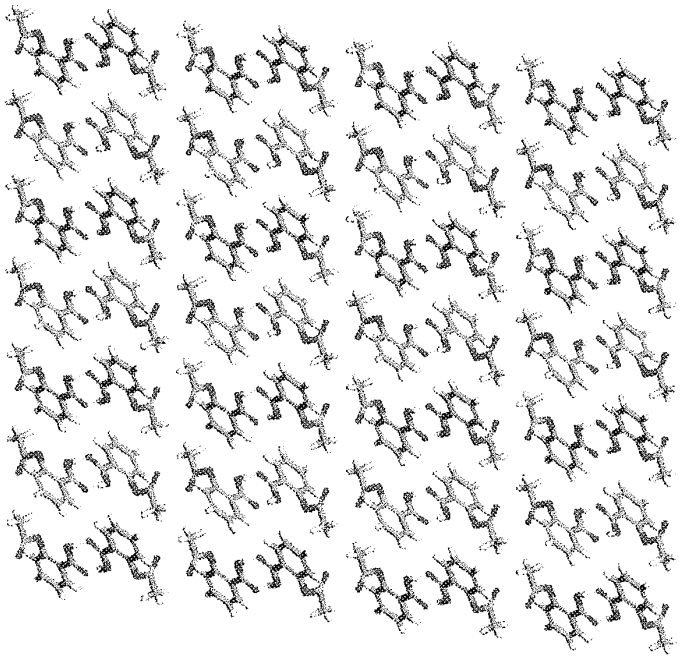


FIG. 6B

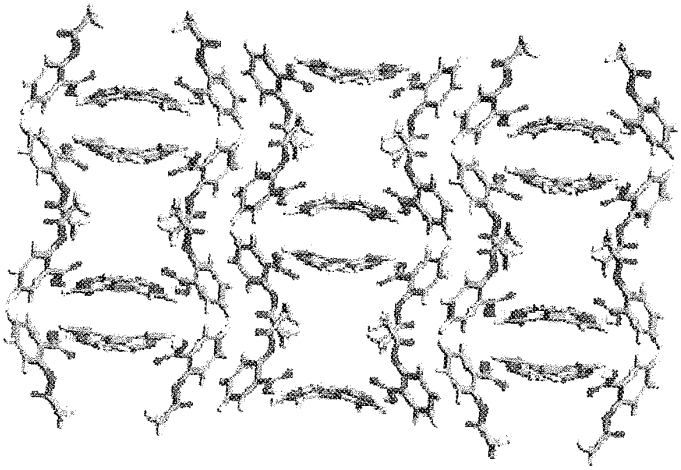


FIG. 6D

FIG. 7A

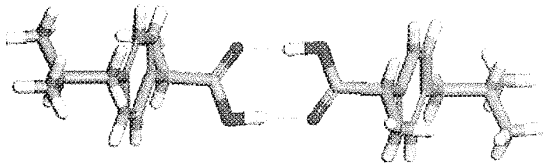
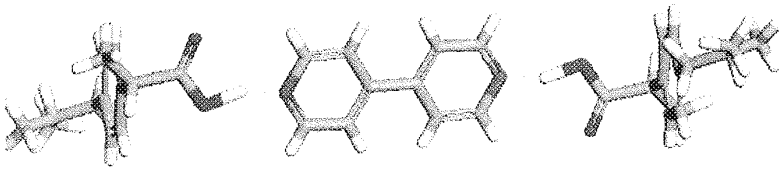


FIG. 7C



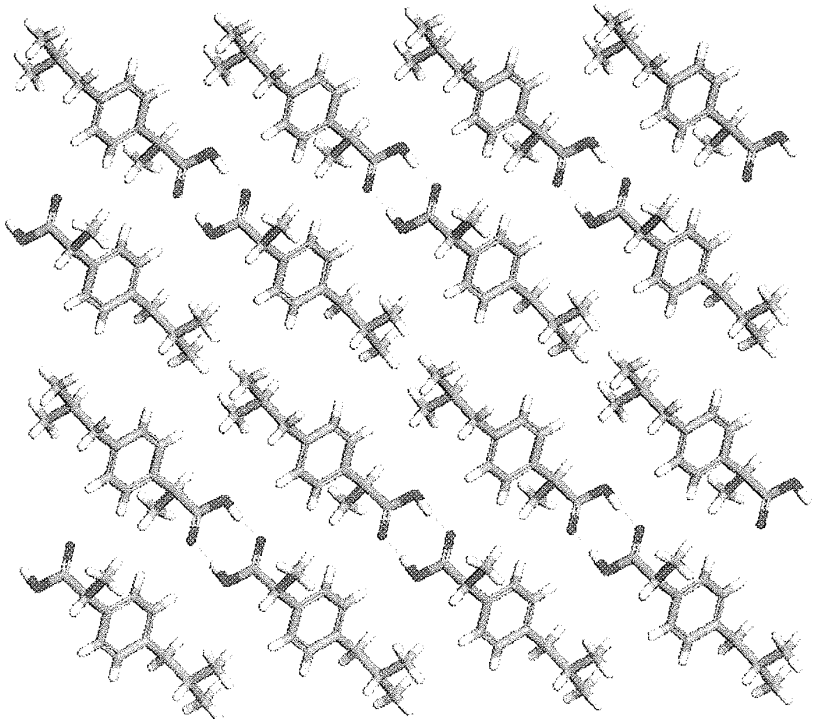


FIG. 7B

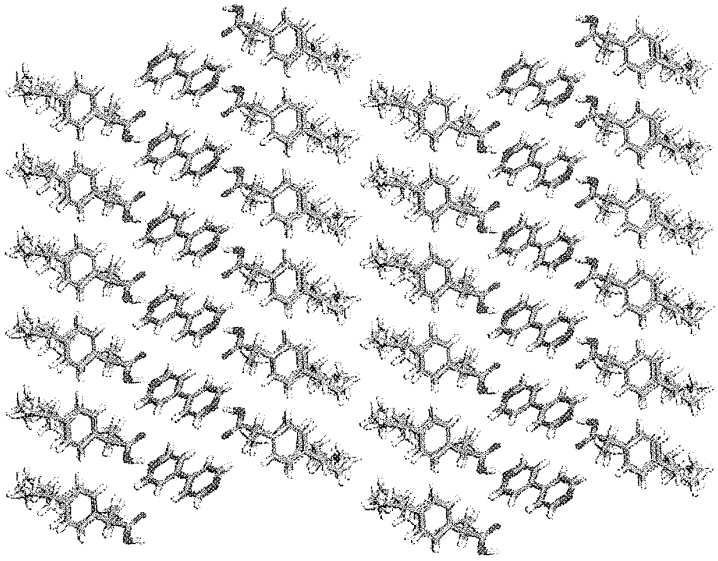


FIG. 7D

FIG. 8A

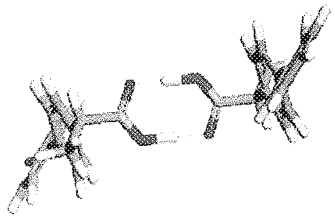
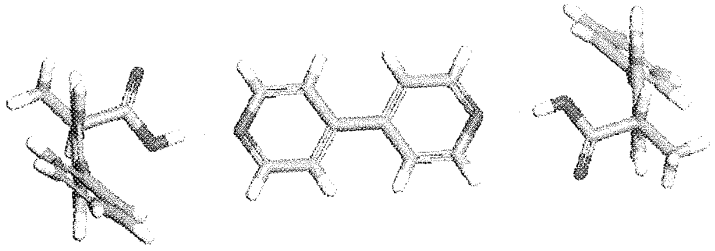


FIG. 8C



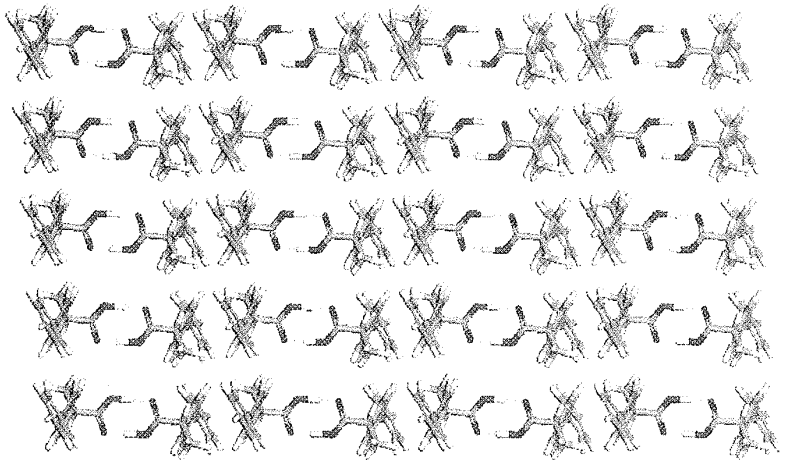


FIG. 8B

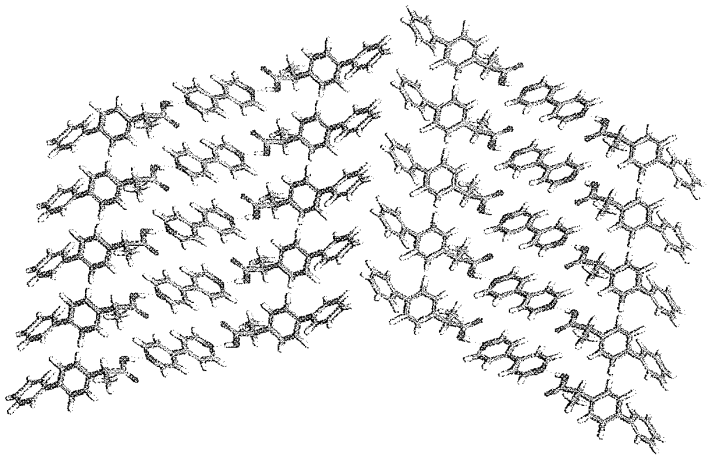


FIG. 8D

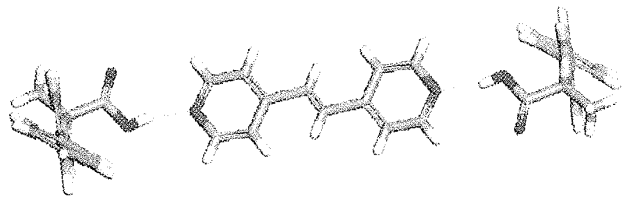


FIG. 9A

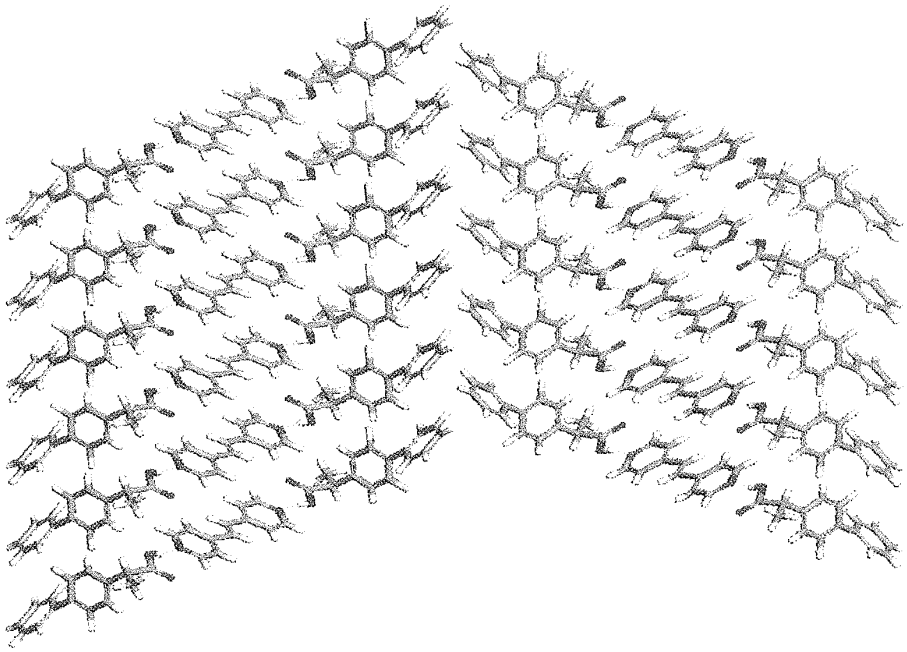


FIG. 9B

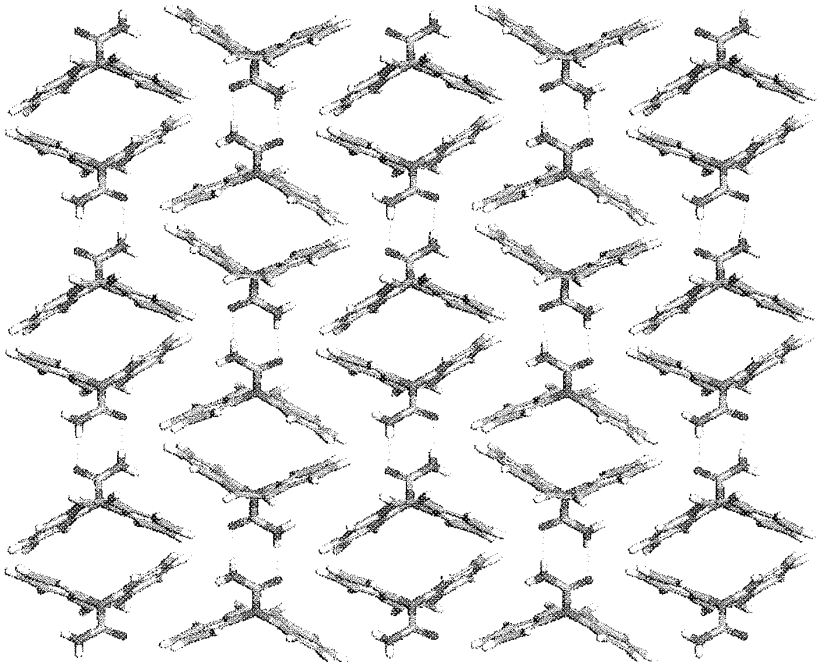


FIG. 10A

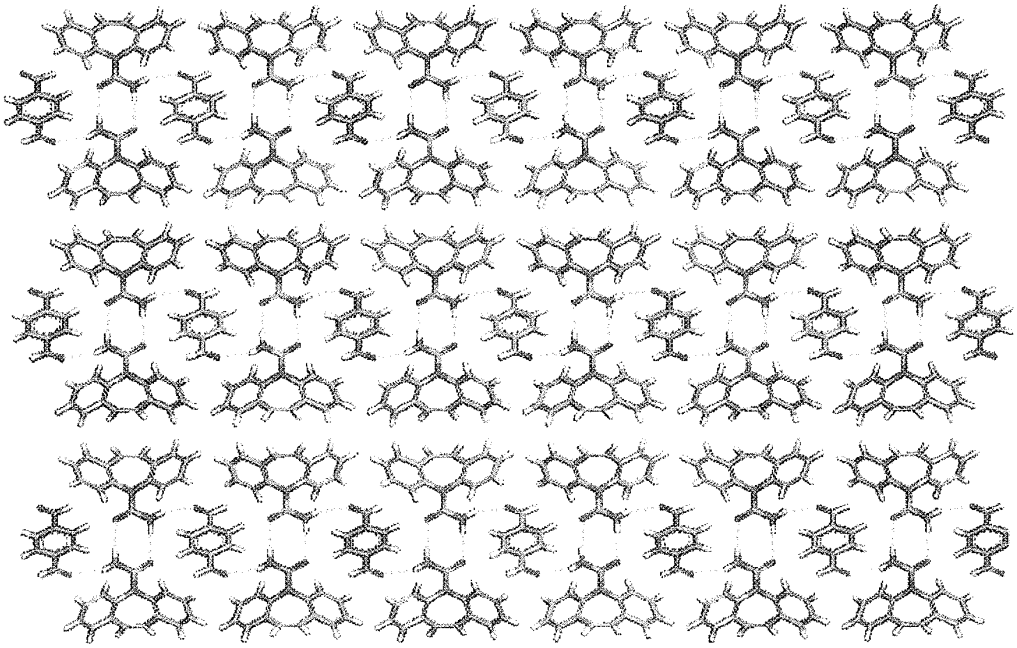


FIG. 10B

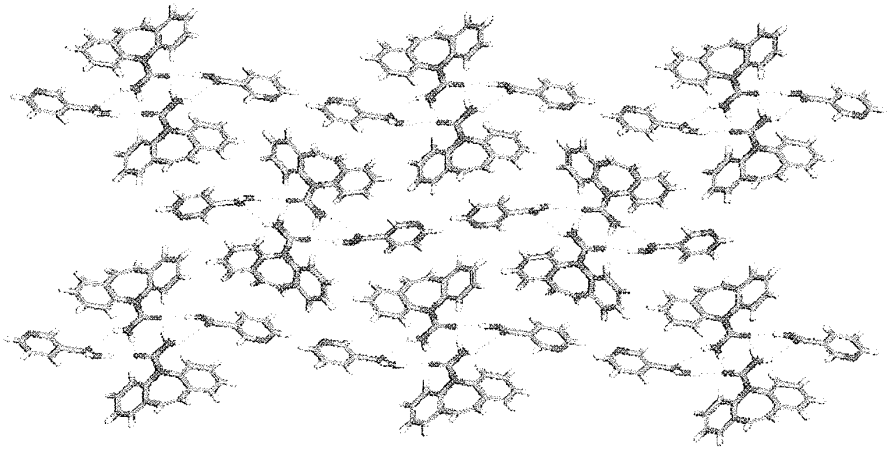


FIG. 11

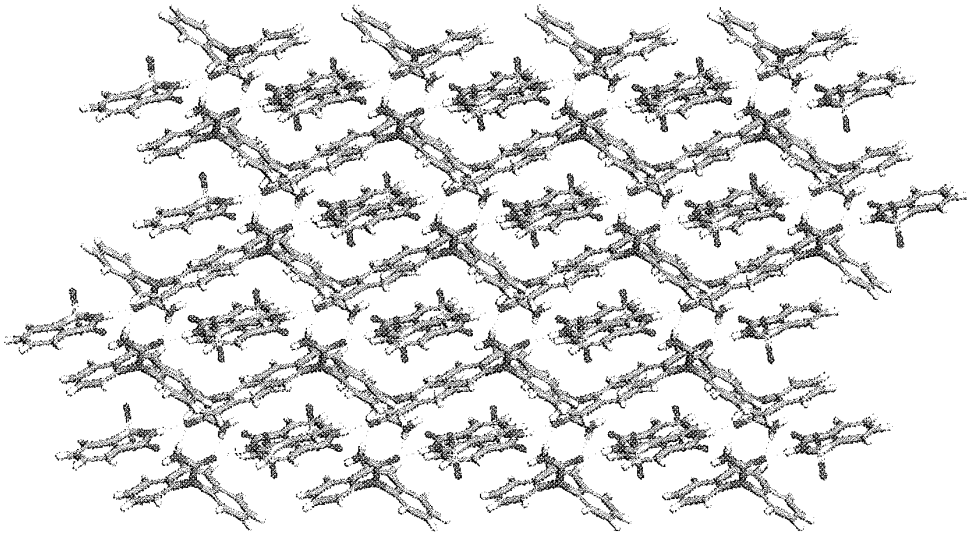


FIG. 12

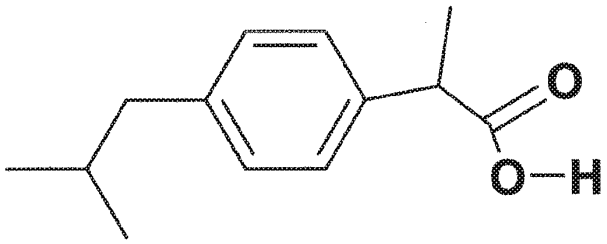


FIG. 13A

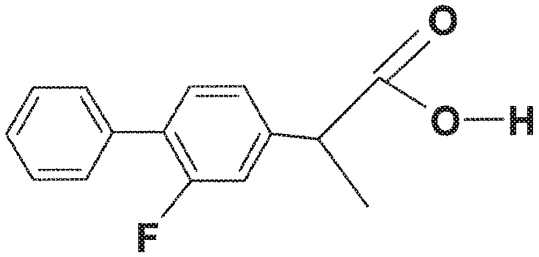


FIG. 13B

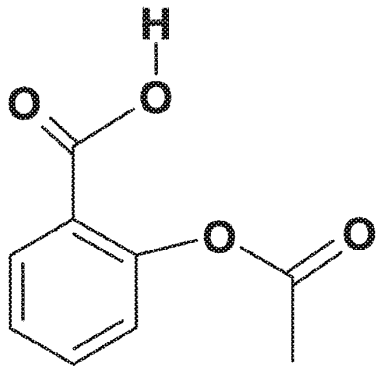


FIG. 13C

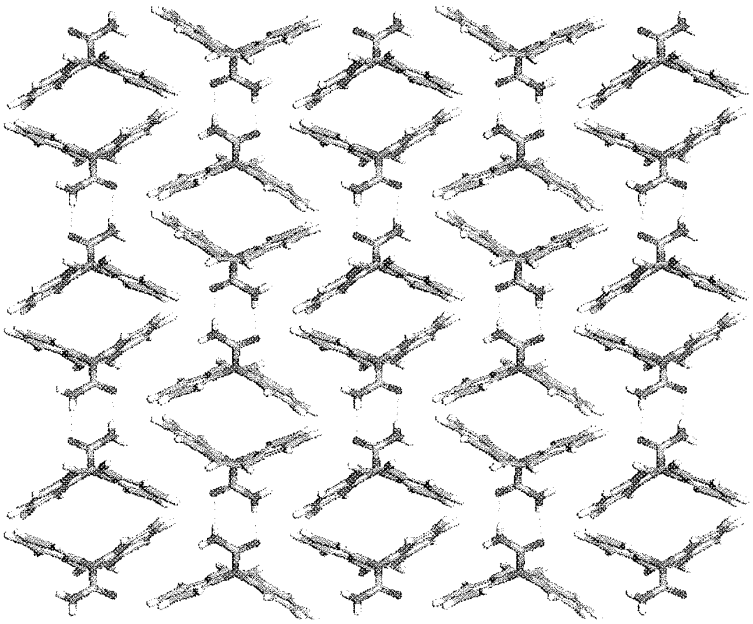


FIG. 14A

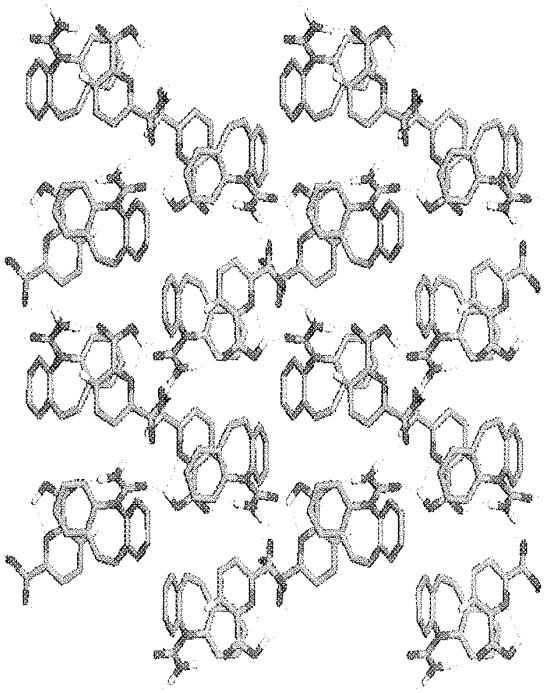


FIG. 14B

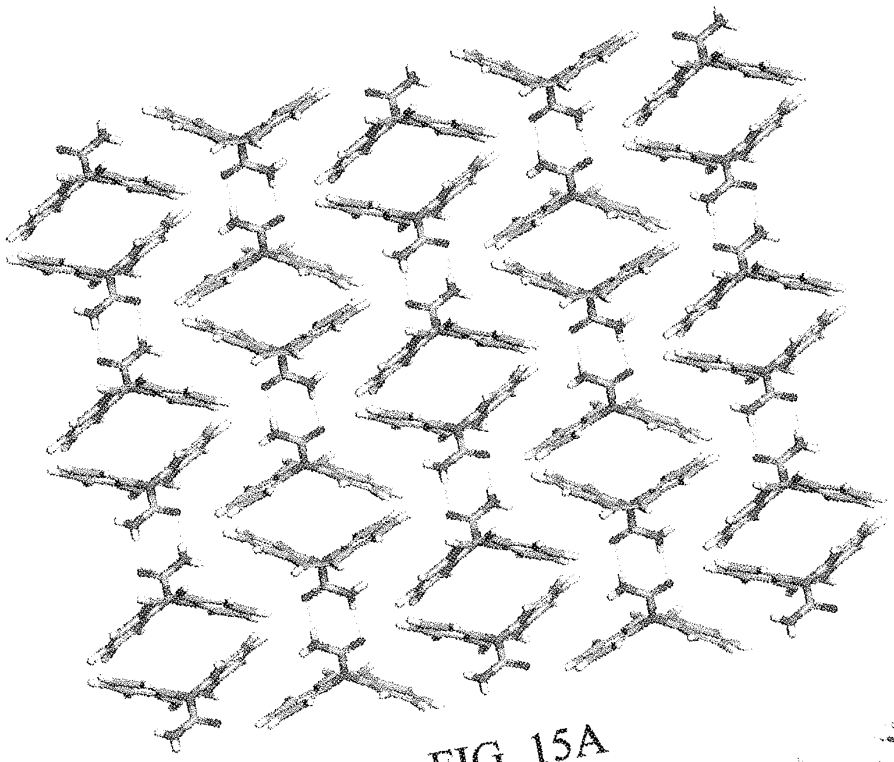


FIG. 15A

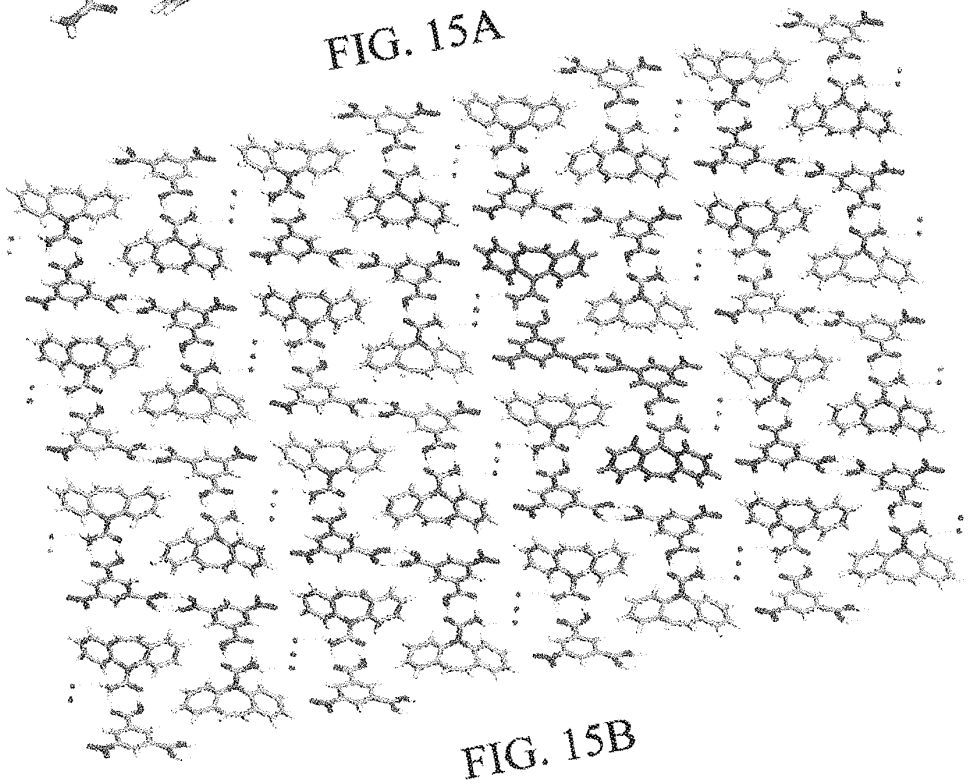


FIG. 15B

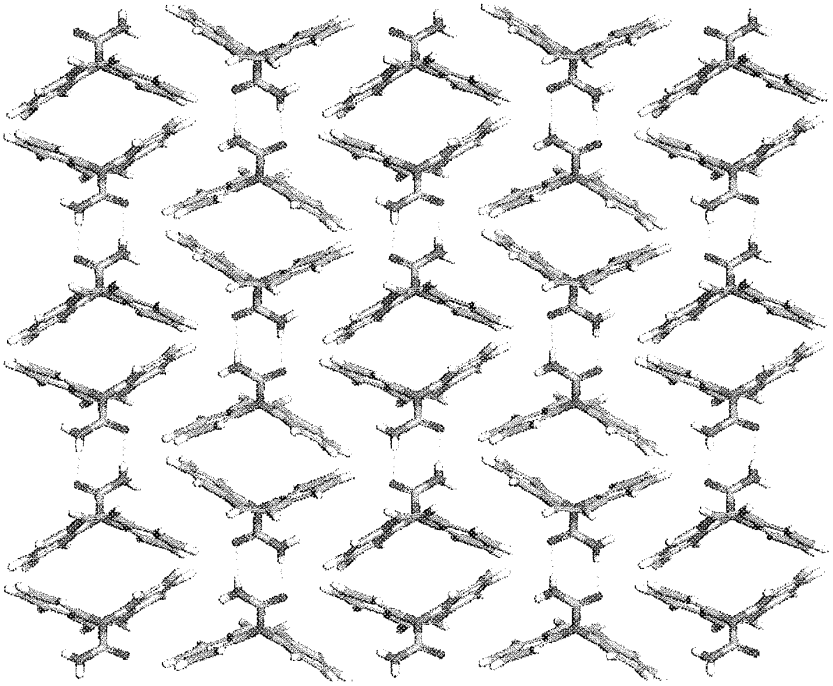


FIG. 16A

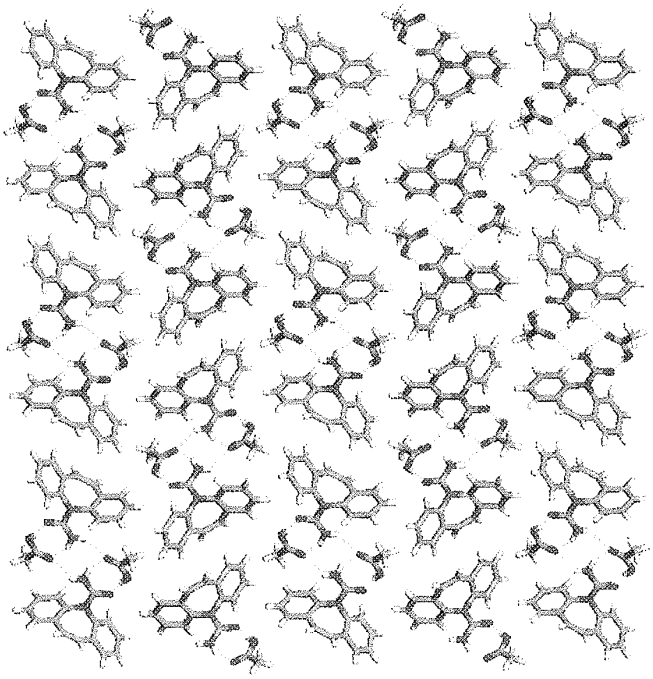


FIG. 16B

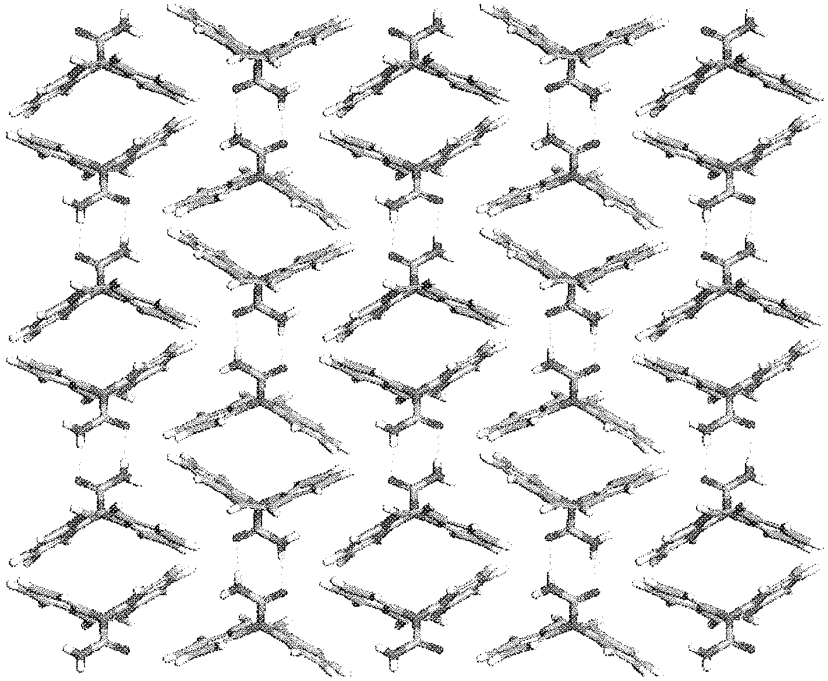


FIG. 17A

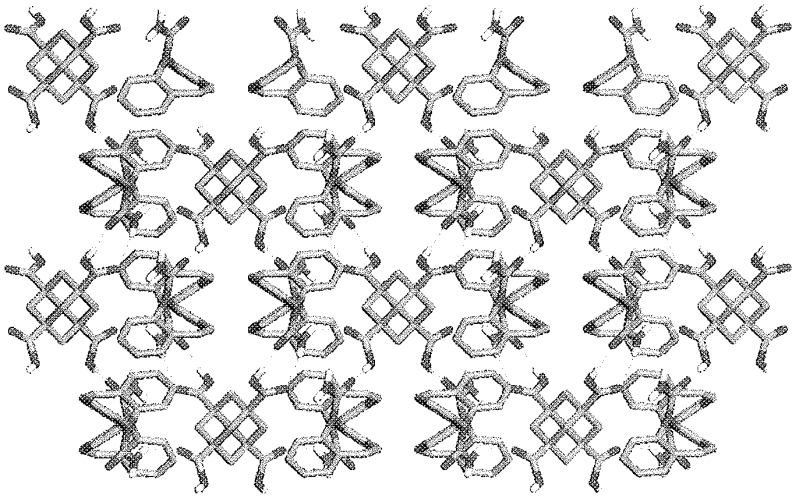


FIG. 17B

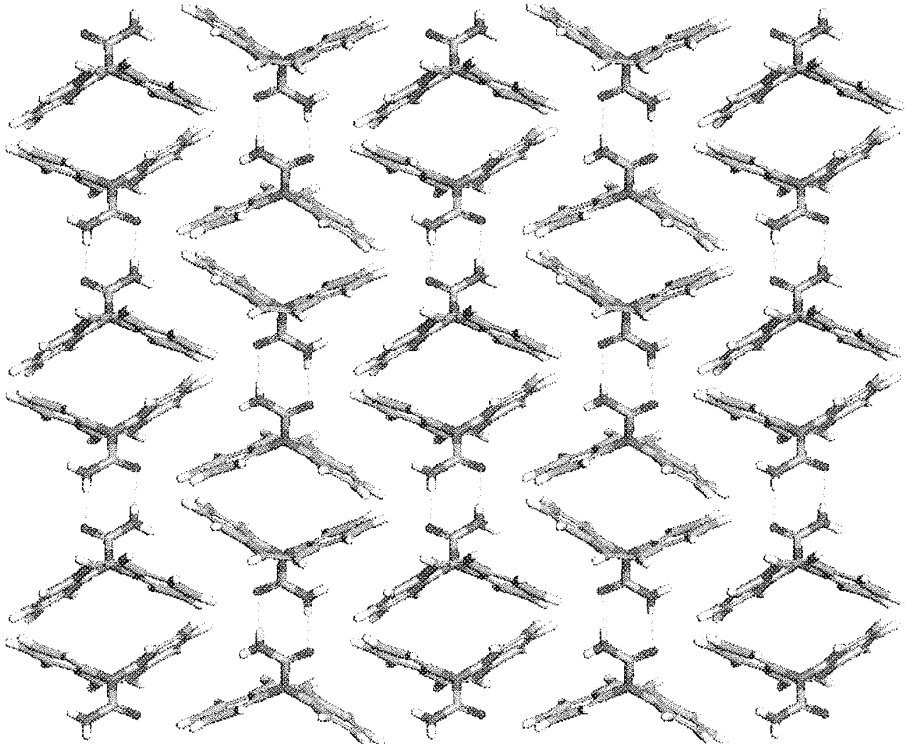


FIG. 18A

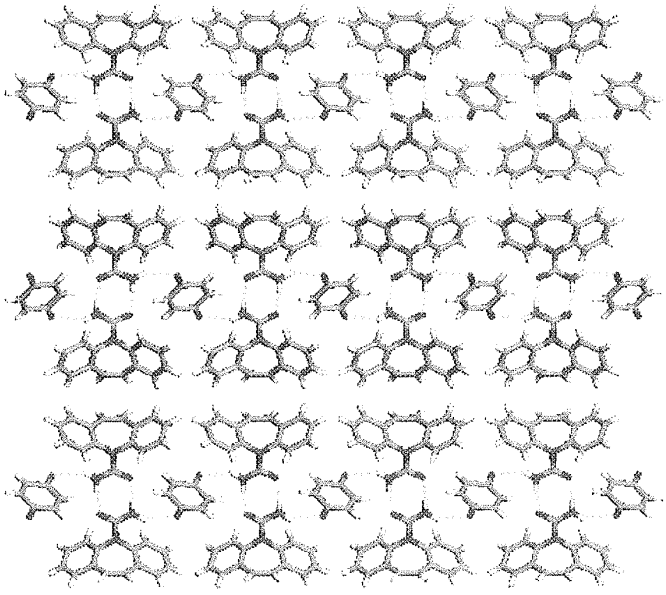


FIG. 18B

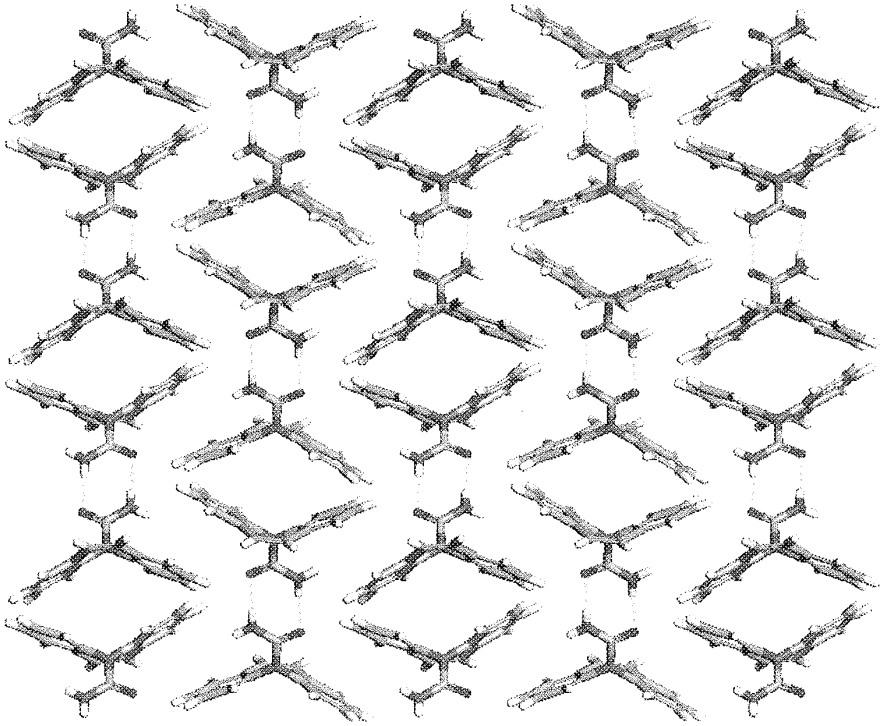


FIG. 19A

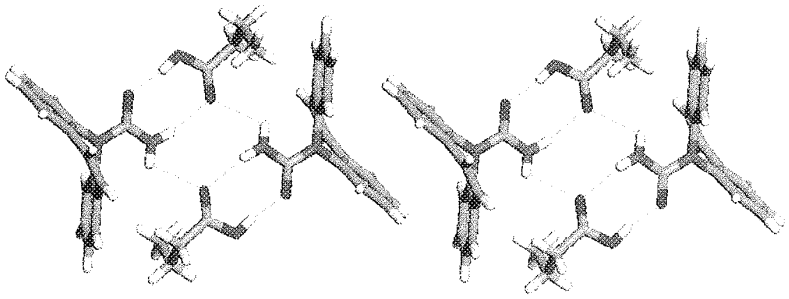


FIG. 19B

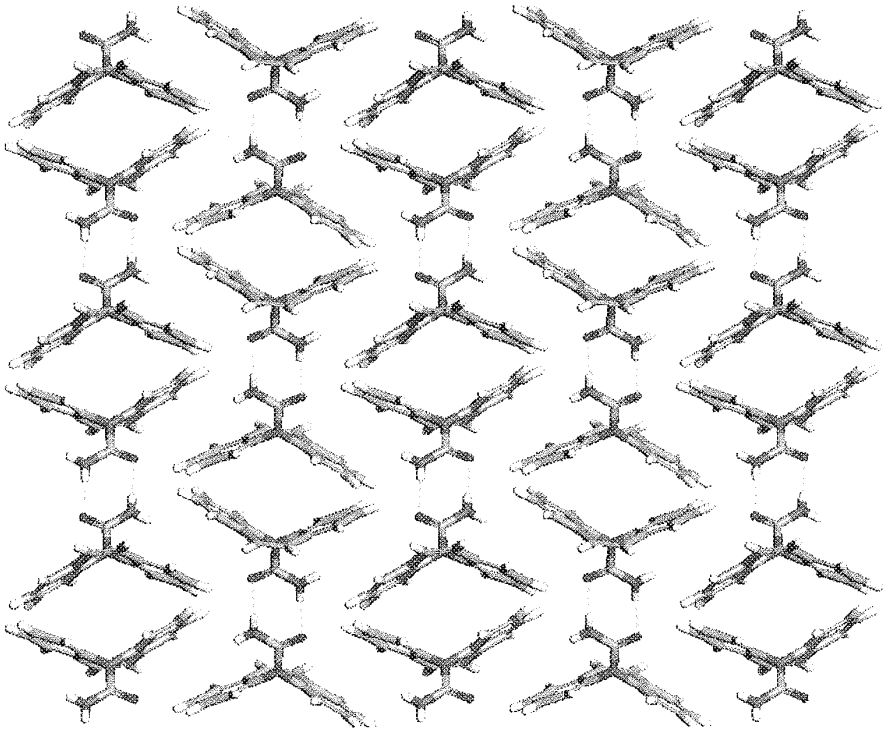


FIG. 20A

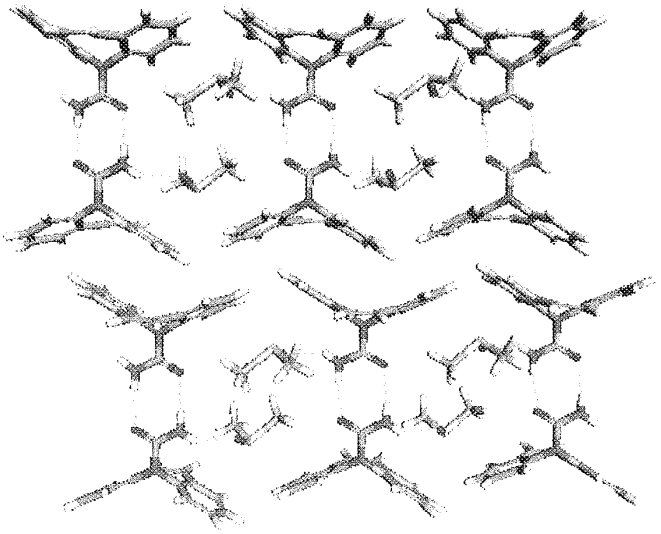


FIG. 20B

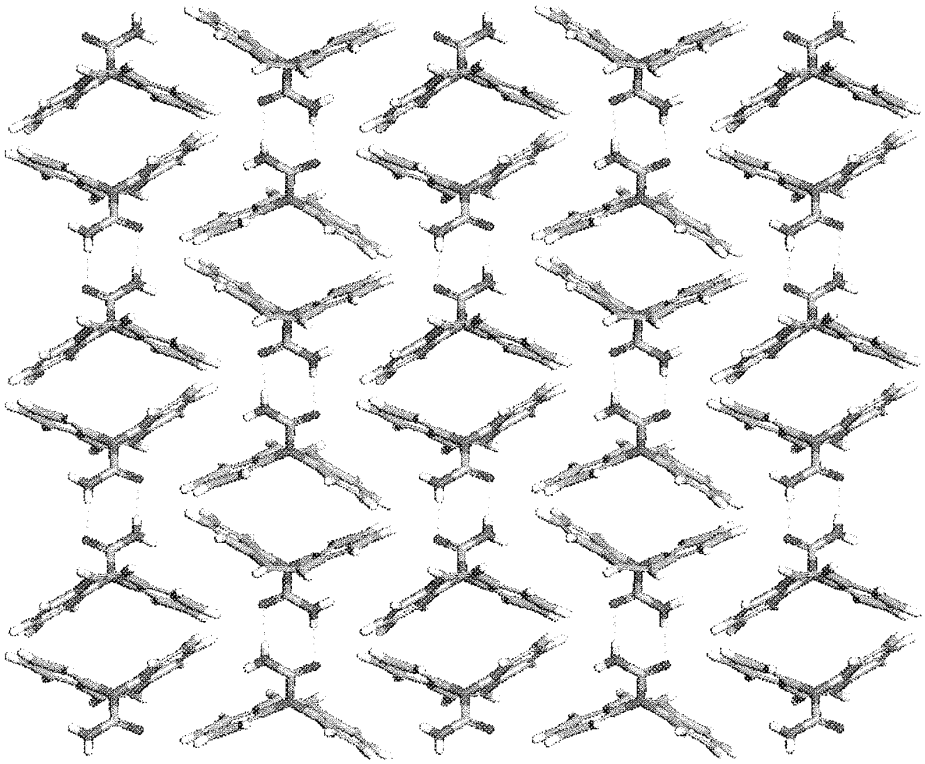


FIG. 21A

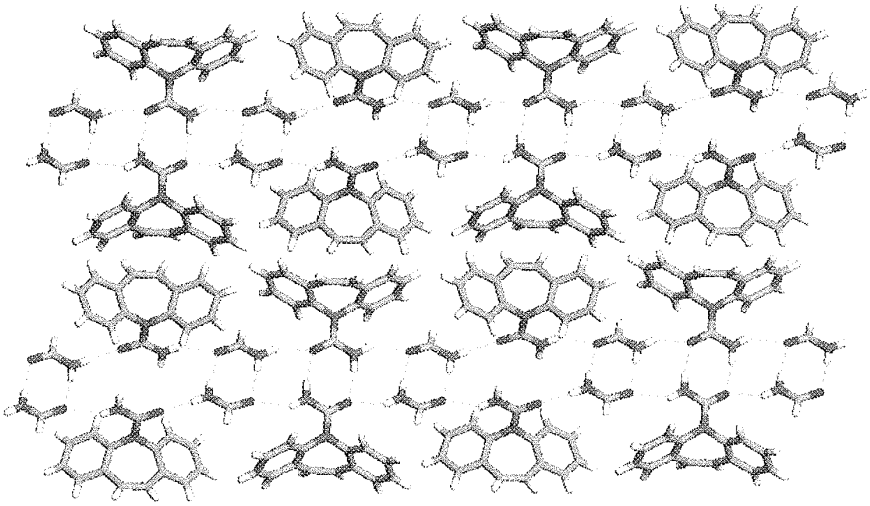


FIG. 21B

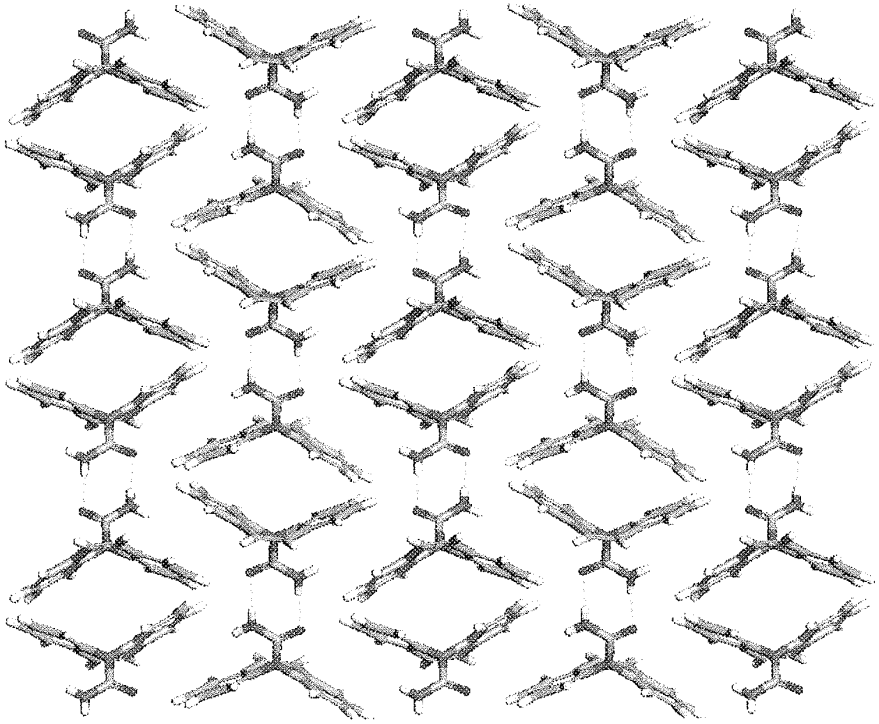


FIG. 22A

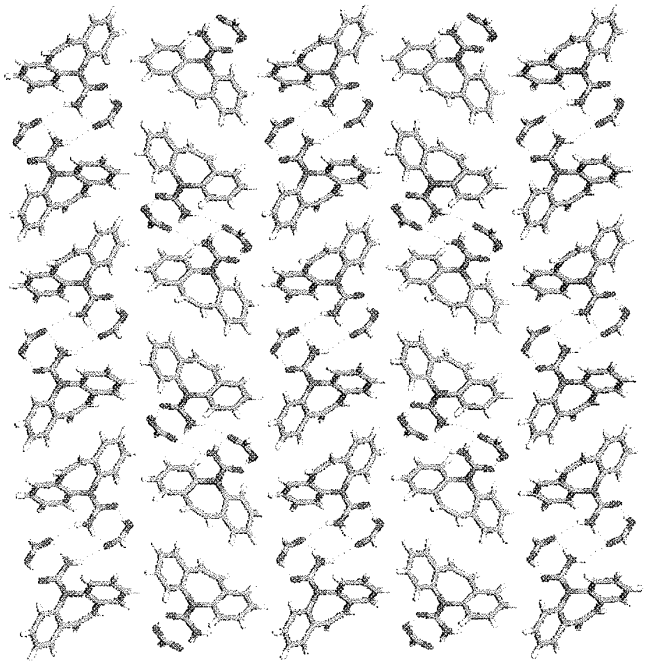


FIG. 22B

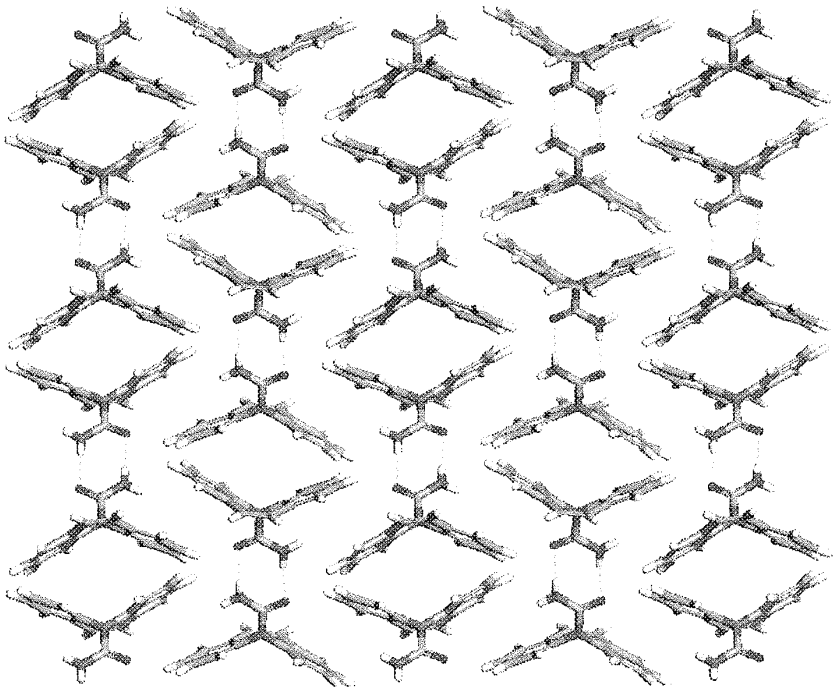


FIG. 23A

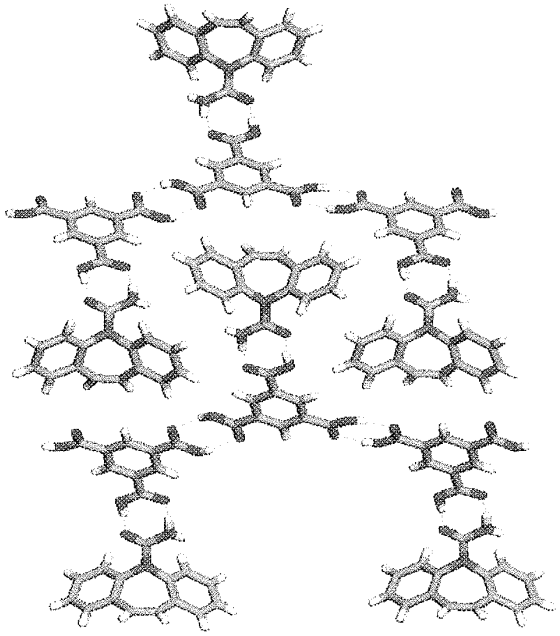


FIG. 23B

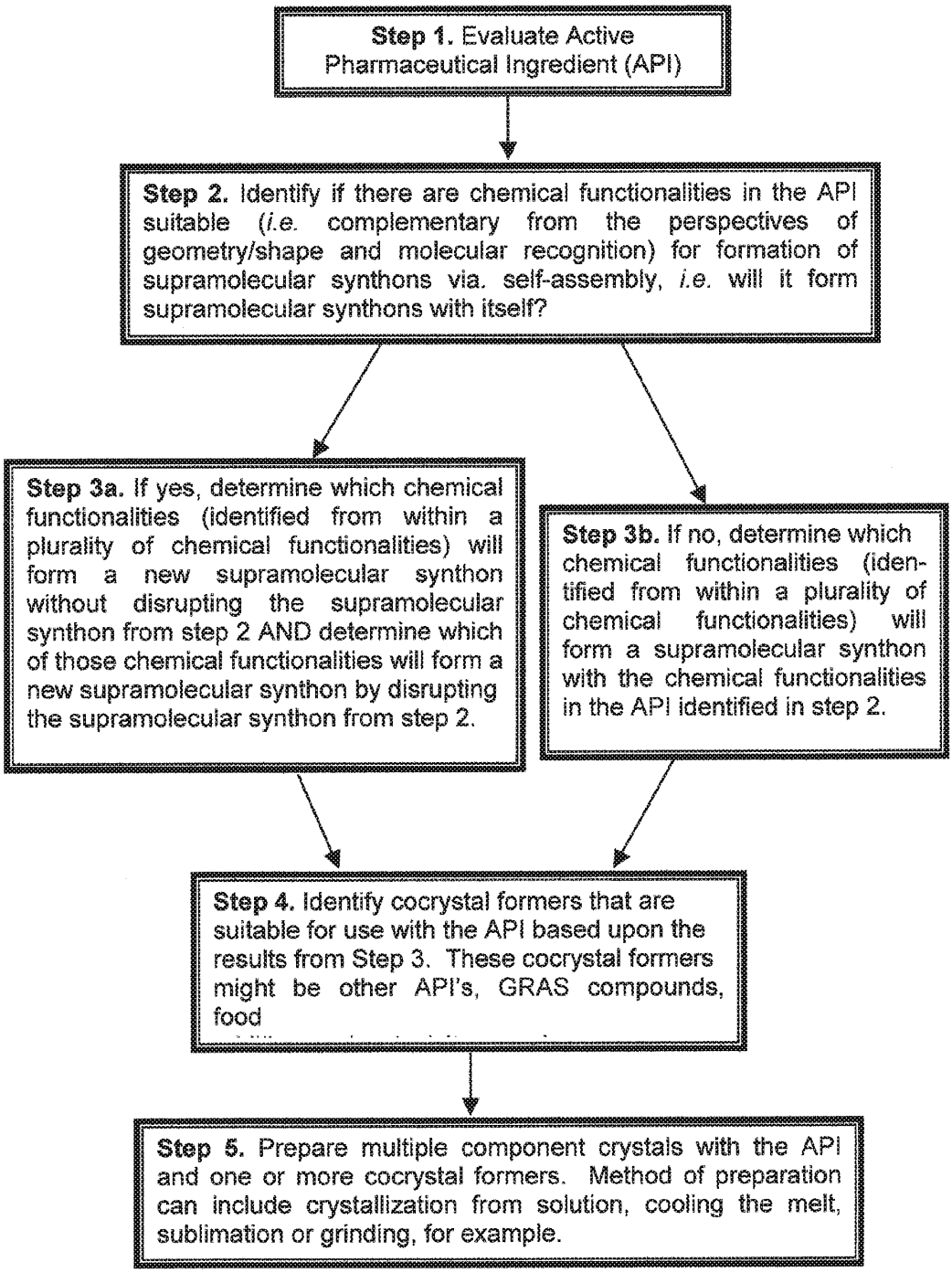

Step 1. Evaluate Active Pharmaceutical Ingredient (API)
Step 2. Identify if there are chemical functionalities in the API suitable (*i.e.* complementary from the perspectives of geometry/shape and molecular recognition) for formation of supramolecular synthons via. self-assembly, *i.e.* will it form supramolecular synthons with itself?
Step 3a. If yes, determine which chemical functionalities (identified from within a plurality of chemical functionalities) will form a new supramolecular synthon without disrupting the supramolecular synthon from step 2 AND determine which of those chemical functionalities will form a new supramolecular synthon by disrupting the supramolecular synthon from step 2.
Step 3b. If no, determine which chemical functionalities (identified from within a plurality of chemical functionalities) will form a supramolecular synthon with the chemical functionalities in the API identified in step 2.
Step 4. Identify cocrystal formers that are suitable for use with the API based upon the results from Step 3. These cocrystal formers might be other API's, GRAS compounds, food
Step 5. Prepare multiple component crystals with the API and one or more cocrystal formers. Method of preparation can include crystallization from solution, cooling the melt, sublimation or grinding, for example.

FIG. 24

Electronic Acknowledgement Receipt

EFS ID:	29667101
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	Edward R. Gates/Nicole Forgrave
Filer Authorized By:	Edward R. Gates
Attorney Docket Number:	U0157.70023US03
Receipt Date:	30-JUN-2017
Filing Date:	
Time Stamp:	14:54:12
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal of New Application	U015770023US03-TRN-ERG.pdf	32113 ce92b40e2f46a38a6f145840e543d52ae47976fe	no	1
Warnings:					

Information:					
2	Application Data Sheet	U015770023US03-ADS-ERG.pdf	30345 2a9857acc3352c0341ad793acdf934685b9cbe06	no	7
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
3	Oath or Declaration filed	U015770023US03-DEC-ERG.pdf	418895 1e7e9c3bec720f1bf8e89d359b11ba9ed2e8527e	no	3
Warnings:					
Information:					
4		U015770023US03-PAMN-ERG.pdf	28906 a9d8e6cc10ccae486a57cbd9a615795e78f9ed26	yes	3

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Preliminary Amendment	1	1
	Specification	2	2
	Applicant Arguments/Remarks Made in an Amendment	3	3

Warnings:					
Information:					
5		U015770023US03-UTLAPL-ERG.pdf	6505872 7a0a8cd5f8c7827c5a816819337b0d82d8b8328f	yes	42

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Specification	1	34
	Claims	35	41
	Abstract	42	42

Warnings:	
Information:	

6	Drawings-only black and white line drawings	U015770023US03-DRW-ERG.pdf	3813052 2e6e1ef04a006c1c742c9098e4f49be7e0cdc75c	no	22
Warnings:					
Information:					
			Total Files Size (in bytes):	10829183	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 15/639,223

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	70		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	300		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	360		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	36 minus 20 =	* 16	x 40 =	640	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	9 minus 3 =	* 6	x 210 =	1260			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	2630		TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)		RATE($)	ADDITIONAL FEE($)
Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
Application Size Fee (37 CFR 1.16(s))									
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
					TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03

CONFIRMATION NO. 8089

23628
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

FORMALITIES LETTER

OC000000092638587

Date Mailed: 07/11/2017

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.
- The application search fee must be submitted.
- The application examination fee must be submitted.
- Additional claim fees of $ **1900** as a small entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.
- Surcharge as set forth in 37 CFR 1.16(f) must be submitted.
  The surcharge is due for any one of:
  - late submission of the basic filing fee, search fee, or examination fee,
  - late submission of inventor's oath or declaration,
  - filing an application that does not contain at least one claim on filing, or
  - submission of an application filed by reference to a previously filed application.

SUMMARY OF FEES DUE:

The fee(s) required within **TWO MONTHS** from the date of this Notice to avoid abandonment is/are itemized below. Small entity discount is in effect. If applicant is qualified for micro entity status, an acceptable Certification of Micro Entity Status must be submitted to establish micro entity status. (See 37 CFR 1.29 and forms PTO/SB/15A and 15B.)

- $ **70** basic filing fee.
- $ **70** surcharge.
- $ **300** search fee.
- $ **360** examination fee.
- $ **1260** for **6** independent claims over 3.
- $ **640** for **16** total claims over 20.

- $(**0**) previous unapplied payment amount.
- $ **2700** TOTAL FEE BALANCE DUE.

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web, including a copy of this Notice and selecting the document description "Applicant response to Pre-Exam Formalities Notice". https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/kgebremichael/

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 84 of 415

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
15/639,223	06/30/2017	2631	0.00	U0157.70023US03	36	9

CONFIRMATION NO. 8089

FILING RECEIPT

23628
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

Date Mailed: 07/11/2017

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Michael J. Zaworotko, Tampa, FL;
Nair Rodriguez-Hornedo, Ann Arbor, MI;
Brian Moulton, Temple Terrace, FL;

Applicant(s)

University of South Florida, Tampa, FL;
The Regents of the University of Michigan, Ann Arbor, MI;

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 10/378,956 03/03/2003 ABN
which claims benefit of 60/360,768 03/01/2002

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 07/10/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/639,223**

Projected Publication Date: To Be Determined - pending completion of Missing Parts

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

Preliminary Class

375

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 87 of 415

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	Not Yet Assigned
Art Unit:	2631

Certificate of Electronic Filing under 37 CFR § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 11, 2017 Signature: /Chelsea E. Dowling/ (Chelsea E. Dowling)

RESPONSE TO NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

In response to the Notice to File Missing Parts of Nonprovisional Application, mailed July 11, 2017, Applicant submits herewith payment of the filing fee, search fee, examination fee, excess claim fee, and the surcharge for late payment of the filing fees. Applicant also submits herewith a Preliminary Amendment to reduce excess claim fees due. Applicant requests that the excess claim fees be calculated after entrance of the Preliminary Amendment being filed herewith.

Please charge our credit card in the amount of $1,010.00 to cover the fees listed above.

The deadline for responding to the Notification is September 11, 2017. Applicant thus submits that the present Response is timely submitted on Monday, September 11, 2017.

Please charge any deficiency in the fees due, or credit any overpayment, to our Deposit Account No. 23/2825, under Docket No. U0157.70023US03, from which the undersigned is authorized to draw.

Dated: September 11, 2017

Respectfully submitted,

By /David F. Cauble/
David F. Cauble
Registration Number: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 89 of 415

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	Not Yet Assigned
Art Unit:	2631

Certificate of Electronic Filing under 37 CFR § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 11, 2017 Signature: /Chelsea E. Dowling/ (Chelsea E. Dowling)

PRELIMINARY AMENDMENT

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

Prior to examination on the merits, please amend the above-referenced U.S. Patent Application as follows:

Amendments to the Claims are reflected in the Listing of Claims, which begins on page 2 of this paper.

Remarks begin on page 7 of this paper.

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, and listings, of claims in the Application:

Listing of Claims

1. (Original) A multiple-component phase composition comprising a solid phase that is sustained by intermolecular interactions between two or more independent molecular entities, wherein at least one of said two or more independent molecular entities is a pharmaceutical molecule.

2. (Currently Amended) The multiple-component phase composition of claim 1, wherein said multiple-component phase composition is a discrete supramolecular entity or a polymeric structure.

3. (Canceled)

4. (Original) The multiple-component phase composition of claim 1, wherein said pharmaceutical molecule is sustained by a supramolecular homosynthon when said pharmaceutical molecule is in its pure phase.

5. (Currently Amended) The multiple-component phase composition of claim 1, wherein said multiple-component phase composition has at least one physical property or chemical property that is different from that of said pharmaceutical when said pharmaceutical molecule is in its pure phase, wherein said at least one physical or chemical property is selected from the group consisting of chemical stability, thermodynamic stability, solubility, dissolution, bioavailability, crystal morphology, and hygroscopicity.

6-8. (Canceled)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 91 of 415

9. (Original) The multiple-component phase composition of claim 1, wherein said pharmaceutical molecule is selected from the group consisting of aspirin, acetaminophen, profen, phenytoin, and carbamazepine.

10. (Original) The multiple-component phase composition of claim 1, wherein said two or more independent molecular entities are selected from the group consisting of: acetaminophen, 4,4'-bipyridine, and water; phenytoin and pyridine; aspirin and 4,4'-bipyridine; ibuprofen and 4,4'- . bipyridine; flurbiprofen and 4,4'-bipyridine; flurbiprofen, trans-1,2-bis (4-pyridyl) ethylene; carbamazepine, p-phthalaldehyde; carbamazepine and nicotinamide; carbamazepine and saccharin; carbamazepine and 2,6-pyridinedicarboxylic acid; carbamazepine and 5- nitroisophthalic acid; carbamazepine and acetic acid; carbamazepine and 1,3,5,7,- adamantanetetracarboxylic acid; carbamazepine and benzoquinone; carbamazepine and butyric acid; carbamazepine and dimethyl stilfoxide; carbamazepine and formamide; carbamazepine and formic acid; and carbamazepine and trimesic acid.

11. (Original) The multiple-component phase composition of claim 1, wherein said intermolecular interactions are selected from the group consisting of hydrogen bonding (weak and/or strong), dipole interactions (induced and/or non-induced), stacking interactions, hydrophobic interactions, and other inter-static interactions.

12. (Original) The multiple-component phase composition of claim 1, wherein said intermolecular interactions are between complementary chemical functionalities on said two or more independent molecular entities.

13. (Currently Amended) The multiple-component phase composition of claim 1[[15]], wherein said complementary chemical functionalities include at least one chemical functionality selected from the group consisting of acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases, amines, alcohols, halogens, sulfones, nitro groups, S-heterocycles, N-heterocycles, O-

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 92 of 415

heterocycles, ethers thioethers, thiols, esters, thioesters, thioketones, epoxides, acetonates, nitrils, oximes, and organohalides.

14. (Original) The multiple-component phase composition of claim 12, wherein said complementary chemical functionalities on said two or more independent molecular entities are the same.

15. (Original) The multiple-component phase composition of claim 14, wherein said complementary chemical functionalities are acids.

16. (Original) The multiple-component phase composition of -.claim 14, wherein said complementary chemical functionalities are amides.

17. (Original) The multiple-component phase composition of claim 12, wherein said complementary chemical functionalities on said two or more independent molecular entities are not the same.

18. (Original) The multiple-component phase composition of claim 17, wherein said complementary chemical functionalities on said two or more independent molecular entities are selected from the group consisting of acids and amides; pyridines and amides; and alcohols and amines.

19-24. (Canceled)

25. (Original) A method for identifying complementary chemical functionalities in order to form a desired supramolecular synthon, said method comprising:

(a) evaluating the structure of an active pharmaceutical ingredient;

(b) determining whether the active pharmaceutical ingredient contains chemical functionalities capable of forming supramolecular synthons with itself;

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 93 of 415

(c) identifying from a plurality of chemical functionalities that are known to form a supramolecular synthon at least one functionality that will form a further supramolecular synthon to the supramolecular synthon formed by the active pharmaceutical ingredient, wherein the identified chemical functionality is not capable of disrupting non-covalent bonding within the supramolecular synthon formed by the supramolecular synthon formed by the active pharmaceutical ingredient, and wherein the selected chemical functionality is capable of forming a noncovalent bond to the supramolecular synthon formed by the active pharmaceutical ingredient; and

(d) identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

26. (Original) The method of claim 25, wherein said method further comprises preparing a multiple-component solid phase composition, wherein the multiple-component solid phase composition comprises the active pharmaceutical ingredient and at least one of the identified co-crystal formers.

27-28. (Canceled)

29. (Original) A method for identifying complementary chemical functionalities in order to form a desired supramolecular synthon, said method comprising:

(a) evaluating the structure of an active pharmaceutical ingredient;

(b) determining whether the active pharmaceutical ingredient contains chemical functionalities capable of forming supramolecular synthons with itself;

(c) identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the active pharmaceutical ingredient, wherein the identified chemical functionality is capable of disrupting non-covalent bonding within the supramolecular synthon formed by the active pharmaceutical ingredient, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the active pharmaceutical ingredient; and

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 94 of 415

(d) identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

30. (Original) The method of claim 29, wherein said method further comprises preparing a multiple-component solid phase composition, wherein the multiple-component solid phase composition comprises the active pharmaceutical ingredient and at least one of the identified co-crystal formers.

31-32. (Canceled)

33. (Original) A method for identifying complementary chemical functionalities in order to form a desired supramolecular synthon, said method comprising:

(a) evaluating the structure of an active pharmaceutical ingredient;

(b) determining whether the active pharmaceutical ingredient contains chemical functionalities capable of forming supramolecular synthons with different molecules;

(c) identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthon with the active pharmaceutical ingredient, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the active pharmaceutical ingredient; and

(d) identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

34. (Original) The method of claim 33, wherein said method further comprises preparing a multiple-component solid phase composition, wherein the multiple-component solid phase composition comprises the active pharmaceutical ingredient and at least one of the identified co-crystal formers.

35-36. (Canceled)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 95 of 415

REMARKS

Applicant requests entrance of this Preliminary Amendment to reduce the number of claims pending in this Application. After entrance of the present Amendment, four (4) independent claims, twenty (20) total claims, and no multiply dependent claims will be pending in this case. Claim(s) 3, 6-8, 19-24, 27-28, 31-32 and 35-36 have been canceled.

Claim 2 has been amended to further recite the element of claim 3. Claim 5 has been amended to further recite the elements of claim 7. Claim 13 has been amended to depend from claim 1.

Applicant reserves the right to pursue subject matter canceled from the claims in future applications claiming priority to the present Application. Applicant submits that no new matter is added to the Application by this Preliminary Amendment.

Applicant believes all fees due are being paid by credit card. However, if any additional fees are due, please charge them, or credit any overpayment, to our Deposit Account No. 23/2825, under Docket No. U0157.70023US03, from which the undersigned is authorized to draw.

Dated: September 11, 2017

Respectfully submitted,

By_____/David F. Cauble/_____
David F. Cauble
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 96 of 415

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Chelsea Dowling
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY FILING FEE (ELECTRONIC FILING)	4011	1	70	70
UTILITY SEARCH FEE	2111	1	300	300
UTILITY EXAMINATION FEE	2311	1	360	360
Pages:				
Claims:				
INDEPENDENT CLAIMS IN EXCESS OF 3	2201	1	210	210
Miscellaneous-Filing:				
LATE FILING FEE FOR OATH OR DECLARATION	2051	1	70	70

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**1010**

Electronic Acknowledgement Receipt	
EFS ID:	30325826
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Chelsea Dowling
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	11-SEP-2017
Filing Date:	30-JUN-2017
Time Stamp:	15:56:12
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$1010
RAM confirmation Number	091217INTEFSW15574100
Deposit Account	232825
Authorized User	Wolf Greenfield
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees)	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	U015770023US03-TRN-DFC.pdf	25132 e8549b89dc09da6d11a8310d3b5f07a87c2821c9	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	31467 57a52de894825f91590dbd086204c116362ec9cd	no	1
Warnings:					
Information:					
3	Applicant Response to Pre-Exam Formalities Notice	U015770023US03-RTMP-DFC.pdf	24196 fb676ac5e6771269580cb47c2191ad04b0aaa08e	no	2
Warnings:					
Information:					
4		U015770023US03-PAMN-DFC.pdf	37336 2a3a216ea4b726950cafb71a723ed8ae3d28967c	yes	7

Multipart Description/PDF files in .zip description

Document Description	Start	End
Preliminary Amendment	1	1
Claims	2	6
Applicant Arguments/Remarks Made in an Amendment	7	7

Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	38711 c642b1153843c4e884e35506410cad9115e11100	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	156842

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM *(to be used for all correspondence after initial filing)*		Application Number	15/639,223-Conf. #8089
		Filing Date	June 30, 2017
		First Named Inventor	Michael J. Zaworotko
		Art Unit	2631
		Examiner Name	Not Yet Assigned
Total Number of Pages in This Submission		Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

[X] Fee Transmittal Form	[ ] Drawing(s)	[ ] After Allowance Communication to TC
[ ] Fee Attached	[ ] Licensing-related Papers	[ ] Appeal Communication to Board of Appeals and Interferences
[X] Amendment/Reply	[ ] Petition	[ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
[ ] After Final	[ ] Petition to Convert to a Provisional Application	[ ] Proprietary Information
[ ] Affidavits/declaration(s)	[ ] Power of Attorney, Revocation Change of Correspondence Address	[ ] Status Letter
[ ] Extension of Time Request	[ ] Terminal Disclaimer	[ ] Other Enclosure(s) (please Identify below):
[ ] Express Abandonment Request	[ ] Request for Refund	
[ ] Information Disclosure Statement	[ ] CD, Number of CD(s) _____	
[ ] Certified Copy of Priority Document(s)	[ ] Landscape Table on CD	
[X] Reply to Missing Parts/ Incomplete Application	Remarks	
[ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble		
Date	September 11, 2017	Reg. No.	73,490

Certificate of Electronic Filing under 37 CFR § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 11, 2017 Signature: /Chelsea E. Dowling/ (Chelsea E. Dowling)

5730928.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	Not Yet Assigned
Art Unit	2631
Practitioner Docket No.	U0157.70023US03

[x] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)1,010.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [x] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[ ] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below [ ] Charge fee(s) indicated below, **except for the filing fee**

[x] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17 [x] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	280	140*	70	600	300	150	720	360	180	730.00
Design	180	90	45	120	60	30	460	230	115	
Plant	180	90	45	380	190	95	580	290	145	
Reissue	280	140	70	600	300	150	2,160	1,080	540	
Provisional	260	130	65	0	0	0	0	0	0	

* The $140 small entity status filing fee for a utility application is further reduced to $70 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	80	40	20
Each independent claim over 3 (including Reissues)	420	210	105
Multiple dependent claims	780	390	195

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- 20 or HP =	_____	x _____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Multiple Dependent Claims

Fee ($)	**Fee Paid ($)**
_____	_____

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
4	- 3 or HP =	1	x 210.00	=	210.00

HP = highest number of independent claims paid for, if greater than 3.

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $400 ($200 for small entity) ($100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**		**Fee ($)**		**Fee Paid ($)**
_____	- 100 =	_____	/50 =	_____	(round **up** to a whole number) x	_____	=	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2051 Surcharge - Late filing fee	70.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble			Date	September 11, 2017

Certificate of Electronic Filing under 37 CFR § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 CFR § 1.6(a)(4).

Dated: September 11, 2017 Signature: /Chelsea E. Dowling/ (Chelsea E. Dowling)

5730927.1

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 15/639,223

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	70		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	300		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	360		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	20 minus 20 =	*	x 40 =	0.00	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	4 minus 3 =	* 1	x 210 =	210			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	940		TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)	OR	RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
15/639,223	06/30/2017	2631	1010	U0157.70023US03	20	4

CONFIRMATION NO. 8089

UPDATED FILING RECEIPT

23628
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206



Date Mailed: 09/14/2017

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

Michael J. Zaworotko, Tampa, FL;
Nair Rodriguez-Hornedo, Ann Arbor, MI;
Brian Moulton, Temple Terrace, FL;

Applicant(s)

University of South Florida, Tampa, FL;
The Regents of the University of Michigan, Ann Arbor, MI;

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 10/378,956 03/03/2003 ABN
which claims benefit of 60/360,768 03/01/2002

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 07/10/2017

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 15/639,223**

Projected Publication Date: 12/21/2017

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

Preliminary Class

375

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign AssetsControl, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit http://www.SelectUSA.gov or call +1-202-482-6800.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 107 of 415

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03

CONFIRMATION NO. 8089

23628
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

PUBLICATION NOTICE

OC000000096240740

Title:MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

Publication No.US-2017-0362182-A1
Publication Date:12/21/2017

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Public Records Division. The Public Records Division can be reached by telephone at (571) 272-3150 or (800) 972-6382, by facsimile at (571) 273-3250, by mail addressed to the United States Patent and Trademark Office, Public Records Division, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently https://portal.uspto.gov/pair/PublicPair. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 108 of 415

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 05/08/2018

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MASSACHUSETTS 02210-2206
UNITED STATES OF AMERICA

EXAMINER
JARRELL, NOBLE E

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
05/08/2018	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 109 of 415

Office Action Summary	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.	
	Examiner NOBLE E JARRELL	**Art Unit** 1625	**AIA Status** No

-- 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 2 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 11 September 2017.

☐ 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) 1-2,4-5,9-18,25-26,29-30 and 33-34 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☐ Claim(s) _____ is/are rejected.

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

9) ☑ Claim(s) 1-2,4-5,9-18,25-26,29-30 and 33-34 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 _____.

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

4) ☐ Other: _____.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 110 of 415

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 2, 4, 5, and 9-18, drawn to a multiple component phase composition comprising a solid phase that is sustained by intermolecular interactions between two or more molecular entities wherein as least one of the molecular entities is a pharmaceutical molecule, classified in C07D213/02.

II. Claims 25 and 26, drawn to a method of identifying complementary chemical functionalities on order to form a supramolecular synthon in which one step is identifying a chemical functionality that is not capable of disrupting non-covalent bonding within the supramolecular synthon, classified in C07D213/02.

III. Claims 29 and 30, drawn to a method of identifying complementary chemical functionalities on order to form a supramolecular synthon in which one step is identifying a chemical functionality that is capable of disrupting non-covalent bonding within the supramolecular synthon, classified in C07D213/02.

IV. Claims 33 and 34, drawn to a method of identifying complementary chemical functionalities in order to form a supramolecular synthon, classified in C07D213/02.

The inventions are independent or distinct, each from the other because:

Inventions I-IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are multiply divergent. Whereas invention I is drawn to a multiple component composition, inventions II-IV are drawn to different methods. Inventions II and III are different due to the following difference: in group II, the

chemical functionality **is not capable of disrupting non-covalent bonding** within the supramolecular synthon; and in group III, the chemical functionality **is capable of disrupting non-covalent bonding** within the supramolecular synthon. Invention IV is drawn to method of identifying complementary functionalities (which is not co-extensive with an invention of group II or III).

Restriction for examination purposes as indicated is proper because all the inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and/or examination burden if restriction were not required because one or more of the following reasons apply:

--the inventions require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search strategies or search queries).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of an invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner

finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 or pre-AIA 35 U.S.C. 103(a) of the other invention.

This application contains claims directed to the following patentably distinct species at least two species of which one is a pharmaceutical molecule. The species are independent or distinct because claim 10 describes groups of compounds which are different in structure and function. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 2, 4, 5, 9-18, 24, 25, 29, 30, 33, and 34 are generic. In the election, a group of compounds meeting the metes and bounds of claim 1, 24, 29, or 33 must be elected.

There is a search and/or examination burden for the patentably distinct species as set forth above because at least the following reason(s) apply:

--the inventions require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search strategies or search queries).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species or grouping of patentably indistinct species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely

traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species or grouping of patentably indistinct species.

Should applicant traverse on the ground that the species, or groupings of patentably indistinct species from which election is required, are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing them to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 or pre-AIA 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be corrected in compliance with 37 CFR 1.48(a) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. A request to correct inventorship under 37 CFR 1.48(a) must be accompanied by an application data sheet in accordance with 37 CFR 1.76 that identifies each inventor by his or her legal name and by the processing fee required under 37 CFR 1.17(i).

The examiner has required restriction between product or apparatus claims and process claims. Where applicant elects claims directed to the product/apparatus, and all product/apparatus claims are subsequently found allowable, withdrawn process claims that include all the limitations of the allowable product/apparatus claims should be considered for rejoinder. All claims directed to a nonelected process invention must include all the limitations of an allowable product/apparatus claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product/apparatus claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product/apparatus are found allowable, an otherwise proper restriction requirement between product/apparatus claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product/apparatus claim will not be rejoined. See MPEP § 821.04. Additionally, in order for rejoinder to occur, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product/apparatus claims. **Failure to do so may result in no rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE E JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on 8:00 AM to 5:00 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Kosar can be reached on 571-372-0913. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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.

/NOBLE E JARRELL/
Primary Examiner, Art Unit 1625

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1625

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 8, 2018 Signature: /Taryn Bollers/ (Taryn Bollers)

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

In response to the Restriction/Election of Species Requirement, dated May 8, 2018, Applicant respectfully requests entrance of the following Amendment and consideration of the following Remarks. The deadline for responding to the Office Action was July 8, 2018. A four-month extension of time from July 8, 2018, up to and including November 8, 2018, is hereby respectfully requested, and the extension fee is being paid using the credit card payment option of the USPTO's Electronic Filing System. Applicant thus submits that the present Response is timely submitted on Thursday, November 8, 2018.

Please amend the above-identified U.S. patent application as follows:

Amendments to the Claims are reflected in the Listing of Claims, which begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, and listings, of claims in the Application:

Listing of Claims

1 – 36. (Canceled)

37. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-crystal former,

wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form,

wherein the co-crystal former has a second chemical functionality complimentary to the first chemical functionality via non-covalent hydrogen bonding,

wherein supramolecular synthons comprise non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-crystal former.

38. (New) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, a GRAS compound, a food additive, a low toxicity organic, and a metal-organic complex.

39. (New) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 118 of 415

40. (New) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and one co-crystal former.

41. (New) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of one active pharmaceutical ingredient (API) and one co-crystal former.

42. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a group selected from acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases, amines, alcohols, halogens, sulfones, and nitro groups.

43. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an acid.

44. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amine.

45. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amide.

46. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an alcohol.

47. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 119 of 415

48. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a heterosynthon.

49. (New) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon and a heterosynthon.

50. (New) The pharmaceutical composition of claim 48, wherein the heterosynthon comprises an alcohol/amine interaction.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 120 of 415

REMARKS

Claims 1-2, 4-5, 9-18, 25-26, 29-30, and 33-34 were pending and under consideration by the Examiner. By this amendment, claims 1-36 are canceled and new claims 37-50 are entered. Support for new claims 37-50 can be found throughout the Application as originally filed. No new matter is added to the Application by the present Amendment.

The Restriction/Election Requirement set forth in the Office Action of May 8, 2018 is moot in view of the foregoing amendments. Applicant submits that new claims 37-50 are drawn to a single invention.

Applicant believes all fees due with this Response are being paid by credit card. However, if any additional fees are due, please charge them, or credit any overpayment, to our Deposit Account No. 23/2825, under Docket No. U0157.70023US03, from which the undersigned is authorized to draw.

Dated: November 8, 2018

Respectfully submitted,

By /David F. Cauble/
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 121 of 415

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1625
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)1,100.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	300	150*	75	660	330	165	760	380	190	
Design	200	100	50	160	80	40	600	300	150	
Plant	200	100	50	420	210	105	620	310	155	
Reissue	300	150	75	660	330	165	2,200	1,100	550	
Provisional	280	140	70	0	0	0	0	0	0	

* The $150 small entity status filing fee for a utility application is further reduced to $75 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	460	230	115
Multiple dependent claims	820	410	205

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- or HP =	_____	x _____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- or HP =	_____	x _____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	
Fee ($)	**Fee Paid ($)**

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $400 ($200 for small entity) ($100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**	**Fee ($)**		**Fee Paid ($)**
_____	- 100 =	_____	/50 =	_____ (round **up** to a whole number)	x _____	=	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2254 Extension for response within fourth month	1,100.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	November 8, 2018

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 8, 2018 Signature: /Taryn Bollers/ (Taryn Bollers)

6751023.1

PTO/AIA/22 (03-13)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) U0157.70023US03
Application Number 15/639,223-Conf. #8089	Filed June 30, 2017
For MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT	
Art Unit 1625	Examiner N. E. Jarrell

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
☐ One month (37 CFR 1.17(a)(1))	$200	$100	$50	$
☐ Two months (37 CFR 1.17(a)(2))	$600	$300	$150	$
☐ Three months (37 CFR 1.17(a)(3))	$1,400	$700	$350	$
☒ Four months (37 CFR 1.17(a)(4))	$2,200	$1,100	$550	$ 1,100.00
☐ Five months (37 CFR 1.17(a)(5))	$3,000	$1,500	$750	$

☒ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

☐ A check in the amount of the fee is enclosed.

☒ Payment by credit card. ~~Form PTO-2038 is attached.~~

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 23/2825 .

☐ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant.

☒ attorney or agent of record. Registration number 73,490 .

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____.

/David F. Cauble/	November 8, 2018
Signature	Date
David F. Cauble, PhD, JD	617.646.8000
Typed or printed name	Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ * Total of 1 forms are submitted.

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 8, 2018 Signature: /Taryn Bollers/ (Taryn Bollers)

6751027.1

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Taryn Bollers
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 4 months with $0 paid	2254	1	1100	1100
Miscellaneous:				
		Total in USD ($)		**1100**

Electronic Acknowledgement Receipt	
EFS ID:	34252236
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Taryn Bollers
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	08-NOV-2018
Filing Date:	30-JUN-2017
Time Stamp:	15:00:22
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$1100
RAM confirmation Number	110918INTEFSW15020000
Deposit Account	232825
Authorized User	Wolf Greenfield
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.21 (Miscellaneous fees and charges)	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	U015770023US03-TRN-DFC.pdf	26448 bcc607dec3224176570e7f620729df195ee964e9	no	1
Warnings:					
Information:					
2		U015770023US03-ERRRAMN-DFC.pdf	32537 21be657227afde2b7e0728887943a6df9b2447c3	yes	5

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Response to Election / Restriction Filed	1	1
	Claims	2	4
	Applicant Arguments/Remarks Made in an Amendment	5	5

Warnings:					
Information:					
3	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	32550 8ccfa08e7bc7d0c93da7d52e80b922284fbf523a	no	1
Warnings:					
Information:					
4	Extension of Time	U015770023US03-EXT-DFC.pdf	24620 00b5079b5a4a5fcf7f4cbc5bacfcc7c5010edc66	no	1
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	30939 157ce3bbd43f3e11529bbcad960183e7073ebf61	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	147094

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM *(to be used for all correspondence after initial filing)*		Application Number	15/639,223-Conf. #8089
		Filing Date	June 30, 2017
		First Named Inventor	Michael J. Zaworotko
		Art Unit	1625
		Examiner Name	N. E. Jarrell
Total Number of Pages in This Submission		Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

[X] Fee Transmittal Form	[ ] Drawing(s)	[ ] After Allowance Communication to TC
[ ] Fee Attached	[ ] Licensing-related Papers	[ ] Appeal Communication to Board of Appeals and Interferences
[ ] Amendment/Reply	[ ] Petition	[ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
[ ] After Final	[ ] Petition to Convert to a Provisional Application	[ ] Proprietary Information
[ ] Affidavits/declaration(s)	[ ] Power of Attorney, Revocation Change of Correspondence Address	[ ] Status Letter
[X] Extension of Time Request	[ ] Terminal Disclaimer	[X] Other Enclosure(s) (please Identify below):
[ ] Express Abandonment Request	[ ] Request for Refund	Amendment and Response to Restriction/Election Requirement
[ ] Information Disclosure Statement	[ ] CD, Number of CD(s) _____	
[ ] Certified Copy of Priority Document(s)	[ ] Landscape Table on CD	
[ ] Reply to Missing Parts/ Incomplete Application	Remarks	
[ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	November 8, 2018	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 8, 2018 Signature: /Taryn Bollers/ (Taryn Bollers)

6751025.1

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	1	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
		2,554,816		Clapp et al.	05-29-1951
		2,665,277		Homeyer et al.	01-05-1954
		2,711,411		Holbert et al.	06-21-1955
		2,980,679		Gianfranco	04-18-1961
		3,028,420		Petrow et al.	04-03-1962
		3,536,809		Schaller et al.	04-09-1991
		3,598,123		Zaffaroni	08-10-1971
		3,664,858		Huffman	05-23-1972
		3,845,770		Theeuwes et al.	11-05-1974
		3,916,899		Theeuwes et al.	11-04-1975
		3,970,651		Kaplan et al.	07-20-1976
		4,008,321		Kamishita et al.	02-15-1977
		4,008,719		Theeuwes et al.	02-22-1977
		4,198,507		Barry et al.	04-15-1980
		4,267,179		Heeres et al.	05-12-1981
		4,368,197		Shefter et al.	01-11-1983
		4,513,006		Maryanoff et al.	04-23-1995
		4,764,604		Muller	08-16-1988
		4,792,569		Maryanoff et al.	12-20-1988
		4,853,379		Shroot et al.	08-01-1989
		4,916,134		Heeres et al.	04-10-1990
		4,925,674		Giannini et al.	05-15-1990
		4,927,855		Lafon	05-22-1990
		4,994,604		Tung et al.	02-19-1991
		5,006,513		Hector et al.	04-09-1991
		5,023,092		DuRoss	07-11-1991
		5,059,595		Le Grazie	10-22-1991

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	2	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		5,073,543		Marshall et al.	12-17-1991
		5,120,548		McClelland et al.	06-09-1992
		5,177,262		Taylor et al.	01-15-1993
		5,242,942		Costanzo et al.	09-07-1993
		5,258,402		Maryanoff	11-02-1993
		5,273,760		Oshlack et al.	12-28-1993
		5,286,493		Oshlack et al.	02-15-1994
		5,324,351		Oshlack et al.	06-28-1994
		5,332,834		Bhattacharya et al.	07-26-1994
		5,338,644		Taylor et al.	08-16-1994
		5,354,556		Sparks et al.	10-11-1994
		5,356,467		Oshlack et al.	10-18-1994
		5,366,738		Rork et al.	11-22-1994
		5,380,867		Bhattacharya et al.	01-10-1995
		5,384,327		Costanzo et al.	01-24-1995
		5,387,700		Maryanoff et al.	02-07-1995
		5,412,094		Amos et al.	05-02-1995
		5,414,997		Tailer	05-16-1995
		5,466,823		Talley et al.	11-14-1995
		5,472,712		Oshlack et al.	12-05-1995
		5,474,997		Gray et al.	12-12-1995
		5,510,496		Talley et al.	04-23-1996
		5,521,207		Graneto	05-28-1996
		5,523,090		Znaiden et al.	06-04-1996
		5,563,165		Talley et al.	10-08-1996
		5,591,767		Mohr et al.	01-07-1997
		5,614,342		Molaire et al.	03-25-1997
		5,631,250		Bunnell et al.	05-20-1997
		5,633,015		Gilis et al.	05-27-1997
		5,633,272		Talley et al.	05-27-1997
		5,635,535		Wagstaff	06-03-1997

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	3	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		5,639,476		Oshlack et al.	06-17-1997
		5,641,512		Cimiluca	06-24-1997
		5,661,151		Saksena et al.	08-26-1997
		5,674,533		Santus et al.	10-07-1997
		5,703,232		Bunnell et al.	12-30-1997
		5,707,975		Francois et al.	01-13-1998
		5,733,566		Lewis	03-31-1998
		5,736,541		Bunnell et al.	04-07-1998
		5,753,688		Talley et al.	05-19-1998
		5,753,693		Shank	05-19-1998
		5,760,007		Shank et al.	06-02-1999
		5,760,068		Talley et al.	06-02-1998
		5,932,598		Talley et al.	08-03-1999
		5,935,933		Shank et al.	08-10-1999
		5,952,187		Stenglein et al.	09-14-1999
		5,972,986		Seibert et al.	10-26-1999
		5,985,902		Talley et al.	11-16-1999
		5,994,365		Zaworotko et al.	11-30-1999
		5,998,380		Ehrenberg et al.	12-07-1999
		5,998,413		Heeres et al.	12-07-1999
		6,001,996		Amos et al.	12-14-1999
		6,054,136		Farah et al.	04-25-2000
		6,071,537		Shank	06-06-2000
		6,132,420		Dionne et al.	10-17-2000
		6,156,781		Talley et al.	12-05-2000
		6,191,117	B1	Kozachuk	02-20-2001
		6,201,010	B1	Cottrell	03-13-2001
		6,245,357	B1	Edgren et al.	06-12-2001
		6,268,385	B1	Whittle et al.	07-31-2001
		6,270,787	B1	Ayer	08-07-2001
		6,283,953	B1	Ayer et al.	09-04-2001

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	4	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		6,287,295	B1	Chen et al.	09-11-2001
		6,294,186	B1	Beerse et al.	09-25-2001
		6,294,192	B1	Patel et al.	09-25-2001
		6,319,903	B1	Carrazana et al.	11-20-2001
		6,323,266	B2	Phillips	11-27-2001
		6,333,050	B2	Wong et al.	12-25-2001
		6,342,249	B1	Wong et al.	01-29-2002
		6,348,458	B1	Hamied et al.	02-19-2002
		6,365,185	B1	Ritschel et al.	04-02-2002
		6,368,626	B1	Bhatt et al.	04-09-2002
		6,375,978	B1	Kleiner et al.	04-23-2002
		6,384,034	B2	Simitchieva et al.	05-07-2002
		6,403,640	B1	Stoner et al.	06-11-2002
		6,413,965	B1	Mylari	07-02-2002
		6,420,394	B1	Supersaxo	07-16-2002
		6,488,962	B1	Berner et al.	12-03-2002
		6,503,884	B1	Ehrenberg et al.	01-07-2003
		6,559,293	B1	Almarsson et al.	05-06-2003
		6,570,036	B1	Reuter	05-27-2003
		6,579,895	B2	Karim et al.	06-17-2003
		6,613,790	B2	Jeffrey Carter	09-02-2003
		6,699,840	B2	Almarsson, et al.	03-02-2004
		7,078,526	B2	Remenar et al.	07-18-2006
		7,132,579	B2	Neckebrock et al.	11-07-2006
		7,205,413	B2	Morissette et al.	04-17-2007
		7,351,695	B2	Almarssoo et al.	04-01-2008
		7,446,107	B2	Remenar et al.	11-04-2008
		7,452,555	B2	Childs	11-18-2008
		7,459,449	B2	Keltjens	12-02-2008
		7,687,091	B2	Moen et al.	03-30-2010
		7,927,613	B2	Almarsson et al.	04-19-2011

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	5	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		2002-0006951	A1	Hageman et al.	01-17-2002
		2002-0013357	A1	Nadkarni et al.	01-31-2002
		2002-0015735	A1	Hedden et al.	02-07-2002
		2002-0034542	A1	Thombre et al.	03-21-2002
		2002-0037925	A1	Dewey et al.	03-28-2002
		2002-0042446	A1	Dewey et al.	04-11-2002
		2002-0071857	A1	Kararli et al.	06-13-2002
		2002-0107250	A1	Hariharan et al.	08-08-2002
		2002-0119193	A1	Le Trang et al.	08-29-2002
		2003-0069190	A1	Abdel-Magid et al.	04-10-2003
		2003-0096014	A1	Sherman	05-22-2003
		2003-0162226	A1	Cima et al.	08-28-2003
		2003-0166581	A1	Almarsson et al.	09-04-2003
		2003-0224006	A1	Zaworotko et al.	12-04-2003
		2004-0019211	A1	Remenar et al.	01-29-2004
		2004-0053853	A1	Almarsson et al.	03-18-2004
		2004-0106052	A1	Molaire	06-03-2004
		2004-0106053	A1	Molaire et al.	06-03-2004
		2004-0106055	A1	Molaire et al.	06-03-2004
		2004-0171062	A1	Hirth et al.	09-02-2004
		2004-0176335	A1	Childs	09-09-2004
		2005-0070551	A1	Remenar et al.	03-31-2005
		2005-0169982	A1	Almarsson et al.	08-04-2005
		2005-0181041	A1	Goldman	08-18-2005
		2005-0252649	A1	Chiu et al.	11-17-2005
		2005-0256127	A1	Ku et al.	11-17-2005
		2006-0134198	A1	Tawa et al.	06-22-2006
		2006-0223794	A1	Bourghol et al.	10-05-2006
		2007-0015841	A1	Tawa et al.	01-18-2007
		2007-0021510	A1	Hickey et al.	01-25-2007
		2007-0026078	A1	Almarsson et al.	02-01-2007

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08)	APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
	FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet 6 of 30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		2007-0059356	A1	Almarsson et al.	03-15-2007
		2007-0293674	A1	Scoppettuolo et al.	12-20-2007
		2009-0088443	A1	Remenar et al.	04-02-2009
		2010-0331285	A1	Almarsson et al.	12-30-2010
		2014-0162989	A1	Zaworotko et al.	06-12-2014

FOREIGN PATENT DOCUMENTS

Examiner's Initials #	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
	*	CA	1 101 840		Sumitomo Chemical Company, Limited	05-26-1981	
		CA	1 148 020	A1	McCoy	06-14-1983	
	*	EP	0 283 992	B1	Janssen Pharma	09-16-1992	
	*	EP	0 310 122	A1	Kaken Pharma	04-05-1989	
	*	EP	0 413 528	B1	Yu, R. et al.	11-15-1995	
	*	EP	0 731 795	B1	G.D. Searle & Co.	12-22-1999	
	*	EP	1 167 355	A1	Fako Ilaclari A.S.	01-02-2002	
	*	EP	1 364 649	A1	Cilag AG	11-26-2003	
	*	FR	769,586		Chemische Fabrik von Heyden	06-11-1934	Y
	*	FR	2 849 029	A1	Laboratoire L. Lafon et al.	06-25-2004	
	*	GB	1 297 261	A	E.R. Squibb & Sons, Inc.	11-22-1972	
	*	GB	2 169 601	A	Tate & Lyle Public Limited Company	07-16-1986	
	*	IN	182620	A1	Bajaj et al.	05-15-1999	
	*	IT	1303251	B1	Industriale Chimica, S.R.L.	11-06-2000	Y
	*	JP	46-33588		Sanzu Inc.	10-01-1971	
	*	JP	54-016494		Yamanouchi Pharmaceutical Co., Ltd.	02-07-1979	Y
	*	JP	54-095589		Sumitomo Chemical Co.	07-28-1979	
	*	JP	B 46-33588		Sanzu Inc.	10-01-1971	
	*	WO	94/16733	A1	Chiesi Farmaceutici S.P.A.	08-04-1994	
	*	WO	95/17407	A1	Schering Corp	06-29-1995	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	7	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	WO	95/23596	A1	The Boots Company PLC	09-08-1995	
	*	WO	96/07331	A1	Xyrofin Oy	03-14-1996	
	*	WO	96/33193	A1	Janssen Pharmaceutica N.V.	10-24-1996	
	*	WO	98/57967	A1	Dong-A Pharmaceutical Co., Ltd.	12-23-1998	
	*	WO	00/07583	A3	Brookhaven Science Associates	02-17-2000	
	*	WO	00/32189	A1	G.D. Searle & Co.	06-08-2000	
	*	WO	00/42021	A1	Merck Frosst Canada & Co.	07-20-2000	
	*	WO	00/50020	A2	University of Cincinnati	08-21-2000	
	*	WO	00/53283	A1	Reuter Chemische Apparatebau KG	09-14-2000	
	*	WO	00/72841	A1	Berlant, Jeffrey	12-07-2000	
	*	WO	01/13904	A2	Ortho-McNeil Pharmaceutical, Inc.	03-01-2001	
	*	WO	01/41536	A2	Pharmacia Corporation	06-14-2001	
	*	WO	01/41760	A3	Pharmacia Corporation	06-14-2001	
	*	WO	01/42221	A1	Pharmacia Corporation	06-14-2001	
	*	WO	01/42222	A2	Pharmacia Corporation	06-14-2001	
	*	WO	01/45706	A1	Pharmacia Corporation	06-28-2001	
	*	WO	01/51919	A2	Transform Pharmaceuticals, Inc.	07-19-2001	
	*	WO	01/78724	A1	Pharmacia Corporation	10-25-2001	
	*	WO	01/91750	A1	Pharmacia Corporation	12-06-2001	
	*	WO	01/97853	A1	Biochemie Gesellschaft MBH	12-27-2001	
	*	WO	02/000627	A1	Fako Ilaclari A.S.	01-03-2002	
	*	WO	02/010125	A1	Teva Pharmaceutical Industries Ltd.	02-07-2002	
	*	WO	02/056878	A2	Pharmacia Corporation	07-25-2002	
	*	WO	02/056915	A2	Cephalon, Inc.	07-25-2002	
	*	WO	02/062318	A2	DSM N.V.	08-15-2002	
	*	WO	02/102376	A1	Pharmacia Corporation	12-27-2002	
	*	WO	03/033462	A2	The Regents of the University of Michigan	04-24-2003	
	*	WO	03/070738	A2	Transform Pharmaceuticals, Inc.	08-28-2003	
	*	WO	03/074474	A2	Univ. South Fla. et al.	09-12-2003	
	*	WO	03/101392	A2	Transform Pharmaceuticals, Inc.	12-11-2003	
	*	WO	2004/054571	A1	Cilag AG	07-01-2004	
	*	WO	2004/060347	A2	Transform Pharmaceuticals, Inc.	07-22-2004	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08)	APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
	FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet 8 of 30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	WO	2004/078161	A1	Transform Pharmaceuticals, Inc.	09-16-2004	
	*	WO	2004/078163	A2	Transform Pharmaceuticals, Inc.	09-16-2004	
	*	WO	2004/089313	A2	Transform Pharmaceuticals, Inc.	10-21-2004	
	*	WO	2005/023198	A2	Transform Pharmaceuticals, Inc.	03-17-2005	
	*	WO	2005/037424	A1	Salvias AG	04-28-2005	
	*	WO	2005/053612	A2	Shire Laboratories, Inc.	06-16-2005	
	*	WO	2005/055983	A2	Medcrystalforms, LCC	06-23-2005	
	*	WO	2005/060968	A1	Sepracor, Inc.	07-07-2005	
	*	WO	2005/077894	A1	Transform Pharmaceuticals, Inc.	08-25-2005	
	*	WO	2005/089375	A2	S.S.C.I., Inc.	09-29-2005	
	*	WO	2005/094804	A1	The Regents of the University of Michigan	10-13-2005	
	*	WO	2005/118577	A1	Transform Pharmaceuticals, Inc.	12-15-2005	
	*	WO	2006/024930	A1	Pharmacia and Upjohn Co., LCC	03-09-2006	

OTHER ART -- NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
		European Search Report for Application No. EP 03711407.1 mailed November 22, 2006 (U0157.70023EP00).	
		International Search Report for Application No. PCT/US2003/06662 mailed October 24, 2003 (U0157.70023WO00).	
	*	Office Action dated April 13, 2011 in U.S. Application No. 12/861,203.	
	*	Notice of Reasons for Rejection dated October 8, 2009 for Japanese Application No. 2003-572946. 11 pages.	Y
	*	Definition of solvate, The Free Dictionary, http://www.thefreedictionary.com/solvate, accessed online on 21 July 2009, pp. 1-3.	
		The Merck Index, 12th Ed. Merck & Co., Inc. Whitehouse Station, NJ. 1996. Entries 5683, 9094.	
	*	Physician's Desk Reference, 56th Ed., pp. 1800-1804, 2002.	
	*	Physician's Desk Reference, 56th Ed., pp. 2590-2595, 2002.	
	*	Press Release. "Clinical Development of Topiramate for Obesity Extended to Simplify Dosing, Improve Tolerability". http://www.orthomcneil.com/news/article020402.html (February 4, 2002), New Jersey, 2 pages.	
	*	The United States Pharmacopoeia, 23rd Edition, U.S. Pharmacopoeia Convention, Inc. Rockville, MD, 1995, pp. 1843.	
	*	[NO AUTHOR LISTED], Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances Q6A. ICH Harmonised Tripartite Guideline. 1999 Oct 6; 4:46.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	9	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	[NO AUTHOR LISTED], X-ray Diffraction. In: The United States Pharmacopeia – The National Formulary (USP #24 NF19). 2000 Jan. Chapter 941: 2005-7	
	*	AAKERÖY, C. et al. "A high-yielding supramolecular reaction" *J. Am. Chem. Soc.*, 2002, 14425-14432, Vol. 124.	
	*	AAKERÖY, C. et al. "A structural study of 2-amino-5-nitropyridine and 2-amino-3-nitropyridine: intermolecular forces and polymorphism" *J. Mater. Chem.*, 1998, pp. 1385- 1389, Vol. 8, No. 6.	
	*	AAKERÖY, C. et al. "A versatile route to porous solids: organic-inorganic hybrid materials assembled through hydrogen bonds" *Angew. Chem. Int. Ed.*, 1999, pp. 1815-1819, Vol. 38, No. 12.	
	*	AAKERÖY, C. et al. "Aromatic dicarboxylic acids as building blocks of extended hydrogen-bonded architectures" *Supramolecular Chemistry*, 1998, pp. 127-135, Vol. 9.	
	*	AAKERÖY, C. et al. "Assembly of 2-D inorganic/organic lamellar structures through a combination of copper (I) coordination polymers and self-complimentary hydrogen bonds" *J. Chem. Soc., Dalton Trans.*, 2000, pp. 3869-3872.	
	*	AAKERÖY, C. et al. "Building organic assemblies with 2-pyridone and dicarboxylic acids: relating molecular conformation and synthon stability to crystal structure" *Crystal Engineering*, 1998, pp. 225-241, Vol. 1, No. 3-4.	
	*	AAKERÖY, C. et al. "Charge-assisted hydrogen bonds and halogen-halogen interactions in organic salts: benzylammonium benzoates and pentaflourobenzoates" *Structural Chemistry*, 1999, pp. 229-242, Vol. 10, No. 3.	
	*	AAKERÖY, C. et al. "Crystal engineering of hydrogen-bonded assemblies- a progress report" *Aust. J. Chem.*, 2001, pp. 409-421, Vol. 54.	
	*	AAKERÖY, C. et al. "Crystal engineering of ionic solids" Modular Chemistry (ed. by Michl, J.), 1997, pp. 153-162, Kluwer Academic Publishers, The Netherlands.	
	*	AAKERÖY, C. et al. "Crystal engineering using intermolecular hydrogen-bonded connectors and classic coordination chemistry" *Transactions ACA*, 1998, pp. 97-103, Vol. 33.	
	*	AAKERÖY, C. et al. "Crystal engineering: strategies and architectures" *Acta Cryst.*, 1997, pp. 569-586, Vol. B53.	
	*	AAKERÖY, C. et al. "Deliberate combination of coordination polymers and hydrogen bonds in a supramolecular design strategy for inorganic/organic hybrid networks" *Chem. Commun.*, 2000, pp. 935-936.	
	*	AAKERÖY, C. et al. "Di-hydroxy malonic acid as a building block of hydrogen-bonded 3-dimensional architectures" *Journal of Chemical Crystallography*, 1998, pp. 111-117, Vol. 28, No. 2.	
	*	AAKERÖY, C. et al. "Do polymorphic compounds make good cocrystallizing agents? A structural case study that demonstrates the importance of synthon flexibility" *Crystal Growth & Design*, 2003, 159-165, Vol. 3, No. 2.	
	*	AAKERÖY, C. et al. "Hydrogen-bonded layers of hydrogentartrate anions: two-dimensional building blocks for crystal engineering" *J. Mater. Chem.*, 1993, 1129-1135, Vol. 3, No. 11.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	10	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	AAKERÖY, C. et al. "Hydrogen-bonding in solids" Crystal Engineering (ed. by Seddon, K. R. et al.), 1999, pp. 303-324, Kluwer Academic Publishers, The Netherlands.	
	*	AAKERÖY, C. et al. "Low-dimensional architectures of silver coordination compounds assembled *via* amide-amide hydrogen bonds" *Crystal Engineering*, 1998, pp. 39-49, Vol. 1, No. 1.	
	*	AAKERÖY, C. et al. "Modular supramolecular synthesis based on a dominance hierarchy of intermolecular interactions (Abstract)" 223rd ACS National Meeting in Orlando, FL., April 7-11, 2002, published by the American Chemical Society, Washington, D.C.	
	*	AAKERÖY, C. et al. "Molecular mechanics and crystal engineering" " Crystal Engineering (ed. by Seddon, K. R. et al.), 1999, pp. 69-82, Kluwer Academic Publishers, The Netherlands.	
	*	AAKERÖY, C. et al. "New building blocks for crystal engineering. Syntheses and crystal structures of oxime-substituted pyridines" *Cryst Eng. Comm.*, 2000, pp. 1-6, Vol. 27.	
	*	AAKERÖY, C. et al. "Novel colorless composite materials for nonlinear optics" *Adv. Mater*, 1993, pp. 364-367, Vol. 5, No. 5.	
	*	AAKERÖY, C. et al. "Organic assemblies of 2-pyridones with dicarboxylic acids" *Tetrahedron*, 2000, pp. 6693-6699, Vol. 56.	
	*	AAKERÖY, C. et al. "Pitfalls in the supramolecular assembly of silver(I) coordination compounds" *Journal of Molecular Structure*, 1999, pp. 91-101, Vol. 474.	
	*	AAKERÖY, C. et al. "Solid state, crystal engineering and hydrogen bonds" Comprehensive Coordination Chemistry II (ed. by McCleverty, J. et al.), pp. 679-688, Elsevier Ltd., Oxford, UK.	
	*	AAKERÖY, C. et al. "Supramolecular assembly of low-dimensional silver (I) architectures *via* amide-amide hydrogen bonds" *Chem. Commun.*, 1998, pp. 1067-1068.	
	*	AAKERÖY, C. et al. "The C-H•••C1 hydrogen bond: does it exist?" *New J. Chem.*, 1999, pp. 145-152.	
	*	AAKERÖY, C. et al. "The crystal structure of the molecular cocristal *L*-malic acid *L*-tartaric acid (1/1)" *Supramolecular Chemistry*, 1996, pp. 153-156, Vol. 7.	
	*	AAKERÖY, C. et al. "The hydrogen bond and crystal engineering" *Chemical Society Reviews*, 1993, pp. 397-407.	
	*	AAKERÖY, C. et al. "Total synthesis' supramolecular style: design and hydrogen-bond-directed assembly of ternary supermolecules" *Angew. Chem. Int Ed.*, 2001, pp. 3240- 3242, Vol. 40, No. 17.	
	*	AAKERÖY, C. et al. "Two-fold interpenetration of 3-D nets assembled via three-co-ordinate silver(I) ions and amide-amide hydrogen bonds" *J. Chem. Soc., Dalton Trans.*, 1998, pp. 1943-1945.	
	*	AAKERÖY, C. et at "Heteromeric intermolecular interactions as synthetic tools for the formation of binary co-crystals" *Cryst. Eng. Comm.*, 2004, pp. 19-24, Vol. 6, No. 5.	
	*	AAKERÖY, C. et at "Hydrogen-bond assisted assembly of organic and organic-inorganic solids" Crystal Enoineerino: From Molecules and Crystals to Materials, 1999, pp. 89-106, Kluwer Academic Publishers, The Netherlands.	

EXAMINER:	DATE CONSIDERED:

[#] EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	11	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	AAKERÖY, C.B. et al. "Do Polymorphic Compounds Make Good Cocrystalizing Agents? A Structural Case Study that Demonstrates the Importance of Synthon Flexibility" *Crystal Growth & Design*, 2003, 3(2):159-165.	
	*	ABOURAHMA et al., Network Hydrogen Bonding in Two New Cocrystals Sustained by [Mn(CO)3(OH)]4, a tetrahedral hydrogen bond donor. J Chem Crystallogr. 1995 Nov; 25:731-736.	
	*	AHN, S. et al. "Polymorphs of a 1:1 cocrystal with tunnel and layer structures: *p,p'*-biphenol/dimethyl sulfoxide" *Crystal Growth & Design*, 2001, pp. 107-111, Vol. 1, No. 2.	
	*	AKAZOME, M. et al. "Enantioselective inclusion of methyl phenyl sulfoxides and benzyl methyl sulfoxides by (*R*)-phenylglycyl-(*R*)-phenylglycine and the crystal structures of the inclusion cavities" *J. Org. Chem.*, 2000, pp. 68-76, Vol. 65.	
	*	AKHTARUZZAMAN, M.D. et al. "One-dimensional hydrogen-bonded molecular tapes in 1, 4-bis[(4-pyridinio) ethynyl]benzene chloranilate" *Acta. Cryst.*, 2001, pp. o353-o355, Vol. E57.	
	*	ALBEROLA, S. et al. "Crystalline and Molecular Structure of Sulfanilimide-Antipyrine" *Acta Cryst.*, 1977, pp. 3337-3341, Vol. B33.	
	*	ALLEN, F. et al. "Systematic analysis of structural data as a research technique in organic chemistry" *Acc. Chem. Res.*, 1983, pp. 146-153, Vol. 16.	
	*	ALMARSSON et al., The A to Z of pharmaceutical cocrystals: a decade of fast-moving new science and patents. Pharm Pat Anal. 2012 Jul;1(3):313-27. doi: 10.4155/ppa.12.29.	
	*	ALMARSSON, Ö. et al. "Crystal engineering of the composition of pharmaceutical phases. Do pharmaceutical co-crystals represent a new path to improved medicines?" *Chem. Commun.*, 2004, pp. 1889-1896.	
	*	AMAI, M. et al. "1:1 complex of octadecanoic acid and 3-pyridinecarboxamide" *Acta Cryst.*, 1998, pp. 1367-1369, Vol. C54.	
	*	AMMAR et al., Effects of Aromatic Hydtotropes on the Solubility of Carbamazepine. Part II: Effect of Nicotinamide, Sodium Salts of Benzoic, Naphthoic and Nicotinic Acids. Egypt J Pharmacol Sci. 1994;35(1-6):209-23.	
	*	ANDERSON, J. "Constitution of aurous compounds: Gold mirrors" *Nature*, October 2, 1937, pp. 583-584, Letters to the Editor.	
	*	ANDERSON, N. et al. "Sulfonation with inversion by mitsunobu reaction: an improvement on the original conditions" *J. Org. Chem.*, 1996, pp. 7955-7958, Vol. 61.	
	*	AOKI, K. et al. "A 1:1 complex of theophylline and p-nitrophenol" *Acta Cryst.*, 1978, pp. 2333-2336, Vol. B34.	
	*	ARONHIME, J. et al. "Crystalline forms of pharmaceuticals and characterization thereof", Oral Presentation, March 8, 2005, USPTO, Alexandria, VA.	
	*	ASHTON, P. et al. "Combining different hydrogen-bonding motifs to self-assemble interwoven superstructures" *Chem. Eur. J.*, 1998, pp. 577-589, Vol. 4, No. 4.	
	*	BALL, P. "Materials Chemistry - Scandal of Crystal Design ...", *Nature*, June 20, 1996, pp. 648-650, Vol. 381.	

EXAMINER:	DATE CONSIDERED:

[#] EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	12	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	BARKER, P. A. et al. "Effect of crystallization temperature on the cocrystallization temperature on the cocrystallization of hydroxybutyrate/ hydroxyvalerate copolymers" *Polymer*, pp. 913-919, Vol. 38, No. 4.	
	*	BASTIN, R.J. et al. "Salt Selection and Optimisation Procedures for Pharmaceutical New Chemical Entities" *Organic Process Research & Development*, 2000, 4:427-435.	
	*	BEDU-ADDO, Understanding Lyophilization Formulation Development. Pharmaceutical Technology. 2004 Mar: 10-18.	
	*	BEERGES, P. et al. "Phenothiazine tetracyanoethylene" *Private Communication*, 1994.	
	*	BERGE et al., Pharmaceutical salts. J Pharm Sci. 1977 Jan;66(1):1-19.	
	*	BERKOVITCH-YELLIN, Z. et al. "Electron density distribution in cumulenes: an x-ray study of the complex allenedicarboxylic acid- acetamide (1:1) at -150°C" *Acta Cryst.*, 1977, pp. 3670-3677, Vol. B33.	
	*	BERKOVITCH-YELLIN, Z. et al. "The role played by C-H•••O and C-H•••N interactions in determining molecular packing and conformation" *Acta Cryst.*, 1984, pp. 159-165, Vol. B40.	
	*	BERL, V. et al. "Induced fit selection of a barbiturate receptor from a dynamic structural and conformational/configurational library" *Eur. J. Org. Chem.*, 1999, pp. 3089-3094.	
	*	BERNSTEIN, J. et al. "Concomitant Polymorphs", *Angew. Chem., Int. Ed.*, 1999, pp. 3440-3461, Vol. 38.	
	*	BERTOLASI, V. et al. "Competition between hydrogen bonding and donor-acceptor interactions in co-crystals of 1,3-dimethylbarbituric acid with aromatic amines" *New J. Chem.*, 2001, pp. 408-415, Vol. 25.	
	*	BERTOLASI, V. et al. "General rules for the packing of hydrogen-bonded crystals as derived from the analysis of squaric acid anions: aminoaromatic nitrogen base co-crystals" *Acta Cryst.*, 2001, pp. 591-598, Vol. B57.	
	*	BETTINETT1, G. et al. "Structure and solid-state chemistry of anhydrous and hydrated crystal forms of the trimethoprim-sulfamethoxypyridazine 1:1 molecular complex" *Journal of Pharmaceutical Sciences*, April 2000, pp. 478-489, Vol. 89, No. 4.	
	*	BETTINETTI, G. et al. "Thermal analysis of binary systems of the pharmaceuticals trimethoprim and benzoic acid" *Journal of Thermal Analysis*, 1983, pp. 285-294, Vol. 28.	
	*	BETTIS, J. et al. "Biopharmaceutics and dosage form design" *Amer. J. Hosp. Pharm.*, March 1973, pp. 240-243, Vol. 30.	
	*	BINGHAM, A. et al. "Over one hundred solvates of sulfathiazole" *Chem. Commun.*, 2001, pp. 603-604.	
	*	BOLTON, S. et al. "Complexes formed in solution by homologs of caffeine" *Journal of the American Pharmaceutical Association*, January 1957, pp. 38-41, Vol. XLVI, No. 1.	
	*	BOND, A. "*In situ* co-crystallisation as a tool for low-temperature crystal engineering" *Chem. Commun.*, 2003, pp. 250-251, Vol. 2.	
	*	BOND, A.D. et al. "On the Polymorphism of Aspirin" *Angew. Chem. Int Ed.*, 2007, 46:615-617.	
	*	BOND, A.D. et al. "On the Polymorphism of Aspirin: Crystalline Aspirin as Intergrowths of Two "Polymorphic" Domains" *Angew. Chem. Int. Ed.*, 2007, 46:618-622.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	13	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	BONIN, M. et al. "Urotropin azelate: a rather unwilling co-crystal" *Acta Cryst.*, 2003, pp. 72-86, Vol. B59.	
	*	BOSSHARD, C. et al. "Microscopic nonlinearities of two-component organic crystals" *J. Opt. Soc. Am. B*, November 2001, pp. 1620-1626, Vol. 18, No. 11.	
	*	BOUCHER, E. et al. "Use of Hydrogen-Bonds to Control Molecular Aggregation. Behavior of Dipyridones and Pyridone-Pyrimidones Designed to Form Cyclic Triplexes", *J. Org. Chem.*, 1995, pp. 1408-1412, Vol. 60.	
	*	BRADER, M.L. et al. "Hybrid insulin cocrystals for controlled release delivery" *Nature Biotechnology*, August 2002, 20:800-804.	
	*	BRAGA, D. et al. "Hydrogen bonding interactions between ions: a powerful tool in molecular crystal engineering" *Structure and Bonding*, 2004, pp. 1-32, Vol. 111.	
	*	BRIERLEY, C. et al. "Preparation and structure of the 1:2 π-molecular complex of phenothiazine with pyromellitic dianhydride" *J. Chem. Phys.*, February 1, 1985, pp. 1522- 1528, Vol. 82, No. 1.	
	*	BRITTAIN, H.G. et al. "Polymorphism in Pharmaceutical Solids" 1999, New York: Marcel Dekker, pp. 183, 202-208, 219.	
	*	BUCZAK, G. et al. "Crystal structure and vibrational spectra of the 1:1 and 1:2 complexes of pyridine betaine with pentachlorophenol" *Journal of Molecular Structure*, 1997, pp. 143- 151, Vol. 436-437.	
	*	BUNICK, G. et al. "The crystal and molecular structure of the complex 2,6-diamino-9-ethylpurine 5,5-diethylbarbituric acid" *American Crystallographic Association, Abstract Papers*" Winter 1976, p. 30.	
	*	BURGI, H. et al. "Crystallisation of supramolecular materials" *Current Opinion in Solid State & Materials Science*, 1998, pp. 425-430, Vol. 3.	
	*	BYRIEL, K., et al. "Molecular cocrystals of carboxylic acids. IX Carboxylic acid interactions with organic heterocyclic bases. The crystal structures of the adducts of (2,4-dichlorophenoxy) acetic acid with 3-hydroxypyridine, 2,4,6,-trinitrobenzoic acid with 2-aminopyrimidine, and 4-nitrobenzoic acid with 3-amino-1,2,4-triazole" *Aust. J. Chem.*, 1992, pp. 969-981, Vol. 45, No. 6.	
	*	BYRN et al., Pharmaceutical solids: a strategic approach to regulatory considerations. Pharm Res. 1995 Jul;12(7):945-54.	
	*	BYRN, S. R. et al. "Solid-state pharmaceutical chemistry" *Chem. Mater.*, 1994, pp. 1148- 1158, Vol. 6.	
	*	CACCIAPUOTI, A. et al. "In vitro and in vivo activities of SCH 56592 (Posaconazole), a new triazole antifungal agent, against *Aspergillus* and *Candida*" *Antimicrobial Agents and Chemotherapy*, August 2000, pp. 2017-2022, Vol. 44, No. 8.	
	*	CAIRA, M. "Molecular complexes of sulfonamides. Part 1. 1:1 complexes between sulfadimidine [4-amino-N-(4,6-dimethyl-2-pyrimidinyl) benzenesulfonamide] and 2- and 4-aminobenzoic acids" *Journal of Crystallographic and Spectroscopic Research*, 1991, pp. 641-648, Vol. 21, No. 5.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	14	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	CAIRA, M. "Molecular complexes of sulfonamides. Part 2. 1:1 complexes between drug molecules: sulfadimidine —acetylsalicylic acid and sulfadimidine-4-aminosalicylic acid" *Journal of Crystallographic and Spectroscopic Research*, 1992, pp. 193-200, Vol. 22, No. 2.	
	*	CAIRA, M. "Molecular complexes of sulfonamides. Part 3. Structure of 5-methoxysulfadiazine (Form II) and its 1:1 complex with acetylsalicylic acid" *Journal of Chemical Crystallography*, 1994, pp. 695-701, Vol. 24, No. 10.	
	*	CAIRA, M. et al. "Order-disorder enantiotropy, monotropy, and isostructurality in a tetroxoprim-sulfametrole 1:1 molecular complex: crystallographic and thermal studies" *Journal of Pharmaceutical Sciences*, November 2003, pp. 2164-2176, Vol. 92, No. 11.	
	*	CAIRA, M. et al. "Selective formation of hydrogen bonded cocrystals between a sulfonamide and aromatic carboxylic acids in the solid state" *J. Chem. Soc. Perkin Trans. 2*, 1995, pp. 2213-2216.	
	*	CAIRA, M. et al. "Structure of a 1:1 complex between the anthelmintic drug mebendazole and propionic acid" *Journal of Chemical Crystallography*, 1998, Vol. 28, No. 1.	
	*	CAIRA, M. et al. "X-ray structure and thermal analysis of a 1:1 complex between (*S*)-naproxen and heptakis (2,3,6-tri-*O*-methyl)-β-cyclodextrin" *Journal of Inclusion Phenomena and Molecular Recognition in Chemistry*, 1995, pp. 277-290, Vol. 20.	
	*	CALLAHAN, J.C. et al. "Equilibrium moisture content of pharmaceutical excipients" *Drug Development and Industrial Pharmacy*, 1982, pp. 355-369, Vol. 8, No. 3.	
	*	CAMERMAN, A. et al. "Hydrogen bonding interaction of diphenylbarbituric acid and 9-ethyladenine. Crystal structure of a 1:1 complex" *Can. J. Chem.*, 2000, pp. 1045-1051, Vol. 78.	
	*	CAMERMAN, A. et al. "Molecular structure of acetylacetone. A crystallographic determination" *J. Am. Chem. Soc.*, 1983, pp. 1584-1586, Vol. 105, No. 6.	
	*	CANNON, A. et al. "Noncovalent derivatization: green chemistry applications of crystal engineering" *Crystal Growth & Design*, 2002, pp. 255-257, Vol. 2. No. 4.	
	*	CARONNA, T. et al. "Halogen bonding and π•••π stacking control reactivity in the solid state" *J. Am. Chem. Soc.*, 2004, pp. 4500-4501, Vol. 126.	
	*	CHANG, Y. L. et al. "An Approach to the Design of Molecular-Solids. Strategies for Controlling the Assembly of Molecules Into Two-Dimensional Layered Structures", *J. Am. Chem. Soc.*, 1993, pp. 5991-6000, Vol. 115.	
	*	CHILDS, S. et al. "Crystal engineering approach to forming cocrystals of amine hydrochlorides with organic acids. Molecular complexes of fluoxetine hydrochloride with benzoic, succinic, and fumaric acids" *J. Am. Chem. Soc.*, 2004, pp. 13335-13342, Vol. 126.	
	*	CHINNAKALI, K. et al. "2-aminopyrimidine and *p*-phenylene-diacetic acid (1:1) co-crystal" *Acta Cryst.*, 1999, pp. 399-401, Vol. C55.	
	*	CHOI, C. et al. "Cocrystallization of melaminium levulinate monohydrate" *Acta Cryst.*, 2004, pp. o295-o296, Vol. C60.	
	*	CHOW, Y. P. et al. "Complexation of acetaminophen with methyl xanthines" *Journal of Pharmaceutical Sciences*, 1972, pp. 1454-1458, Vol. 61.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	15	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	CHRISTIAN, S. et al. "Activity coefficient effects in spectral and solubility studies of molecular complex equilibria" *Journal of the American Chemical Society*, September 20, 1972, pp. 6861-6862, Vol. 94, No. 19, Communications to the editor.	
	*	COLL, M. et al. "Molecular structure of the complex formed between the anticancer drug cisplatin and d(pGpG): $C222_1$ crystal form" *Journal of Biomolecular Structure & Dynamics*, 1990, pp. 315-330, Vol. 8, No. 2.	
	*	COPP, S. et al. "Supramolecular chemistry of $[Mn(CO)_3(\mu 3\text{-}OH)]_4$: Assembly of a cubic hydrogen-bonded diamondoid network with 1,2-diamineothane" *J. Am. Chem. Soc.*, 1992, pp. 8719-8720, Vol. 114.	
	*	CORDI, A. et al. "(*S*)-Spiro [(1, 3-diazacyclopent-1-ene)-5, 2' -(7'-methyl-1,2',3',4'-tetrahydronaphthalene)]: resolution, stereospecific synthesis, and preliminary pharmacological characterization as a partial α-adrenergic agonist" *J. Med. Chem.*, 1997, pp. 2931-2935, Vol. 40.	
	*	COWAN, J.A. et al. "Neutron diffraction studies of the 1:1 and 2:1 cocrystals of benzene-1,2,4,5-tetracarboxylic acid and 4,4'-bipyridine" *Acta Crystallographica Section C: Crystal Structure Communications*, 2006, C62:o157-o161.	
	*	COX, J.R. et al., "Selective Crystal Growth of the Anhydrous and Monohydrate Forms of Theophylline on Self-Assembled Monolayers," *Angew, Chem. Int. Ed.*, 2007, pp. 1988-1991, Vo. 46.	
	*	CRAVEN, M. et al. "The 2:1 crystal complex of 5, 5-diethylbarbituric acid (barbital) and caffeine" *Acta Cryst.*, 1974, pp. 1191-1195, Vol. B30.	
	*	CRAVEN, M. et al. "The crystal structures of two polymorphs of 5,5'-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1969, pp. 1978-1993, Vol. 825.	
	*	CRIHFIELD, A. et al. "Crystal engineering through halogen bonding. 2. Complexes of diacetylene-linked heterocycles with organic iodides" *Crystal Growth & Design*, 2003, pp. 313-320, Vol. 3, No. 3.	
	*	CUDNEY, B. et al. "Screening and optimization strategies for macromolecular crystal growth" *Acta Cryst.*, 1994, pp. 414-423, Vol. D50.	
	*	CUTSEM, J. V. et al. "Oral and parenteral therapy with saperconazole (R 66905) of invasive aspergillosis in normal and immunocompromised animals" *Antimicrobial Agents and Chemotheraphy*, December 1989, pp. 2063-2068, Vol. 33, No. 12.	
	*	DANNAOUI, E. et al. "Acquired itraconazole resistance in *Aspergillus fumigatus*" *Journal of Antimicrobial Chemotherapy*, 2001, pp. 333-340, Vol. 47.	
	*	DATABASE WPI, Section Ch, Week 197936, Derwent Publishing Ltd., London, Great Britain, Class B02, AN 1979-65538B, XP002282989 and JP 54 095589A (Sumitomo) 1979 Abstract.	
	*	DATTA, S. et al. "Crystal structures of drugs: advances in determination, prediction and engineering" *Nature*, January 2004, pp. 42-57, Vol. 3.	
	*	DATTA, S. et al. "Molecular complex formation between riboflavin and salicylate in an aqueous medium" *Bult Chem. Soc. Jpn.*, 2003, pp. 1729-1734, Vol. 76.	
	*	DAVEY, R. J. et al. "Crystal engineering- nucleation, the key step" *Cryst Eng. Comm.*, 2002, pp. 257-264, Vol. 4, No. 47.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	16	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	DAVEY, R. J. et al. "Crystallisation in polymer films: control of morphology and kinetics of an organic dye in a polysilicone matrix" *J. Mater. Chem.*, 1997, pp. 237-241, Vol. 7, No. 2.	
	*	DAVIDOVICH, M. et al. "Detection of Polymorphism by Powder X-Ray Diffraction Interference by Preferred Orientation" *American Pharmaceutical Review*, 2004, pp. 10, 12, 14, 16, 100, Vol. 7, No. 1.	
	*	DAVIES, N.M. ef al. "Clinical Pharmacokinetics and Pharmacodynamics of Celecoxib: A Selective Cyclo-Oxygenase-2 Inhibitor" *Clin Pharmacokinet*, March 2000, 38(3):225-242.	
	*	DE JONG, E.M.G.J. et al. "Dystrophic Psoriatic Fingernails Treated with 1% 5-Fluorouracil in a Nail Penetration-Enhancing Vehicle: A Double-Blind Study" *Dermatology*, 1999, 199:313-318.	
	*	DEAN, J.A. "Analytical Chemistry Handbook" 1995, New York: McGraw-Hill, Inc., pp. 10.24-10.26.	
	*	DEBERNARDIS, J. et al. "Conformationally defined adrenergic agents. 5. Resolution, absolute configuration, and pharmacological characterization of the enantiomers of 2-(5,6-dihydroxy-1,2,3,4-tetrahydro-1-naphthyl) imidazoline: a potent agonist at α-adrenoceptors" *J. Med. Chem.*, 1987, pp. 1011-1017, Vol. 30.	
	*	DENNING, D. W. et al. "In vitro activity of Saperconazole (R66 905) compared with Amphotericin B and ltraconazole against *Aspergillus* species" *Eur. J. Clin. MicrobiaL Infect. Dis.*, 1990, pp. 693-697, Vol. 9.	
	*	DESIRAJU, G. "Supramolecular synthons in crystal engineering- A new organic synthesis" *Angew. Chem. Int. Ed. Engl*, 1995, pp. 2311-2327, Vol. 34.	
	*	DESIRAJU, G. et al. "Crystal and co-crystal" *Cryst. Eng. Comm.*, 2003, pp. 466-467, Vol. 5, No. 82.	
	*	DESIRAJU, G. et al. "Crystal engineering: outlook and prospects" *Current Science*, October 25, 2001, pp. 1038-1042, Vol. 81, No. 8.	
	*	DESIRAJU, G. R. "Chemistry beyond the molecule" *Nature*, July 26, 2001, pp. 397-400, Vol. 412.	
	*	DESIRAJU, G. R. "Crystal Gazing: Structure Prediction and Polymorphism", *Science*, October 17, 1997, pp. 404-405, Vol. 278, No 5337.	
	*	DESIRAJU, G. R. "The C--H•••O Hydrogen Bond in Crystals: What Is It?" *Acc. Chem. Res.*, 1991, pp. 24:290-296.	
	*	DESIRAJU, G. R., "Crystal engineering: A brief overview," *J. Chem. Sci.*, September 2010, pp. 667-675, Vol. 122, No. 5.	
	*	DOELKER, E. "Crystalline Modifications and Polymorphism changes during drug manufacturing" *Annales Pharmaceutiques Francaises*, 2002, 60(3):161-176.	
	*	DOELKER, E. "Physicochemical behavior of active substances. Consequences for the feasibility and stability of pharmaceutical forms" *S.T.P. Pharma Practiques*, 1999, 9(5):399- 409.	
	*	DOI, M. et al. "Conformational study of a potent human renin inhibitor: x-ray crystal structure of isopropyl (2*R*, 3*S*) -4-cyclohexyl-2-hydroxy-3-{*N*-[(2R)-2-morpholinocarbonylmethyl-3-(1-naphthyl) propionyl] -L-histidylamino}butyrate (KRI-1314), a pentapeptide analogue with amino acid sequence corresponding to the cleavage site of angiotensinogen" *J. Chem. Soc. Perkin Trans. 1*, 1991, pp. 1153-1158.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	17	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	DRESSMAN, J. B. et al. "Dissolution testing as a prognostic tool for oral drug absorption: immediate release dosage forms" *Pharmaceutical Research*, 1998, pp. 11-22, Vol. 15, No. 1.	
	*	DUAX, W. et al. "The structure of the crystalline complex estradiol. Urea (1:1)" *Acta Cryst.*, 1972, pp. 1864-1871, Vol. B28.	
	*	DUKE, Handbook of Phytochemical Constituents of GRAS Herbs and Other Economic Plants, 2001, CRC Press LLC, page 419.	
	*	DUNITZ, J. "Crystal and co-crystal: a second opinion" *Cryst. Eng. Comm.*, 2003, pp. 506, Vol. 5, No. 91.	
	*	DUNITZ, J. "New light on an old story: the solid-state transformation on ammonium cyanate into urea" *J. Am. Chem. Soc.*, 1998, pp. 13274-13275, Vol. 120.	
	*	DUNITZ, J. D. "Are crystal structures predictable" *Chem Commun.*, 2003, pp. 545-548.	
	*	DVORKIN et al. "Crystal and Molecular Structure of a Complex 18-crown-6 with 6-chloro-7-sulfamido-3,4-dihydro-1,2,4-benzothiadiazine-1, 1-dioxide (hypothiazide) of 1:1 Composition" *Kristallagrafiya*, 1990, 35(3):682-686.	
	*	EBERT, W. R. "Soft elastic gelatin capsules: a unique dosage form" *Pharmaceutical Technology*, October 1977, pp. 44-50, Vol. 1, No. 5.	
	*	EL-NAHHAS, S.A. "Physico-Chemical characteristics of Carbamazepine-beta-cyclodextrin inclusion compounds and carbamazepine-peg solid dispersions" *Pharmazie,* 1996, 51(12):960-963.	
	*	ENRIGHT, G. et al. "Thermally programmable gas storage and release in single crystals of an organic van der Waals host" *J. Am. Chem. Soc.*, 2003, pp. 9896-9897, Vol. 125.	
	*	EPSTEIN, R. et al. "The x-ray crystal structure of the molecular complex 8-bromo-9-ethyladenine-5-allyI-5-isobutylbarbituric acid" *Acta Cryst.*, 1976, pp. 2180-2188, Vol. B32.	
	*	ERMER, O. et al. "Molecular recognition among alcohols and amines: super-tetrahedral crystal architectures of linear diphenol-diamine complexes and aminophenols" *J. Chem. Soc. Perkins Trans. 2*, 1994, pp. 925-944.	
	*	ETTER, M. "Encoding and decoding hydrogen-bond patterns of organic compounds" *Acc. Chem. Res.*, 1990, pp. 120-126, Vol. 23.	
	*	ETTER, M. "Hydrogen bonds as design elements in organic chemistry" *J. Phys. Chem.*, 1991, pp. 4601-4610, Vol. 95.	
	*	ETTER, M. et al. "Graph-set analysis of hydrogen-bond patterns in organic crystals" *Acta Cryst.*, 1990, pp. 256-262, Vol. B46.	
	*	ETTER, M. et al. "Hydrogen bond directed cocrystallization and molecular recognition properties of acyclic imides" *J. Am. Chem. Soc.*, 1991, pp. 2586-2598, Vol. 113.	
	*	EVGEN'EV et al., Selective determination of 4-aminobenzoic and 4-aminosalicylic acid derivatives in mixtures by flow-injection analysis. J Anal Chem. 2000 July;55(7):696-702.	
	*	FABIAN, L. et al. "Volumetric measure of isostructurality" *Acta Cryst.*, 1999, pp. 1099- 1108, Vol. B55.	
	*	FALLON III, L. "The crystal and molecular structure of 5-fluorouracil" *Acta Cryst.*, pp. 2549-2556, Vol. B29.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	18	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	FAUGHT, E. et al. "Topiramate Dose-Ranging Trial in Refractory Partial Epilepsy" *Amer. Epilepsy Soc. Proc.*, 1995,pg. 33, Vol. 36, Supp. 4.	
	*	FEIBUSH, B. et al. "Chiral separation of heterocyclic drugs by HPLC: solute-stationary phase base-pair interactions" *J. Am. Chem. Soc.*, 1986, pp. 3310-3318, Vol. 108.	
	*	FELTHOUSE et al., Maleic Anhydride, Maleic Acid, And Fumaric Acid. 2001. http://www.huntsman.com/performance_products/media/komaleic.pdf	
	*	FEYNMAN, R. "There's Plenty of Room at the Bottom", *Engineering and Science*, February 1960, pp. 22-36.	
	*	FIFER, E. et al. "Fentanyl analogues 3. 2-(1,2,3,4-tetrahydro)-naphthyl substituted 4-anilidopiperidines" *Eur. J. Med. Chem.- Chim. Ther.*, 1984, pp. 519-524, Vol. 19, No. 6.	
	*	FITZGERALD, G.A. et aL "The Coxibs, Selective Inhibitors of Cyclooxygenase-2", *New England Journal of Medicine*, August 9, 2001, 345(6):433-442.	
	*	FLEISCHMAN, S.G. et al. "Crystal Engineering of the Composition of Pharmaceutical Phases: Multiple-Component Crystalline Solids Involving Carbamazepine" *Crystal Growth & Design.*, 2003, 3(6):909-919.	
	*	FLEISCHMAN, Scott et al. , "Crystal engineering of binary crystals that contain pharmaceutical molecules, Abstracts of Papers, 23rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002, IEC-076.	
	*	FOXMAN, B. M. et al. "Environmentally benign synthesis using crystal engineering: steric accommodation in non-covalent derivatives of hydroquinones" *Crystal Engineering*, 1998, pp. 109-118, Vol. 1, No. 1.	
	*	FOXMAN, B. M. et al. "Noncovalent derivatives of hydroquinone: *BIS*- (*N,N*-dialkyl) bicyclo[2.2.2]octane-1,4-dicarboxamide complexes" *Crystal Engineering*, 1999, pp. 55-64, Vol. 2. No. 1.	
	*	FREEMONT, Cocrystal structure of an editing complex of Klenow fragment with DNA. PNAS. 1988 Dec;85(23):8924-8.	
	*	FRITCHIE, C. et al. "The configuration of phenothiazine in various molecular complexes" *Chem. Commun.*, 1968, pp. 833-834.	
	*	FUJII, S. et al. "Crystal and molecular structure of a 1:1 molecular complex of adenine and riboflavin" *Archives of Biochemistry and Biophysics*, 1977, pp. 363-370, Vol. 181.	
	*	FUNG, H.L. et al. "Solvent Effects on Comparative Dissolution of Pharmaceutical Solvates" *Chemical and Pharmaceutical Bulletin*, 1974, 22(2):454-458.	
	*	GAO, X et al. "Supramolecular construction of molecular ladders in the solid state" *Angew. Chem. Int. Ed.*, 2004, pp. 232-236, Vol. 43.	
	*	GARTLAND, G. L. et al. "Hydrogen bonding NH•••O=C of barbiturates: the (1:1) crystal complex of urea and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 980-987, Vol. B30.	
	*	GASCON, M. -P. et al. "In vitro forecasting of drugs which may interfere with the biotransformation of midazolam" *Eur. J. Clin. Pharmacol.*, 1991, pp. 573-578, Vol. 41.	
	*	GAVEZZOTTI, A. "Are crystal structures predictable?" *Acc. Chem. Res.*, 1994, pp. 309- 314, Vol. 27.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	19	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	GHOSH, M. "Structure and conformation of the 1:1 molecular complex sulfaproxyline-caffeine" *Acta Cryst.*, 1991, pp. 577-580, Vol. C47.	
	*	GIUSEPPETTI, G. P. et al. "The crystal structure of a sulfamethoxazole-trimethoprim 1:1 molecular compound" *II Farmaco- Ed. Sc.*, pp. 138-151, Vol. 35.	
	*	GLUZMAN, M. Kh. et al. "Investigation of Eutectic Melting in Systems Composed of Organic Salts and Acids" *Journal of Physical Chemistry*, 1960, pp. 2742-2747, Vol. 34.	
	*	GOSWAMI, S. et al. "1:1 Hetero-assembly of 2-amino-pyramidine and (+)-camphoric acid" *Acta Cryst.*, 2000, pp. 477-478, Vol. C56.	
	*	GOSWAMI, S. et al. "2-aminopyrimidine-fumaric acid cocrystal" *Acta Cryst.*, 1999, pp. 583-585, Vol. C55.	
	*	GOSWAMI, S. et al. "Molecular recognition induced supramolecular array of 2-aminopyrimidine with terephthalic acid, 1,4-phenylenediacetic acid and furmaric acid in solid state *via* H-bonding and π-stacking interactions" *Supramolecular Chemistry*, 1999, pp. 25-33, Vol. 11.	
	*	GRAJA, A. et al. "Interplay of acceptor molecule shape, crystal structure and physical properties of a new molecular complex C_{70} • 2[(Ph_3P) AuCl]" *Chemical Physics Letters*, November 19, 1999, pp. 725-732. Vol. 313.	
	*	GROTH, P. "*d*-Glucose-sodium chloride-monohydrate (glucose-sodium chloride) = $2C_6H_{12}O_6.NaCl.H_2O$" *Chemische Krystallographie*, 1910, pp. 438-439.	
	*	GUARRERA, D. et al. "Molecular self-assembly in the solid state. The combined use of solid state NMR and differential scanning calorimetry for the determination of phase constitution" *Chem. Mater.*, 1994, pp. 1293-1296, Vol. 6.	
	*	HAIXIN, L. et at "Structure of the 1:1 complex of 6,6'-diquinolyl ether with 5,5-diethylbarbituric acid" *Acta Cryst.*, 1992, pp. 2096-2098, Vol. C48.	
	*	HARKEMA, S. et al. "The crystal structure of urea oxalic acid (2:1)" *Acta Cryst.*, 1972, pp. 1646-1648, Vol. B28.	
	*	HAYNES, D. "Supramolecular synthon competition in organic sulfonates: A CSD survey" *Cryst Eng. Comm.*, 2004, pp. 584-588, Vol. 6, No. 95.	
	*	HEERES, J. et al. "Antimycotic azoles. 7. Synthesis and antifungal properties of a series of novel triazol-3-ones" *J. Med. Chem.*, 1984, pp. 894-900, Vol. 27.	
	*	HELFRICH, B. et al. "Polymorphism as an indication of structural versatility (Abstract)" 223rd ACS National Meeting in Orlando, FL., April 7-11, 2002, published by the American Chemical Society, Washington, D.C.	
	*	HENCK, J. et al. "Disappearing and reappearing polymorphs. The benzocaine:picric acid system" *J. Am. Chem. Soc.*, 2001, pp. 1834-1841, Vol. 123.	
	*	HEPPERLE, M. et al. "Mono *N*-arylation of piperazine(III): metal-catalyzed *N*-arylation and its application to the novel preparations of the antifungal posaconazole and its advanced intermediate" *Tetrahedron Letters*, 2002, pp. 3359-3363, Vol. 43.	
	*	HIGUCHI, T. et al. "Complexation of organic substances in aqueous solution by hydroxyaromatic acids and their salts" *J. Pharm. Sci.*, 1961, pp. 905-909, Vol. 50.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	20	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	HINO, T. et al. "Assessment of nicotinamide polymorphs by differential scanning calorimetry" *Thermochimica Acta*, 2001, pp. 85-92, Vol. 374.	
	*	HÖGBERG, T. et al. "Crystallographic, theoretical and molecular modelling studies on the conformations of the salicylamide, raclopride, a selective dopamine-D_2 antagonist" *J. Pharm. Pharmacol.*, 1987, pp. 787-796, Vol. 39.	
	*	HONIG, P. K. et al. "Itraconazole affects single-dose Terfenadine pharmacokinetics and cardiac repolarization pharmacodynamics" *J. Clin. Pharmacol.*, 1993, pp. 1201-1206, Vol. 33.	
	*	HSU, I. et al. "Hydrogen bonding NH...N of barbiturates: The 1:1 crystal complex of imidazole and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 988-993, Vol. 830.	
	*	HSU, I. et al. "The 1:1 crystal complex of *N*-methyl-2-pyridone and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 998-1001, Vol. B30.	
	*	HSU, I. et al. "The 2:1 crystal complex of 2-aminopyridine and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 994-997, Vol. B30.	
	*	HSU, I. et al. "The crystal structure of the 1:1 complex of acetamide with 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 974-979, Vol. B30.	
	*	HSU, I. et al. "The crystal structure of the triclinic 1:2 complex of hexamethylphosphoramide with 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 1299-1304, Vol. B30.	
	*	HSU, I. et al. "The crystalline complex (1:1) of salicylamide and 5-ethyl-5-isoamylbarbituric acid (amobarbital)" *Acta Cryst.*, 1974, pp. 843-846, Vol. B30.	
	*	HU, Z. et al. "Separation of 4-aminobenzoic acid by cocrystallization: Crystal structure of the complex of 4-aminobenzoic acid with (2*R*,3*R*)-tartaric acid" *Journal of Chemical Crystallography*, December 2002, pp. 525-529, Vol. 32, No. 12.	
	*	HUANG, C.-M. et al. "Molecular packing modes. Part XI. Crystal structures of the 2:1 complexes of benzamide with succinic acid and furamide with oxalic acid" *J. Chem. Soc. Perkins Trans. 2: Physical Organic Chemistry*, 1973, pp. 503-508, Vol. 5.	
	*	IBRAGIMOV, B. "A simple correlation between the structures of different crystal modifications of a given host-guest complex and their crystallization temperatures" *Journal of Inclusion of Phenomena and Macrocyclic Chemistry*, 1999, pp. 345-353, Vol. 34.	
	*	IMAI, T. et al. "Successful treatment of cerebral Aspergillosis with a high oral dose of Itraconazole after excisional surgery" *Internal Medicine*, October 1999, pp. 829-832, Vol. 38, No. 10.	
	*	ISHIDA, T. et al. "Structural study of histamine H_2-receptor antagonists. Five 3-[2-(diaminomethyleneamino)-4-thiazolymethylthio] propionamidine and -amide derivatives" *Acta Cryst.*, 1989, pp. 505-512, Vol. 645.	
		ITO et al., Compelled Orientational Control of the Solid-State Photodimerization of *trans*-Cinnamamides: Dicarboxylic Acid as a Non-covalent Linker. Tetrahedron. 2000;56:6833-44.	
		IWAMOTO et al., Structure of Cinnamamide. Acta Cryst. 1989;C45:1110-2.	
	*	JACKISCH, M. et al. 'Structures of three related biphenyl compounds: 4,4'-biphenyldiol, 3, 3',5,5'-tetra-*tert*-butyl-4,4'-biphenyldiol, and 3,3',5,5'- tetra-*tert*-butyl-1,1'-bicyclohexa-2,5-dienylidene-4,4'-dione" *Acta Cryst.*, 1990, pp. 919-922, Vol. C46.	
	*	JAIN, N.K. et al. "Polymorphism in Pharmacy" *Indian Drugs*, 1986, 23(6):315-329.	

EXAMINER:	DATE CONSIDERED:

[#] EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	21	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		JIANG et al., Cinnamamide, an antitumor agent with low cytotoxicity acting on matrix metalloproteinase. Anti-Cancer Drugs. 2000 Jan;11(1):49-54.	
	*	KATAKAI, R. et al. "Stepwise synthesis of oligopeptides with N-carboxy-α-amino acid anhydrides. IV. Glycine NCA" *J. Org. Chem.*, 1972, pp. 327-329, Vol. 37, No. 2.	
	*	KAWAKAMI, Y. et al. "The rationale for E2020 as a potent acetylcholinesterase inhibitor" *Bioorganic & Medicinal Chemistry*, 1996, pp. 1429-1446, Vol. 4, No. 9.	
	*	KELDERS, H. et al. "Automated protein crystallization and a new crystal form of a subtilisin: eglin complex" *Protein Engineering*, 1987, pp. 301-303, Vol. 1, No. 4.	
	*	KHALIL, R. M. "Complexation of paracetamol with xanthine derivatives" *Egypt. J. Pharm. Sol.*, 1992, pp. 757-769, Vol. 33, No. 5-6.	
	*	KIM, H. et al. "High-performance liquid chromatographic analysis of the anti-fungal agent SCH 56592 in dog serum" *Journal of Chromatography B*, 2000, pp. 93-98, Vol. 738.	
	*	KIM, S. "Crystal structure of the 1:1 complex of 5-fluorouracil and 9-ethylhypoxanthine" *Science*, November 24, 1967, pp. 1046-1048, Vol. 158, No. 3804.	
	*	KIM, S. et al. "The structure of a crystalline complex containing one phenobarbital molecule and two adenine derivatives" P*roc. Natl. Acad. Sci. USA*, 1968, pp. 402-408, Vol. 60.	
	*	KIRCHNER, M.T. et al. "Co-crystals with Acetylene: Small Is not Simple" *Chem. Eur J.*, 2010, 16:2131-2146.	
	*	KIRYU, S. et al. "Crystal structure of a 1:1 aminopyrine-barbital complex" *Journal of Pharmaceutical Sciences*, May 1971, pp. 699-703, Vol. 60, No. 5.	
	*	KIRYU, S. et al. "Crystal structure of a 1:1 aminopyrine-cyclobarbital complex" *Chem. Pham. Bull.*, 1974, pp. 1588-1592, Vol. 22.	
	*	KLEIN, C.L. et al. "Molecular Structure of Two Conformationally Restrained Fentanyl Analogues: cis- and trans-Isomers of *N*-{3-Methyl-1-[2-(1,2,3,4-tetrahydro)naphthyl]-4-piperidinyl}-*N*-phenylpropanamide" *Journal of Pharmaceutical Sciences*, November 1985, 74(11):1147-1151.	
	*	KOBAYASHI, H. et al. "Sinusoidal structure of the 1:1 complex of phenothiazine and 7,7,8,8-tetracyanoquinodimethane, PTZ-TCNQ" *Acta Cryst.*, 1974, pp. 1010-1017, Vol. B30.	
	*	KOFLER, L. et al., Thermal micromethods for the study of organic compounds and their mixtures, pp. 1-145, 148-351, 354-386, Innsbruck, Austria, 1980.	
	*	KOSHIMA, H. et al. "Photoreactivities of two kinds of bimolecular crystals formed from acridine and phenothiazine" *J. Chem. Soc., Perkins Trans. 2*, 1997, pp. 2033-2038.	
	*	KOSHIMA, H. et al. "Polymorphs of a cocrystal with achiral and chiral structures prepared by pseudoseeding: tryptamine/hydrocinnamic acid" *Crystal Growth & Design*, 2001, pp. 355-357, Vol. 1, No. 5.	
	*	KOVACS, J. et al. "New type of bridged monoamino-β-cyclodextrins" *Journal of Inclusion Phenomena and Molecular Recognition in Chemistry*, 1996, pp. 53-56, Vol. 25.	
	*	KRANTZ, J. et al. "Sodium theophylline glycinate" *Journal of the American Pharmaceutical Association*, 1946, pp. 248-250.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	22	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	KRISHNAMOHAN SHARMA, C. V. et al. "X-ray crystal structure of C_6H_3 $(CO_2H)_3$-1,3,5•1.5(4,4'-bipy): a 'super trimesic acid' chicken-wire grid" *Chem. Commun.*, 1996, pp. 2655-2656.	
	*	KURODA, R. et al. "Generation of a co-crystal phase with coloristic properties *via* solid state grinding procedures" *Chem. Commun.*, 2002, pp. 2848-2849.	
	*	LAVRIJSEN, A. P. M. et al. "Hepatic injury associated with itraconazole" *The Lancet*, July 25, 1992, pp. 251-252, Vol. 340.	
	*	LE JEUNNE, C. et al. "Comparative efficacy and safety of calcium carbasalate plus metoclopramide versus ergotamine tartrate plus caffeine in the treatment of acute migraine attacks" *Eur. Neurol.*, 1999, pp. 37-43, Vol. 41.	
	*	LEGER, J.M. et al. "Crystal Structure of the 1:1 Sulfacetamide-Caffeine Complex" *Acta Cryst.*, 1977, pp. 1455-1459, Vol. 633.	
	*	LEHN, J.-M. et al. "Molecular recognition directed self-assembly of ordered supramolecular strands by cocrystallization of complementary molecular components" *Chem. Soc., Chem. Commun.*, 1990, pp. 479-481.	
	*	LEISEROWITZ, L. "Molecular packing modes. Carboxylic acids" *Acta Cryst.*, 1976, pp. 775-802, Vol. B32.	
	*	LEISEROWITZ, L. et al. "The molecular packing modes and hydrogen-bonding properties of amide: dicarboxylic acid complexes" *Acta Cryst.*, 1977, pp. 2719-2733, Vol. B33.	
	*	LEVIN, B. et al. "The not-so-trivial synthesis and characterization of heterocyclic boronic acids (Abstract)" 38th Midwest Regional Meeting of the American Chemical Society in Columbia, MO., November 5-7, 2003, published by the American Chemical Society, Washington, D.C.	
	*	LYNCH, D. et al. "1:1 Molecular complexes of 4-amino-N-(4,6-dimethylpyrimidin-2-yl) benzene-sulfonamide (sulfamethazine) with indole-2-carboxylic acid and 2,4-dinitrobenzoic acid" *Aust. J. Chem.*, 2000, pp. 383-387, Vol. 53.	
	*	LYNCH, D. et al. "Molecular cocrystals of carboxylic acids. XV Preparation and characterization of heterocyclic base adducts with a series of carboxylic acids, and the crystal structures of the adducts of 2-aminopyrimidine with 2,6-dihydroxybenzoic acid, 4-aminobenzoic acid, phenoxyacetic acid, (2,4-dichlorophenoxy) acetic acid, (3,4-dichlorophenoxy)- acetic acid and salicylic acid, and 2-aminopyridmine with 2,6-dihydroxybenzoic acid" *Aust. J. Chem.*, 1994, pp. 1097-1115, Vol. 47.	
	*	LYNCH, D. et al. "Molecular cocrystals of carboxylic acids. XXXI adducts of 2-aminopyrimidine and 3-amino-1,2,4-triazole with heterocyclic carboxylic acids" *Aust. J. Chem.*, 1998, pp. 403-408, Vol. 51.	
	*	MACGILLIVRAY, L. et al. "Supramolecular control of reactivity in the solid state using linear molecular templates" *J. Am. Chem. Soc.*, 2000, pp. 7817-7818, Vol. 122.	
	*	MADARASZ, J. et al. "Thermal, ftir and xrd study on some 1:1 molecular compounds of theophylline" *Journal of Thermal Analysis and Calorimetry*, 2002, pp. 281-290, Vol. 69.	
	*	MARTIN, R. et al. "Polyphenal-caffeine complexation" *J. Chem. Soc., Chem. Commun.*, 1986, pp. 105-106.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	23	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	MARTIN, R. et al. 'The caffeine-potassium chlorogenate molecular complex" *Phytochemistry*, 1987, pp. 273-279, Vol. 26, No. 1.	
	*	MARTINS, F.T. et al., "Intermolecular Contacts Influencing the Conformational and Geometric Features of the Pharmaceutically Preferred Mebendazole Polymorph C," *Journal of Pharmaceutical Sciences*, July 2009, pp. 2336-2344, Vol. 98, No. 7.	
	*	MARYANOFF, B. "Stereochemistry in a medium-sized ring. Highly diastereoselective N-oxidation of a substituted 3-benzazonine. X-ray crystal structure of an unusual complex between an amine *N*-oxide and saccharin" *J. Org. Chem.*, 1990, pp. 760-764, Vol. 55.	
	*	MASTROPAOLO, D. et al. "Hydrogen bonding interaction of diphenylhydantoin and 9-ethyladenine" *Molecular Pharmacology*, 1983, pp. 273-277, Vol. 23.	
	*	MATHIAS, J. et al. "Structural preferences of hydrogen-bonded networks in organic solution-the cyclic $CA_3{\bullet}M_3$ 'rosette'" *J. Am. Chem. Soc.*, 1994, pp. 4316-4325, Vol. 116.	
	*	MCCRONE, W. C. "Polymorphism", In: The Physics and Chemistry of the Organic Solid State, Vol. II, FOX, D. et al. (eds.), 1965, pp. 725-767, Interscience, New York.	
	*	MCINTOSH, J. et al. "Chemotherapeutic drugs in anaerobic infections of wounds" *The Lancet*, June 26, 1943, pp. 793-795.	
	*	MCINTOSH, J. et al. "Further observations on the chemotherapy of experimental gas gangrene: flavazole, marfanil, V187 and V335" *British Journal of Experimental Pathology*, 1946, pp. 46-54, Vol. 27.	
	*	MCINTOSH, J. et al. "Zinc peroxide, proflavine and penicillin in experimental *cl. welchii* infections" *The Lancet*, December 26, 1942, pp. 750-752.	
	*	MCMAHON, J. et al. "Crystal engineering of the composition of pharmaceutical phases. 3^1. Primary amide supramolecular heterosynthons and their role in the design of pharmaceutical co-crystals" *Z. Kristallogr.*, 2005, pp. 340-350, Vol. 220.	
	*	MEEJOO, S. et al. "The interplay of aryl-perfluoroaryl stacking interactions and interstack hydrogen bonding in controlling the structure of a molecular cocrystal" *Chemphyschem*, 2003, pp. 766-769, Vol. 4.	
	*	MIRMEHRABI, M. et al. "Improving the filterability and solid density of ranitidine hydrochloride form 1" *Journal of Pharmaceutical Sciences*, July 2004, pp. 1692-1700, Vol. 93, No. 7.	
	*	MORRIS, K. et al. "Theoretical approaches to physical transformations of active pharmaceutical ingredients during manufacturing processes" *Advanced Drug Delivery Reviews*, 2001, pp. 91-114, Vol. 48.	
	*	MOULTON, B. et al. "From Molecules to Crystal Engineering: Supramolecular Isomerism and Polymorphism in Network Solids", *Chem. Rev.*, 2001, pp. 1629-1658, Vol. 101.	
	*	MUNN, R. et al. "A Model for resonance-assisted hydrogen bonding in crystals and its graph set analysis" *J. Phys. Chem. A*, 2001, pp. 6938-6942, Vol. 105.	
	*	MUZAFFAR, N.A. et al. "Polymorphism and Drug Availability" *Journal of Pharmacy (Lahore)*, 1997, 1(1):59-66.	
	*	NAKANISHI, I. et aL "X-ray structural studies on two forms of β-cyclodextrin barbital complexes" *Journal of Inclusion Phenomena*, 1984, pp. 689-699, Vol. 2.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	24	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	NAKAO, S. et al. "The crystal and molecular structure of the 2:1 molecular complex of theophylline with phenobarbital" *Acta Cryst.*, 1977, pp. 1373-1378, Vol. B33.	
	*	NATARAJAN, S. et al. "Reinvestigation of the crystal structure of diglycine hydrochloride" *Zeitschrift für Kristallographic*, 1992, pp. 265-270, Vol. 198.	
	*	NEUVONEN, P. J. et al. "Itraconazole drastically increases plasma concentrations of lovastatin and lovastatin acid" *Clinical Pharmacology & Therapeutics*, 1996, pp. 54-61, Vol. 60, No. 1	
	*	NOMEIR, A. A. et al. "Pharmacokinetics of SCH 56592, a new azole broad-spectrum antifungal agent, in mice, rats, rabbits, dogs, and cynomolgus monkeys" *Antimicrobial Agents and Chemotherapy*, March 2000, pp. 727-731, Vol. 44, No. 3.	
	*	ODDS, F. C. "Antifungal activity of saperconazole (R 66 905) *in vitro*" *Journal of Antimicrobial Chemotherapy*, 1989, pp. 533-537, Vol. 24.	
	*	OLENIK, B. et al. "Cooperative and anticooperative effects in the cocrystals of mono- and diazanaphthalenes with *meso*-1, 2-diphenyl-1,2-ethanediol" *Crystal Growth & Design*, 2003, pp. 175-181, Vol. 3, No. 2.	
	*	OLENIK, B. et al. "Supramolecular synthesis by cocrystallization of oxalic and fumaric acid with diazanaphthalenes" *Crystal Growth & Design*, 2003, pp. 183-188, Vol. 3, No. 2.	
	*	OSORIO-LOZADA, A. et al. "Synthesis and determination of the absolute stereochemistry of the enantiomers of adrafinil and modafinil" *Tetrahedron: Asymmetry*, 2004, 15:3811-3815.	
	*	OSWALD, I. et al. "Rationalisation of co-crystal formation through knowledge-mining" *Crystallography Reviews*, 2004, pp. 57-66, Vol. 10, No. 1.	
	*	OSWALD, I.D.H. et al. "The formation of paracetamol (acetaminophen) adducts with hydrogen-bond acceptors" *Acta Crystallographica Section B*, 2002, B58:1057-1066.	
	*	OTSUKA, M. et al. "Effect of Polymorphic Forms of Bulk Powders on Pharmaceutical Properties of Carbamazepine Granules" *Chem Pharm Bull*, 1999, 47(6):852-856.	
	*	OUYANG, X. et al. "Single-crystal-to-single-crystal topochemical polymerizations of a terminal diacetylene: two remarkable transformations give the same conjugated polymer" *J. Am. Chem. Soc.*, 2003, pp. 12400-12401, Vol. 125.	
	*	PATEL, U. et al. "Structure of the 1:1 complex between 4-amino-*N*-(4,6-dimethyl-2-pyrimidinyl)- benzenesulfonamide (sulfadimidine) and 2-hydroxybenzoic acid (salicylic acid)" *Acta Cryst.*, 1988, pp. 1264-1267, Vol. C44.	
	*	PEDIREDDI, V.R. et al. "Layered Structures Formed by Dinitrobenzoic Acids" *Tetrahedron Letters*, 1998, 39:9831-9834.	
	*	PRIVITERA, M. et al. "Dose-Ranging Trial with Higher Doses of Topiramate in Patients with Resistant Partial Seizures", *Amer. Epilepsy Soc. Proc.*, 1995, pg. 33, Vol. 36, Supp. 4.	
	*	QUEHENBERGER, H. "Concerning organic molecular compounds and their polymorphism" Monatshefte für Chemie, 1949, pp. 595-606, Vol. 80, No. 5.	
	*	RASENACK, N. et al. "Dissolution Rate Enhancement by *in Situ* Micronization of Poorly Water-Soluble Drugs" *Pharmaceutical Research*, December 2002, 19(12):1894-1900.	
	*	RECK, G. et al. "Crystal structures of the carbamazepine/ammonium chloride and carbamazepine/ammonium bromide adducts and their transformation into carbamazepine dihydrate" *Pharmazie*, 1991, pp. 509-512, Vol. 46, No. 7.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	25	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	REDDY, L. et al. "Phenyl-perfluorophenyl synthon mediated cocrystallization of carboxylic acids and amides" *Crystal Growth & Design*, 2004, pp. 89-94, Vol. 4., No. 1.	
	*	REMENAR, J. F. et al. "Celecoxib sodium salt: engineering crystal forms for performance" *CrystEngComm*, 2011, 13:1081-1089.	
	*	REMENAR, J. F. et al. "Crystal engineering of novel cocrystals of a triazole drug with 1,4-dicarboxylic acids" *J. Am. Chem. Soc.*, 2003, pp. 8456-8457, Vol. 125.	
	*	REYNOLDS, J. E. F. (ed). Martindale, The Extra Pharmacopoeia, 1993, The Pharmaceutical Press, London, England, 13th Edition, pp. 1431 (e.g., Acetaminophen, Aspirin, and Caffeine Tablets), 1465 (e.g., Aspirin plus C), 1521 (Codafen Continus), 1610 (Gaboril Complex).	
	*	ROBBINS, A. H. et al. "The crystal structure of the 1:2 adduct of potassium triiodide and 5,5-diethylbarbituric acid (barbital)" *American Crystallographic Association- Series 2 Papers and Abstracts*, 1973, p. 87.	
	*	ROSENFELD, W. E. "Topiramate: A Review of Preclinical, Pharmacokinetic, and Clinical Data" *Clinical Therapeutics*, 1997, 1916):1294-1308.	
	*	RUBINO, J.T. et al. "Influence of solvent composition on the solubilities and solid-state properties of the sodium salts of some drugs" *International Journal of Pharmaceutics*, 1990, 65:141-145.	
	*	SACHDEO, S.K. et al. "Topiramate: Double-Blind Trial as Monotherapy", *Amer. Epilepsy Soc. Proc.*, 1995, pg. 33, Vol. 36, Supp. 4.	
	*	SAKSENA, A. K. et al. "Advances in the chemistry of novel broad-spectrum orally active azole antifungals: recent studies leading to the discovery of SCH 56592" in Advances in the Chemistry of Novel Broad-Spectrum Orally Active Azole Antifunoals (Royal Soc. Chem., Cambridge), 1997, pp. 180-199.	
	*	SAKSENA, A. K. et al. "Concise asymmetric routes to 2,2,4-trisubstituted tetrahydrofurans via chiral titanium imide enolates: key intermediates towards synthesis of highly active azole antifungals SCH 51048 and SCH 56592" *Tetrahedron Letters*, 1996, pp. 5657-5660, Vol. 37, No. 32.	
	*	SALEM, M.S. et al. "Preparation, characterisation and transformation of terfenadine polymorphic forms" *International Journal of Pharmaceutics,* 1996, 141:257-259.	
	*	SALMON, J. et al. "Supramolecular chemistry of boronic acids (Abstract)" 38th Midwest Regional Meeting of the American Chemical Society in Columbia, MO., November 5-7, 2003, published by the American Chemical Society, Washington, D.C.	
	*	SCARBROUGH, F. et al. "Crystal structure of a complex between lumiflavin and 2,6-diamino-9-ethylpurine: a flavin adenine dinucleotide model exhibiting charge-transfer interactions" *Proc. Natl. Acad. Sci. USA*, November 1976, pp. 3807-3811, Vol. 73, No. 11.	
	*	SCHMIDT, G. "Photodimerization in the solid state" *Pure Appl. Chem.*, 1971, pp. 647-678, Vol. 27.	
	*	SHAN, N. et al. "Co-crystal of 4,7-phenanthroline and carboxylic acids: synthon competition and prediction" *Tetrahedron Letters*, 2002, pp. 8721-8725, Vol. 43.	
	*	SHAN, N. et al. "Crystal engineering using 4,4'-bipyridyl with di- and tricarboxylic acids" *Crystal Engineering*, 2002, pp. 9-24, Vol. 5.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	26	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	SHAN, N. et al. "Mechanochemistry and co-crystal formation: effect of solvent on reaction kinetics" *Chem. Commun.*, 2002, pp. 2372-2373.	
	*	SHAN, N. et al. "Supramolecular synthons in the co-crystal structures of 2-aminopyrimdine with diols and carboxylic acids" *Tetrahedron Letters*, 2002, pp. 3101-3104, Vol. 43.	
	*	SHATTOCK, T. R. et al. "Hierarchy of Supramolecular Synthons: Persistent Carboxylic Acid ••• Pyridine Hydrogen Bonds in Cocrystals that also contain a Hydroxyl Moiety" *Crystal Growth 7 Design*, 2008, pp. 4533-4545, Vol. 8, No. 12.	
	*	SHAVIV, R. et al. "Magnetochemistry of the tetrahaloferrate (III) ions 6. Crystal structure and magnetic ordering in $[(pyH)_3Cl]$ $[FeCl_4]_2$" *Inorganica Chimica Acta*, 1992, pp. 613-621, Vol. 198-200.	
	*	SHEFTER, E. "Structural studies on complexes IV: Crystal structure of a 1:1 5-chlorosalicylic acid and theophylline complex" *Journal of Pharmaceutical Sciences*, 1969, pp. 710-714, Vol. 58.	
	*	SHEFTER, E. et al., ACS, Abstr. Papers (Summer), 1970, 35, compound name: sulfathiazole-theophylline complex.	
	*	SHIMIZU, N. et al. "Structure of 2,4-diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine-5,5-diethylbarbituric acid (1:1)" *Acta Cryst.*, 1982, pp. 2309-2311, Vol. B38.	
	*	SIMONOV, Y. et al. "Structure of the caffeine-copper(II) acetate additional compound", *Izvestiya Akademii Nauk Moldavskoi SSR, Seriya Fiziko-Tekhnicheskikh i Matematicheskikh Nauk*, 1972, Vol. 3, pp. 83-84, abstract only.	
	*	SINGH, N. B. et al. "Solid state reaction between 8-hydroxyquinoline and *p*-nitrobenzoic acid" *Indian Journal of Chemistry*, May 1988, pp. 429-432, Vol. 37B.	
		SMITH et al., The Determination of the Crystal Structure of Anhydrous Theophylline by X-ray Powder Diffraction with a Systematic Search Algorithm, Lattice Energy Calculations, and ^{13}C and ^{15}N Solid-State NMR: A Question of Polymorphism in a Given Unit Cell. J Phys Chem B. 2001;105(24):5818-26.	
	*	SMITH et al., The utility of 4-aminobenzoic acid in promotion of hydrogen bonding in crystallization processes: the structures of the cocrystals with halo and nitro subsituted aromatic compounds, and the crystal structures of the adducts with 4-nitroaniline (1:1), 4-(4-nitrobenzyl)pyridine (1:2), and (4-nitrophenyl)acetic acid (1:1). J Chem Crystallogr. 1997 May; 27(5):307-317.	
	*	SMITH, D. et al. "Structure confirmation by single crystal X-ray diffraction of a series of new schiff bases and theoretical computations on 3-(N-2-α, α, α-triflourotoluylidene amino) tetrahydrothiophene-1, 1-dioxide (Abstract)" 216th ACS National Meeting in Boston, MA., August 23-27, 1998, published by the American Chemical Society, Washington, D.C.	
	*	SMITH, G. et al. "Interactions of aromatic carboxylic acids with quinolin-8-ol (oxine): Synthesis and the crystal structures of the proton-transfer compounds with the nitro-substituted benzoic acids" *Aust. J. Chem.*, 2001, pp. 171-175, Vol. 54.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	27	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	SMITH, G. et al. "Molecular cocrystals of carboxylic acids. XXI The role of secondary group interactions in adduct formation between 2-aminopyramidine and substituted benzoic acids: the crystal structures of the adducts with *o*-phthalic acid, *o*-nitrobenzoic acid, *o*-aminobenzoic acid and *m*-aminobenzoic acid" *Aust. J. Chem.*, 1995, pp. 1151- 1166, Vol. 48.	
	*	SMITH, G. et al. "The 1:1 adduct of 4-aminobenzoic acid with 4-aminobenzonitrile" *Acta Cryst.*, 2000, pp. 1155-1156, Vol. C56.	
	*	STAHL, P.H. *The Practice of Medicinal Chemistry*; "Chapter 35: Preparation of water-soluble compounds through salt formation" 1 January 2003, Elsevier, NL, pp. 601-615, XP002566271.	
	*	STAHLY, G. P. "A Survey of Cocrystals Reported prior to 2000" *Crystal Growth & Design*, 2009, 9:4212-4229.	
	*	STALKER, R. et al. "Asymmetric synthesis of two new conformationally constrained lysine derivatives" *Tetrahedron*, 2002, pp. 4837-4849, Vol. 58.	
	*	STEINER, T. "Donor and acceptor strengths in C-H•••0 hydrogen bonds quantified from crystallographic data of small solvent molecules" *New. J. Chem.*, 1998, pp. 1099-1103.	
	*	STEZOWSKI, J. J. et al. "Characterization of a 1:1 complex of an unusual structure in the phenothiazine/phenazine binary phase diagram" *Zeitschrift fur Kristallographie* in International Journal for Structural, Physical, Chemical Aspects of Crystalline Materials, 1983, pp. 213-215, Vol. 162, No. 1-4.	
	*	STOREY, R. et al. "Automation of solid form screening procedures in the pharmaceutical industry- how to avoid the bottlenecks" *Crystallography Reviews*, 2004, pp. 45-56, Vol. 10, No. 1.	
	*	SUMMERS, M.P. et al. "The polymorphism of aspirin" *J. Pharm. Pharmac.*, 1970, 22:615-616.	
	*	SZAFRAN, M. et al. "Molecular structures and hydrogen bonding in the 1:1 and 1:2 complexes of pyridine betaine with 2,6-dichloro-4-nitrophenol; an example of strongly coupled hydrogen bonds, 0-H•••O=C-0-H•••0-" *Journal of Molecular Structure*, 1997, pp. 145-160, Vol. 416.	
	*	TAKEUCHI, M. et al. "Synchrotron radiation SAXS/WAXS study of polymorph-dependent phase behavior of binary mixtures of saturated monoacid triacylglycerols" *Crystal Growth & Design*, 2003, pp. 369-374, Vol. 3, No. 3.	
	*	TANG, C. P. et al. "Reaction pathways in crystalline host-guest inclusion complexes: rotation by a net 180° of the acetyl group on photoaddition of guest- acetophenone and —*m*-Chloroacetophenone to the atom C5 of host deoxycholic acid" *J. Am. Chem. Soc.*, 1985, pp. 4058-4070, Vol. 107.	
	*	TAYLOR, R. et aL "Rules governing the crystal packing of mono- and dialcohols" *Acta Crystallographica Section B, Structural Science*, 2001, pp. 815-827, Vol. B57.	
	*	THALLAPALLY, P. et al. "Polymorphism of 1,3,5-trinitrobenzene induced by a trisindane additive" *Angew. Chem. Mt. Ed.*, 2004, pp. 1149-1155, Vol. 43.	
	*	THAYER, A.M. et al. "Form and Function" *Chemical & Engineering News*, June 18, 2007, 85(25):17-30 (8 pages).	
	*	TIMMERMAN, P. et al. "Noncovalent Assembly of functional groups on calix[4]arene molecular boxes" *Chem. Eur. J.*, 1997, pp. 1823-1832, Vol. 3., No. 11.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	28	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	TOMURA, M. et al. "One-dimensional zigzag chain structures with intermolecular C-H•••π and C-H•••O interactions consisted of phthalic acid and pyridine derivatives" *Chemistry Letters*, 2001, pp. 532-533.	
	*	TRASK, A. et al. "Crystal engineering of organic cocrystals by the solid-state grinding approach" *Top Curr. Chem.*, 2005, pp. 41-70, Vol. 254.	
	*	TRASK, A. et al. "Pharmaceutical cocrystallization: engineering a remedy for caffeine hydration" *Crystal Growth & Design*, 2005, pp. 1013-1021, Vol. 5, No. 3.	
	*	TRASK, A. et al. "Solvent-drop grinding: green polymorph control of cocrystallisation" *Chem. Commun.*, 2004, pp. 890-891 in addition to supplemental materials.	
	*	TROWBRIDGE, L. et al. "Composites for nonlinear optics: Crystal growth and polymorphism" *University of Sussex, Falmer Brighton UK, School of Chemistry and Molecular Sciences*, pp. 272.	
	*	UNO, T. et al. "Structure of 5,5-diphenylhydantoin-1- (4-bromophenyl)-4-dimethylamino-2,3-dimethyl-3-pyrazolin-5-one (1:1)" *Acta Cryst.*, 1980, pp. 2794-2796, Vol. B36.	
	*	URBINA, J. et al. "Supramolecular design of inorganic/organic networks using flexible ligands with self-complementary hydrogen bonds (Abstract)" 38th Midwest Regional Meeting of the American Chemical Society in Columbia, MO., November 5-7, 2003, published by the American Chemical Society, Washington, D.C.	
	*	VAN ROEY, P. et al. "Structure of *cis*-1-{[4-(1-imidazolylmethyl) cyclohexyl] methyl} imidazole- succinic acid complex" *Acta Cryst.*, 1991, pp. 1015-1018, Vol. C47.	
	*	VAN ROEY, P. et al. "Structure-activity studies of non-steroidal aromatase inhibitors: the crystal and molecular structures of CGS 16949A and CGS 18320B" *J. Enzyme Inhibition*, 1991, pp. 119-132, Vol. 5.	
	*	VILLA, L. A. et al. "Central nervous system paracoccidioidomycosis. Report of a case successfully treated with itraconazol" *Rev. Inst. Med. Trop. S. Paulo*, July-August, 2000, pp. 231-234, Vol. 42, No. 4.	
	*	VIPPAGUNTA, S. R. et al. "Crystalline solids" *Advanced Drug Delivery Reviews*, 2001, pp. 3-26, Vol. 48.	
	*	VISHWESHWAR, P. et al. "Crystal engineering of pharmaceutical co-crystals from polymorphic active pharmaceutical ingredients" *Chem. Commun.*, 2005, pp. 4601-4603.	
	*	VISHWESHWAR, P. et al. "Molecular complexes of homologous alkanedicarboxylic acids with isonicotinamide: X-ray crystal structures, hydrogen bond synthons, and melting point alternation" *Dotal Growth & Design*, 2003, pp. 783-790, Vol. 3, No. 5.	
	*	VISHWESHWAR, P. et al. "Recurrence of carboxylic acid- pyridine supramolecular synthon in the crystal structures of some pyrazinecarboxylic acids" *J. Org. Chem.*, 2002, pp. 556-565, Vol. 67.	
	*	VISHWESHWAR, P. et al. "Supramolecular synthons based on N-H•••N and C-H•••0 hydrogen bonds. Crystal engineering of a helical structure with 5,5-diethylbarbituric acid" *Chem. Commun.*, 2002, pp. 1830-1831.	
	*	VISHWESHWAR, P. et al. "Supramolecular synthons in phenol-isonicotinamide adducts" *Cryst Eng. Comm.* 2003, pp. 164-168, Vol. 5, No. 31.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	29	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	VOET, D. et al. "Barbiturates and adenine derivatives. Molecular structure of a hydrogen-bonded complex" *Joumal of the American Chemical Society*, August 9, 1972, pp. 5888- 5891, Vol. 94, No. 16.	
	*	VOET, D. et al. "The crystal and molecular structure of the intermolecular complex 9-ethyladenine-5, 5-diethylbarbituric acid" *Journal of the American Chemical Society*, November 15, 1972, pp. 8213-8222, Vol. 94, No. 23.	
	*	VOET, D. et al. "The structure of an intermolecular complex between cytosine and 5-fluorouracil" *Journal of the American Chemical Society*, May 21, 1969, pp. 3069-3075, Vol. 91, No. 11.	
	*	WALSH, R.D.B. et al. " Crystal Engineering of the composition of pharmaceutical phases". *Chem. Commun.*, 2003, pp. 186-187.	
	*	WANG, A. et al. "Crystal structure of 1:1 complex of barbital with 1-methylimidazole" *Journal of Pharmaceutical Sciences*, March 1979, pp. 361-363, Vol. 68, No. 3.	
	*	WEBER, E. et al. "Synthesis of new Schiff bases: reaction of monofluorobenzaldehydes with 3-aminosulfolane hydrochloride (Abstract)" 216th ACS National Meeting in Boston, MA., August 23-27, 1998, published by the American Chemical Society, Washington, D.C.	
	*	WEISSBUCH, I. et al. "Crystal morphology control with tailor-made additives; a stereochemical approach" *Advances in Crystal Growth Research*, 2001, pp. 381-400.	
	*	WEISSBUCH, I. et al. "Understanding and Control of Nucleation, Growth, Habit, Dissolution and Structure of Two- and Three-Dimensional Crystals Using 'Tailor-Made' Auxiliaries" *Acta Cryst.*, 1995, B51:115-148.	
	*	WEST, A. R., "Solid Solutions" In: Solid State Chemistry and its Applications, 1988, p. 358, p. 365, Wiley, NY.	
	*	WHEATLEY, P.J., "The Crystal and Molecular Structure of Aspirin," *J. Chem. Soc.*, 1964, pp. 6036- 6048.	
	*	WIEDENFELD, H. et al. "Solubilization of aminophenazone" *Arch. Pharm.*, 1982, pp. 633- 641, Vol. 315.	
	*	WIEDENFELD, H. et al. "The crystal structure of the theophylline-urea complex" *Arch. Pharm.*, 1986, pp. 654-659, Vol. 319.	
	*	WOOD, R. A. et at "2,5-O-methylene-D-mannitol sodium-chloride, $C_7 H_{14} O_6$. NaCl" *Cryst. Struct. Comm.*, 1976, 207-210, Vol. 5.	
	*	WUNDERLICH, H.F. et al. " The Derivatives of carbamazepine with ammonium halogenides and formamide" *Pharmazie*, 1991,46(7):507-509.	
	*	XU, J. et al. "Effect of composition distribution on miscibility and co-crystallization phenomena in the blends of low density polyethylene with conventional and metallocene-based ethylene-butene copolymers" *Polymer*, 2001, pp. 3867-3874, Vol. 42.	
	*	YADAV, A.V. et al. "Co-crystals: A novel approach to modify physicochemical properties of active pharmaceutical ingredients" *Indian Journal of Pharmaceutical Sciences*" 2009, 71(4):359-370.	
	*	YOO, J. et at "Cocrystallization of a dinuclear platinum complex as a monomer and a one-dimensional polymer" *Polyhedron*, 2002, pp. 715-719, Vol. 21.	

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	30	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	ZAITU, S. et al. "1:1 Molecular complex of theophylline and *p*-nitroaniline" *Acta Cryst.*, 1995, pp. 2390-2392, Vol. C51.	
	*	ZAITU, S. et al. "A 2:1 molecular complex of theophylline and 5-fluorouracil as the monohydrate" *Acta Cryst.*, 1995, pp. 1857-1859, Vol. C51.	
	*	ZAMAN, M. B. et al. "Crystal Engineering Using Anilic Acids and Dipyridyl Compounds through a New Supramolecular Synthon" *J. Org. Chem.*, 2001, pp. 5987-5995, Vol. 66.	
	*	ZAMAN, M. B. et at "Linear hydrogen-bonded molecular tapes in the cocrystals of squaric acid with 4,4'-dipyridylacetylene and 1,2-bis(4-pyridyl) ethylene" *Acta Cryst.*, 2001, pp. 621-624, Vol. C57.	
	*	ZAMAN, M.B. et al. "Crystal Engineering Using Anilic Acids and Dipyridyl Compounds through a New Supramolecular Synthon" *J. Org. Chem.*, 2001, 66:5987-5995.	
	*	ZAWOROTKO, M. J. "Crystal Engineering of Diamondoid Networks", *Chem. Soc. Rev.*, 1994, pp. 283-288, Vol. 23.	
	*	ZAWOROTKO, Michael J., "Binary Crystals by Design," Abstracts of Papers, 23rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002, IEC-030.	
	*	ZERKOWSKI, J. et al. "Design of organic structures in the solid state: hydrogen-bonded molecular "tapes"[1]" *J. Am. Chem. Soc.*, 1990, pp. 9025-9026, Vol. 112.	
	*	ZERKOWSKI, J. et al. "Design of organic structures in the solid state: molecular tapes based on the network of hydrogen bonds present in the cyanuric acid•melamine complex" *J. Am. Chem. Soc.*, 1994, pp. 2382-2391, Vol. 116.	
	*	ZERKOWSKI, J. et al. "Investigations into the robustness of secondary and tertiary architecture of hydrogen-bonded crystalline tapes" *Chem. Mater*, 1994, pp. 1250-1257, VoI. 6.	
	*	ZERKOWSKI, J. et al. "New varieties of crystalline architecture produced by small changes in molecular structure in tape complexes of melamines and barbiturates" *J. Am. Chem. Soc.*, 1994, pp. 4305-4315, Vol. 116.	
	*	ZERKOWSKI, J. et al. "Polymorphic packing arrangements in a class of engineered organic crystals" Chem. Mater., 1997, pp. 1933-1941, Vol. 9.	
	*	ZERKOWSKI, J. et al. "Solid-state structures of "Rosette" and "Crinkled Tape" motifs derived from the cyanuric acid-melamine lattice" *J. Am. Chem. Soc.*, 1992, pp. 5473-5475, Vol. 114.	
	*	ZERKOWSKI, J. et al. "Steric control of secondary, solid-state architecture in 1:1 complexes of melamines and barbiturates that crystallize as crinkled tapes" *J. Am. Chem. Soc.*, 1994, pp. 4298-4304, Vol. 116.	
	*	ZHANG, R. et al. "Atmospheric new particle formation enhanced by organic acids" *Science*, June 4, 2004, pp. 1487-1490 with additional supporting online material, Vol. 304.	
	*	ZHU, H. et al. "Influence of water activity in organic solvent + water mixtures on the nature of the crystallizing drug phase. 1. theophylline" *International Journal of Pharmaceutics*, 1996, pp. 151-160, Vol. 135.	

[NOTE – No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR § 1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR § 1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR § 1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. § 120.]

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

Electronic Acknowledgement Receipt

EFS ID:	34253019
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Chelsie Bailey
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	08-NOV-2018
Filing Date:	30-JUN-2017
Time Stamp:	15:33:19
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	CA1148020A1.pdf	1069724 63d21f07e46a9e6b5155f030b13a1e9212b5a14f	no	29

Warnings:

Information:					
2	Other Reference-Patent/App/Search documents	U015770023WO00_ISR_mailed_10-24-2003_QC.pdf	322961 670b5740aa18e0f8aeca9e68a6db7a782bcbe326	no	9
Warnings:					
Information:					
3	Non Patent Literature	The_Merck_Index_12th_ed_1996_Entries_5683_9094_QC.pdf	835931 e1eadff9e41f657b41af609497c359a81ebfb6c7	no	4
Warnings:					
Information:					
4	Non Patent Literature	Ito_et_al_Tetrahedron_2000_v56_p6833_QC.PDF	749913 0849a9d3ede60fc6395e7d6725f72fa47ae4590f	no	12
Warnings:					
Information:					
5	Non Patent Literature	Iwamoto_et_al_Acta_Cryst_1989_vC45_p1110_QC.PDF	226687 aecef3be960afc2318ea5de13ba39a3772056dc6	no	3
Warnings:					
Information:					
6	Non Patent Literature	Jiang_et_al_Anti_Cancer_Drugs_2000_v11_p49_QC.pdf	131612 40fcf2a53ba8adc161936d35ab131d475309ba6b	no	6
Warnings:					
Information:					
7	Non Patent Literature	Smith_et_al_J_Phys_Chem_B_2001_v105_p5818_QC.pdf	357514 ae64037c687307745d3745db337f903ef99fef76	no	9
Warnings:					
Information:					
8	Miscellaneous Incoming Letter	U015770023US03-TRN-DFC.pdf	26275 d568ff74609eccf71fac4c9c103f1c6e97e26a9b	no	1
Warnings:					
Information:					

9	Transmittal Letter	U015770023US03-IDSBODY-DFC.pdf	31149 95e840f3d2f8196732c86b582bd3ce25908abeae	no	3
Warnings:					
Information:					
10	Information Disclosure Statement (IDS) Form (SB08)	U015770023US03-IDS1449-DFC.pdf	300166 9b90f04e3fa7ef0639ffac421f5b09e733618edd	no	30
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
11	Other Reference-Patent/App/Search documents	U015770023EP00_ESR_mailed_11-22-2006_QC.pdf	516809 d76f239178f9c8ff9ecaf1b3ea62fb31d0300fe5	no	4
Warnings:					
Information:					
		Total Files Size (in bytes):	4568741		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/06662

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C233/25 C07C69/86 C07D233/74 C07C57/30 C07C57/58
C07D223/26 C07D213/22 C07D213/16 C07C47/544 C07D213/82
C07D275/06 C07D213/80 C07C53/08 C07C61/125 C07C50/04

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C C07D

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	BAILEY WALSH ET AL.: "Crystal engineering of the composition of pharmaceutical phases" CHEM. COMMUN., 2003, pages 186-187, XP002248827 the whole document	1-20,22
P,X	OSWALD, I.D.H. ET AL.: "The formation of paracetamol (acetaminophen) adducts with hydrogen-bond acceptors" ACTA CRYST., vol. B58, 2002, pages 1057-1066, XP009014505 the whole document	1-9, 11-19,21

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 July 2003	24. 10. 03

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Johnson, C.

Form PCT/ISA/210 (second sheet) (July 1992)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 163 of 415

INTERNATIONAL SEARCH REPORT

International Application No
PCT/ 03/06662

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EL-NAHHAS S A: "PHYSICO-CHEMICAL CHARACTERISTICS OF CARBAMAZEPINE-BETA-CYCLODEXTRININ CLUSION COMPOUNDS AND CARBAMAZEPINE-PEG SOLID DISPERSIONS" PHARMAZIE, VEB VERLAG VOLK UND GESUNDHEIT. BERLIN, DD, vol. 51, no. 12, 1 December 1996 (1996-12-01), pages 960-963, XP000633833 ISSN: 0031-7144 paragraph [3.2.4.3]	1-9, 11-19,24
X	JAMES E. F. REYNOLDS, EDITOR: "Martindale. The extra pharmacopoeia" 1993, THE PHARMACEUTICAL PRESS , LONDON , XP002248828 page 1431 (e.g. acetaminophen, aspirin, and caffeine tablets), page 1465 (e.g. Aspirin plus C), page 1521 (Codafen Continus), page 1610 (Gaboril Complex)	1-9, 11-23
X	GB 1 297 261 A (E.R. SQUIBB & SONS INC.) 22 November 1972 (1972-11-22) the whole document	1-9, 11-19,21

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 164 of 415

INTERNATIONAL SEARCH REPORT

In ional application No.
PCT/US 03/06662

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 25,29,33
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iii) PCT - Scheme, rules and method for performing mental acts
The methods of independent claims 25, 29 and 33 comprise 4 purely intellectual steps and therefore constitute methods for performing mental acts, for which no search is necessary.

2. [X] Claims Nos.: 1-9,11-24
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

10, 26-28, 30-32, 34-36 (all part)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 165 of 415

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 25,29,33

Rule 39.1(iii) PCT - Scheme, rules and method for performing mental acts

The methods of independent claims 25, 29 and 33 comprise 4 purely intellectual steps and therefore constitute methods for performing mental acts, for which no search is necessary.

Continuation of Box I.2

Claims Nos.: 1-9,11-24

The technical features of claim 1 are: i) a solid composition ii) having at least 2 components iii) at least one of which is a pharmaceutical molecule.

Pharmaceuticals which are administered in a solid form (e.g. as tablets) rarely contain 100% pharmaceutical - in the majority of cases other components such as fillers are present. All such pharmaceutical compositions fall within the scope of claim 1. None of the features of dependent claims 2-9 appear to add any characteristic that would distinguish the subject matter of these claims from the vast majority of solid pharmaceutical compositions currently on the market. An extract of "Martindale" has been cited to illustrate examples of compositions falling within the scope of claim 9 (see e.g. acetaminophen, aspirin and caffeine tablets, acetaminophen and codeine tablets, aspirin and ascorbic acid). Pharmazie 51 (1996) 12 960-963 is cited to illustrate an example of a carbamazepine composition falling within present claim 9. The dependent claims 11-24 also do not contain any feature that would distinguish their subject matter from well-known pharmaceutical preparations such as those cited in the documents mentioned above.

In view of the huge number of pharmaceutical compositions that fall within the scope of present claims 1-9 and 11-24, of which the compositions cited above form only an arbitrary selection, it is not possible to perform any meaningful search of these claims.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 166 of 415

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 167 of 415

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are acetaminophen, 4,4'-bipyridine and water, and its method of preparation.

---

2. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are phenytoin and pyridine, and its method of preparation.

---

3. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are aspirin and 4,4'-bipyridine, and its method of preparation.

---

4. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are ibuprofen and 4,4'-bipyridine, and its method of preparation.

---

5. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are flurbiprofen and 4,4'-bipyridine, and its method of preparation.

---

6. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are flurbiprofen and trans-1,2-bis(4-pyridyl)ethylene, and its method of preparation.

---

7. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and p-phthalaldehyde, and its method of preparation.

---

8. claims: 10, 26-28, 30-32, 34-36 (all part)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 168 of 415

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Composition according to claim 1 wherein the two or more components are carbamazepine and nicotinamide, and its method of preparation.

---

9. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and saccharin, and its method of preparation.

---

10. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and 2,6-pyridinedicarboxylic acid, and its method of preparation.

---

11. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and 5-nitroisophthalic acid, and its method of preparation.

---

12. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and acetic acid, and its method of preparation.

---

13. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and 1,3,5,7-adamantanetetracarboxylic acid, and its method of preparation.

---

14. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and benzoquinone, and its method of preparation.

---

15. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and butyric acid, and its method of preparation.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 169 of 415

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

16. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and dimethyl sulfoxide, and its method of preparation.

---

17. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and formamide, and its method of preparation.

---

18. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and formic acid, and its method of preparation.

---

19. claims: 10, 26-28, 30-32, 34-36 (all part)

Composition according to claim 1 wherein the two or more components are carbamazepine and trimesic acid, and its method of preparation.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 170 of 415

INTERNATIONAL SEARCH REPORT

mation on patent family members

International Application No
PCT/US 03/06662

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 1297261 A	22-11-1972	CA 948642 A1	04-06-1974
		CH 507253 A	15-05-1971
		DE 2000210 A1	23-07-1970
		FR 2034467 A1	11-12-1970

Form PCT/ISA/210 (patent family annex) (July 1992)

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM *(to be used for all correspondence after initial filing)*	Application Number	15/639,223-Conf. #8089
	Filing Date	June 30, 2017
	First Named Inventor	Michael J. Zaworotko
	Art Unit	1625
	Examiner Name	N. E. Jarrell
Total Number of Pages in This Submission	Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

☐ Fee Transmittal Form	☐ Drawing(s)	☐ After Allowance Communication to TC
☐ Fee Attached	☐ Licensing-related Papers	☐ Appeal Communication to Board of Appeals and Interferences
☐ Amendment/Reply	☐ Petition	☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
☐ After Final	☐ Petition to Convert to a Provisional Application	☐ Proprietary Information
☐ Affidavits/declaration(s)	☐ Power of Attorney, Revocation Change of Correspondence Address	☐ Status Letter
☐ Extension of Time Request	☐ Terminal Disclaimer	☒ Other Enclosure(s) (please Identify below):
☐ Express Abandonment Request	☐ Request for Refund	Form PTO-1449
☒ Information Disclosure Statement	☐ CD, Number of CD(s) _____	Copies of cited references
☐ Certified Copy of Priority Document(s)	☐ Landscape Table on CD	
☐ Reply to Missing Parts/ Incomplete Application	Remarks	
☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	November 8, 2018	Reg. No.	73,490

Certificate of Electronic Filing under 37 CFR § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 8, 2018 Electronic Signature for Chelsie Bailey: /Chelsie Bailey/

6224460.1

DOCKET NO.: U0157.70023US03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1625

Certificate of Electronic Filing under 37 CFR §1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 8, 2018 Electronic Signature for Chelsie Bailey: /Chelsie Bailey/

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF DISCLOSURE UNDER 37 C.F.R. §§ 1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, the undersigned requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. § 1.97

This Information Disclosure Statement has been filed before the mailing of a first Office Action on the merits in the above-identified case.

No fee or certification is required.

PART II: Information Cited

The undersigned hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified PTO/SB/08). The order of presentation of the references should not be construed as an indication of the importance of the references.

The undersigned hereby makes the following additional information of record in the above-identified application.

The undersigned would like to bring to the Examiner's attention the following co-pending applications that may contain subject matter related to this application:

Serial No.	Filing Date	Inventor(s)	Docket No.
*10/378,956	March 3, 2003	Zaworotko et al.	U0157.70023US01
*14/179,862	February 13, 2014	Zaworotko et al.	U0157.70023US02

*A copy of this reference is not provided as the Office has waived the requirement under 37 C.F.R. § 1.98(a)(2)(iii) for submitting a copy of a cited U.S. patent application if it is scanned to the Image File Wrapper system and is available on Private PAIR .

The undersigned would like to bring to the Examiner's attention the enclosed search report or other communication from a corresponding or related International or Foreign National Application:

Serial No.	Date of Mailing	Type(s) of Communication	Docket No.
EP 03711407.1	11-22-2006	European Search Report	U0157.70023EP00
PCT/US2003/06662	10-24-2003	International Search Report	U0157.70023WO00

PART III: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;

2. The enclosed form PTO-1449 (modified PTO/SB/08) be signed by the Examiner to evidence that the cited information has been fully considered by the United States Patent and Trademark Office during the examination of this application;

3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the undersigned makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. § 102.

Notwithstanding any statements by the undersigned, the Examiner is urged to form his or her own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

The Director is hereby authorized to charge any deficiency or credit any overpayment in the fees occasioned by the filing of this Information Disclosure Statement to our Deposit Account No. 23/2825 under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Respectfully submitted,

By: /David F. Cauble/

David F. Cauble, PhD, JD, Reg. No. 73,490
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
Telephone: (617) 646-8000

Docket No.: U0157.70023US03
Date: November 8, 2018

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/639,223	Filing Date 06/30/2017	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT **11/08/2018**

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 14	Minus	** 36	= 0	X $50 =	0
Independent (37 CFR 1.16(h))	* 1	Minus	***9	= 0	X $230 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	**0**

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

SLIE
SHARON M. WEST

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 02/26/2019

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
02/26/2019	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Office Action Summary	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.	
	Examiner NOBLE E JARRELL	**Art Unit** 1625	**AIA Status** No

-- 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 08 November 2018.

☐ 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) 37-50 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 37-50 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 30 June 2017 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 8 November 2018.

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

4) ☐ Other: _____.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 178 of 415

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Election/Restrictions

Applicant's election without traverse of a cocrystal of an active pharmaceutical ingredient and a conformer in the reply filed on 8 November 2018 is acknowledged.

Information Disclosure Statement

The information disclosure statements filed 8 November 2018 are acknowledged and considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

> (a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-50 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, because the specification, while being enabling for preparation of cocrystals of examples 1-17 in specification, does not reasonably provide enablement for preparation of the scope of cocrystals claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some

experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a stoichiometric cocrystal of an active pharmaceutical ingredient and a coformer. Thus, the claims taken together with the specification imply a stoichiometric cocrystal can be formed.

The state of the prior art and (4) the predictability or unpredictability of the art:

KUMAR (*Indian Journal of Pharmaceutical Sciences*, **2017**, *79(6)*, 858-71) describes that many steps are required to make a cocrystal (page 862, column 2, paragraph 3 to page 865, column 1, paragraph 1). Additionally, different methods of making cocrystalas are known (page 865, column 1, paragraph 2 to page 866, column 1, paragraph 4). The formation of cocrystals has challenges: selection of a suitable conformer and stability in the presence of excipients (page 867, column 2, paragraph 2 to page 868, column 1, paragraph 2). Development, screening, and evaluation of a new cocrystals of drugs require lot of time due to the steps required for each part.

The relative skill of those in the art:

While the artisan generally would have an advanced degree in cocrystal formation and analysis, their high level of skill and knowledge is insufficient to overcome the lack of understanding as to how cocrystal formation occurs.

The amount of direction or guidance presented and the presence or absence of working examples:

The specification has provided guidance for preparation of the following cocrystals (examples 1-17 in specification):acetaminophen: 4,4'-bipyridine:water (1:1:1); phenytoin/pyridine (1:1); aspirin and 4,4'-bipyridine (2:1); ibuprogen and 4,4'-bipyridine (2:1); flurbiprofen and [4,4'-bipyridine or trans-1,2-bis(4-pyridyl)ethylene] (2:1); carbamazepine and [one of *p*-phthalaldehyde, nicotinamide, saccharin, 5-nitroisophthalic acid, acetic acid, 1,3,5,7-adamantanetetracarboxylic acid, benzoquinone, butyric acid, DMSO, or formamide] (1:1); carbamazepine and 2,6-pyridinecarboxylic acid (2:3)

However, the specification does not provide guidance for the scope of stoichiometric cocrystals claimed.

The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to cocrystal formation and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 102

In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

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

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 37-42, 45, 46, and 48 is/are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by HSU (*Acta Crystallographica*, **1974**, *B30*, 843-846, cited in IDS). Hsu describes a 1:1 cocrystal of salicylamide and 5-ethyl-5-isoamylbarbituric acid (title and abstract). Hydrogen bonding is used to bind the compounds together (abstract; page 845, column 2 to page 846, column 1, paragraph 1).

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 conflicting claims 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 re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *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 nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application,

or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) 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 www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 37-50 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37and 45 of copending Application No. 14/179862 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of 14/179862. Claim 37 of '862 overlaps with instant claims 37 and 39. Claim 45 of '862 is embraced by instant claims 37 and 40.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Conclusion

Claims 37-50 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE E JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on 8:00 AM to 5:00 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Kosar can be reached on 571-372-0913. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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.

/NOBLE E JARRELL/
Primary Examiner, Art Unit 1625

Notice of References Cited	Application/Control No. 15/639,223	Applicant(s)/Patent Under Reexamination Zaworotko et al.	
	Examiner NOBLE E JARRELL	Art Unit 1625	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
	A					
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	KUMAR. Indian Journal of Pharmaceutical Sciences, 2017, 79(6), 858-71. (Year: 2017)
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 185 of 415

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/639,223	Zaworotko et al.
	Examiner	Art Unit
	NOBLE E JARRELL	1625

CPC - Searched*		
Symbol	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystalcocrystals co near crystals).clm.	02/19/2019	NJ

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystalcocrystals co near crystals).clm.	02/19/2019	NJ
stn registry and hcaplus	02/19/2019	NJ
inventor search in PALM and EAST	02/19/2019	NJ

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
C07D	223/26	02/19/2019	NJ

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1625	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 186 of 415

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	1	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite No.	U.S. Patent Document Number	U.S. Patent Document Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY
		2,554,816		Clapp et al.	05-29-1951
		2,665,277		Homeyer et al.	01-05-1954
		2,711,411		Holbert et al.	06-21-1955
		2,980,679		Gianfranco	04-18-1961
		3,028,420		Petrow et al.	04-03-1962
		3,536,809		Schaller et al.	04-09-1991
		3,598,123		Zaffaroni	08-10-1971
		3,664,858		Huffman	05-23-1972
		3,845,770		Theeuwes et al.	11-05-1974
		3,916,899		Theeuwes et al.	11-04-1975
		3,970,651		Kaplan et al.	07-20-1976
		4,008,321		Kamishita et al.	02-15-1977
		4,008,719		Theeuwes et al.	02-22-1977
		4,198,507		Barry et al.	04-15-1980
		4,267,179		Heeres et al.	05-12-1981
		4,368,197		Shefter et al.	01-11-1983
		4,513,006		Maryanoff et al.	04-23-1995
		4,764,604		Muller	08-16-1988
		4,792,569		Maryanoff et al.	12-20-1988
		4,853,379		Shroot et al.	08-01-1989
		4,916,134		Heeres et al.	04-10-1990
		4,925,674		Giannini et al.	05-15-1990
		4,927,855		Lafon	05-22-1990
		4,994,604		Tung et al.	02-19-1991
		5,006,513		Hector et al.	04-09-1991
		5,023,092		DuRoss	07-11-1991
		5,059,595		Le Grazie	10-22-1991

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	2	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		5,073,543		Marshall et al.	12-17-1991
		5,120,548		McClelland et al.	06-09-1992
		5,177,262		Taylor et al.	01-15-1993
		5,242,942		Costanzo et al.	09-07-1993
		5,258,402		Maryanoff	11-02-1993
		5,273,760		Oshlack et al.	12-28-1993
		5,286,493		Oshlack et al.	02-15-1994
		5,324,351		Oshlack et al.	06-28-1994
		5,332,834		Bhattacharya et al.	07-26-1994
		5,338,644		Taylor et al.	08-16-1994
		5,354,556		Sparks et al.	10-11-1994
		5,356,467		Oshlack et al.	10-18-1994
		5,366,738		Rork et al.	11-22-1994
		5,380,867		Bhattacharya et al.	01-10-1995
		5,384,327		Costanzo et al.	01-24-1995
		5,387,700		Maryanoff et al.	02-07-1995
		5,412,094		Amos et al.	05-02-1995
		5,414,997		Tailer	05-16-1995
		5,466,823		Talley et al.	11-14-1995
		5,472,712		Oshlack et al.	12-05-1995
		5,474,997		Gray et al.	12-12-1995
		5,510,496		Talley et al.	04-23-1996
		5,521,207		Graneto	05-28-1996
		5,523,090		Znaiden et al.	06-04-1996
		5,563,165		Talley et al.	10-08-1996
		5,591,767		Mohr et al.	01-07-1997
		5,614,342		Molaire et al.	03-25-1997
		5,631,250		Bunnell et al.	05-20-1997
		5,633,015		Gilis et al.	05-27-1997
		5,633,272		Talley et al.	05-27-1997
		5,635,535		Wagstaff	06-03-1997

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)	APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
	FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet 3 of 30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		5,639,476		Oshlack et al.	06-17-1997
		5,641,512		Cimiluca	06-24-1997
		5,661,151		Saksena et al.	08-26-1997
		5,674,533		Santus et al.	10-07-1997
		5,703,232		Bunnell et al.	12-30-1997
		5,707,975		Francois et al.	01-13-1998
		5,733,566		Lewis	03-31-1998
		5,736,541		Bunnell et al.	04-07-1998
		5,753,688		Talley et al.	05-19-1998
		5,753,693		Shank	05-19-1998
		5,760,007		Shank et al.	06-02-1999
		5,760,068		Talley et al.	06-02-1998
		5,932,598		Talley et al.	08-03-1999
		5,935,933		Shank et al.	08-10-1999
		5,952,187		Stenglein et al.	09-14-1999
		5,972,986		Seibert et al.	10-26-1999
		5,985,902		Talley et al.	11-16-1999
		5,994,365		Zaworotko et al.	11-30-1999
		5,998,380		Ehrenberg et al.	12-07-1999
		5,998,413		Heeres et al.	12-07-1999
		6,001,996		Amos et al.	12-14-1999
		6,054,136		Farah et al.	04-25-2000
		6,071,537		Shank	06-06-2000
		6,132,420		Dionne et al.	10-17-2000
		6,156,781		Talley et al.	12-05-2000
		6,191,117	B1	Kozachuk	02-20-2001
		6,201,010	B1	Cottrell	03-13-2001
		6,245,357	B1	Edgren et al.	06-12-2001
		6,268,385	B1	Whittle et al.	07-31-2001
		6,270,787	B1	Ayer	08-07-2001
		6,283,953	B1	Ayer et al.	09-04-2001

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	4	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		6,287,295	B1	Chen et al.	09-11-2001
		6,294,186	B1	Beerse et al.	09-25-2001
		6,294,192	B1	Patel et al.	09-25-2001
		6,319,903	B1	Carrazana et al.	11-20-2001
		6,323,266	B2	Phillips	11-27-2001
		6,333,050	B2	Wong et al.	12-25-2001
		6,342,249	B1	Wong et al.	01-29-2002
		6,348,458	B1	Hamied et al.	02-19-2002
		6,365,185	B1	Ritschel et al.	04-02-2002
		6,368,626	B1	Bhatt et al.	04-09-2002
		6,375,978	B1	Kleiner et al.	04-23-2002
		6,384,034	B2	Simitchieva et al.	05-07-2002
		6,403,640	B1	Stoner et al.	06-11-2002
		6,413,965	B1	Mylari	07-02-2002
		6,420,394	B1	Supersaxo	07-16-2002
		6,488,962	B1	Berner et al.	12-03-2002
		6,503,884	B1	Ehrenberg et al.	01-07-2003
		6,559,293	B1	Almarsson et al.	05-06-2003
		6,570,036	B1	Reuter	05-27-2003
		6,579,895	B2	Karim et al.	06-17-2003
		6,613,790	B2	Jeffrey Carter	09-02-2003
		6,699,840	B2	Almarsson, et al.	03-02-2004
		7,078,526	B2	Remenar et al.	07-18-2006
		7,132,579	B2	Neckebrock et al.	11-07-2006
		7,205,413	B2	Morissette et al.	04-17-2007
		7,351,695	B2	Almarssoo et al.	04-01-2008
		7,446,107	B2	Remenar et al.	11-04-2008
		7,452,555	B2	Childs	11-18-2008
		7,459,449	B2	Keltjens	12-02-2008
		7,687,091	B2	Moen et al.	03-30-2010
		7,927,613	B2	Almarsson et al.	04-19-2011

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	5	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		2002-0006951	A1	Hageman et al.	01-17-2002
		2002-0013357	A1	Nadkarni et al.	01-31-2002
		2002-0015735	A1	Hedden et al.	02-07-2002
		2002-0034542	A1	Thombre et al.	03-21-2002
		2002-0037925	A1	Dewey et al.	03-28-2002
		2002-0042446	A1	Dewey et al.	04-11-2002
		2002-0071857	A1	Kararli et al.	06-13-2002
		2002-0107250	A1	Hariharan et al.	08-08-2002
		2002-0119193	A1	Le Trang et al.	08-29-2002
		2003-0069190	A1	Abdel-Magid et al.	04-10-2003
		2003-0096014	A1	Sherman	05-22-2003
		2003-0162226	A1	Cima et al.	08-28-2003
		2003-0166581	A1	Almarsson et al.	09-04-2003
		2003-0224006	A1	Zaworotko et al.	12-04-2003
		2004-0019211	A1	Remenar et al.	01-29-2004
		2004-0053853	A1	Almarsson et al.	03-18-2004
		2004-0106052	A1	Molaire	06-03-2004
		2004-0106053	A1	Molaire et al.	06-03-2004
		2004-0106055	A1	Molaire et al.	06-03-2004
		2004-0171062	A1	Hirth et al.	09-02-2004
		2004-0176335	A1	Childs	09-09-2004
		2005-0070551	A1	Remenar et al.	03-31-2005
		2005-0169982	A1	Almarsson et al.	08-04-2005
		2005-0181041	A1	Goldman	08-18-2005
		2005-0252649	A1	Chiu et al.	11-17-2005
		2005-0256127	A1	Ku et al.	11-17-2005
		2006-0134198	A1	Tawa et al.	06-22-2006
		2006-0223794	A1	Bourghol et al.	10-05-2006
		2007-0015841	A1	Tawa et al.	01-18-2007
		2007-0021510	A1	Hickey et al.	01-25-2007
		2007-0026078	A1	Almarsson et al.	02-01-2007

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	6	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		2007-0059356	A1	Almarsson et al.	03-15-2007
		2007-0293674	A1	Scoppettuolo et al.	12-20-2007
		2009-0088443	A1	Remenar et al.	04-02-2009
		2010-0331285	A1	Almarsson et al.	12-30-2010
		2014-0162989	A1	Zaworotko et al.	06-12-2014

FOREIGN PATENT DOCUMENTS

Examiner's Initials #	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
	*	CA	1 101 840		Sumitomo Chemical Company, Limited	05-26-1981	
		CA	1 148 020	A1	McCoy	06-14-1983	
	*	EP	0 283 992	B1	Janssen Pharma	09-16-1992	
	*	EP	0 310 122	A1	Kaken Pharma	04-05-1989	
	*	EP	0 413 528	B1	Yu, R. et al.	11-15-1995	
	*	EP	0 731 795	B1	G.D. Searle & Co.	12-22-1999	
	*	EP	1 167 355	A1	Fako Ilaclari A.S.	01-02-2002	
	*	EP	1 364 649	A1	Cilag AG	11-26-2003	
	*	FR	769,586		Chemische Fabrik von Heyden	06-11-1934	Y
	*	FR	2 849 029	A1	Laboratoire L. Lafon et al.	06-25-2004	
	*	GB	1 297 261	A	E.R. Squibb & Sons, Inc.	11-22-1972	
	*	GB	2 169 601	A	Tate & Lyle Public Limited Company	07-16-1986	
	*	IN	182620	A1	Bajaj et al.	05-15-1999	
	*	IT	1303251	B1	Industriale Chimica, S.R.L.	11-06-2000	Y
	*	JP	46-33588		Sanzu Inc.	10-01-1971	
	*	JP	54-016494		Yamanouchi Pharmaceutical Co., Ltd.	02-07-1979	Y
	*	JP	54-095589		Sumitomo Chemical Co.	07-28-1979	
	*	JP	B 46-33588		Sanzu Inc.	10-01-1971	
	*	WO	94/16733	A1	Chiesi Farmaceutici S.P.A.	08-04-1994	
	*	WO	95/17407	A1	Schering Corp	06-29-1995	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)	APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
	FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet 7 of 30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	WO	95/23596	A1	The Boots Company PLC	09-08-1995	
	*	WO	96/07331	A1	Xyrofin Oy	03-14-1996	
	*	WO	96/33193	A1	Janssen Pharmaceutica N.V.	10-24-1996	
	*	WO	98/57967	A1	Dong-A Pharmaceutical Co., Ltd.	12-23-1998	
	*	WO	00/07583	A3	Brookhaven Science Associates	02-17-2000	
	*	WO	00/32189	A1	G.D. Searle & Co.	06-08-2000	
	*	WO	00/42021	A1	Merck Frosst Canada & Co.	07-20-2000	
	*	WO	00/50020	A2	University of Cincinnati	08-21-2000	
	*	WO	00/53283	A1	Reuter Chemische Apparatebau KG	09-14-2000	
	*	WO	00/72841	A1	Berlant, Jeffrey	12-07-2000	
	*	WO	01/13904	A2	Ortho-McNeil Pharmaceutical, Inc.	03-01-2001	
	*	WO	01/41536	A2	Pharmacia Corporation	06-14-2001	
	*	WO	01/41760	A3	Pharmacia Corporation	06-14-2001	
	*	WO	01/42221	A1	Pharmacia Corporation	06-14-2001	
	*	WO	01/42222	A2	Pharmacia Corporation	06-14-2001	
	*	WO	01/45706	A1	Pharmacia Corporation	06-28-2001	
	*	WO	01/51919	A2	Transform Pharmaceuticals, Inc.	07-19-2001	
	*	WO	01/78724	A1	Pharmacia Corporation	10-25-2001	
	*	WO	01/91750	A1	Pharmacia Corporation	12-06-2001	
	*	WO	01/97853	A1	Biochemie Gesellschaft MBH	12-27-2001	
	*	WO	02/000627	A1	Fako Ilaclari A.S.	01-03-2002	
	*	WO	02/010125	A1	Teva Pharmaceutical Industries Ltd.	02-07-2002	
	*	WO	02/056878	A2	Pharmacia Corporation	07-25-2002	
	*	WO	02/056915	A2	Cephalon, Inc.	07-25-2002	
	*	WO	02/062318	A2	DSM N.V.	08-15-2002	
	*	WO	02/102376	A1	Pharmacia Corporation	12-27-2002	
	*	WO	03/033462	A2	The Regents of the University of Michigan	04-24-2003	
	*	WO	03/070738	A2	Transform Pharmaceuticals, Inc.	08-28-2003	
	*	WO	03/074474	A2	Univ. South Fla. et al.	09-12-2003	
	*	WO	03/101392	A2	Transform Pharmaceuticals, Inc.	12-11-2003	
	*	WO	2004/054571	A1	Cilag AG	07-01-2004	
	*	WO	2004/060347	A2	Transform Pharmaceuticals, Inc.	07-22-2004	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	8	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	WO	2004/078161	A1	Transform Pharmaceuticals, Inc.	09-16-2004	
	*	WO	2004/078163	A2	Transform Pharmaceuticals, Inc.	09-16-2004	
	*	WO	2004/089313	A2	Transform Pharmaceuticals, Inc.	10-21-2004	
	*	WO	2005/023198	A2	Transform Pharmaceuticals, Inc.	03-17-2005	
	*	WO	2005/037424	A1	Salvias AG	04-28-2005	
	*	WO	2005/053612	A2	Shire Laboratories, Inc.	06-16-2005	
	*	WO	2005/055983	A2	Medcrystalforms, LCC	06-23-2005	
	*	WO	2005/060968	A1	Sepracor, Inc.	07-07-2005	
	*	WO	2005/077894	A1	Transform Pharmaceuticals, Inc.	08-25-2005	
	*	WO	2005/089375	A2	S.S.C.I., Inc.	09-29-2005	
	*	WO	2005/094804	A1	The Regents of the University of Michigan	10-13-2005	
	*	WO	2005/118577	A1	Transform Pharmaceuticals, Inc.	12-15-2005	
	*	WO	2006/024930	A1	Pharmacia and Upjohn Co., LCC	03-09-2006	

OTHER ART -- NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
		European Search Report for Application No. EP 03711407.1 mailed November 22, 2006 (U0157.70023EP00).	
		International Search Report for Application No. PCT/US2003/06662 mailed October 24, 2003 (U0157.70023WO00).	
	*	Office Action dated April 13, 2011 in U.S. Application No. 12/861,203.	
	*	Notice of Reasons for Rejection dated October 8, 2009 for Japanese Application No. 2003-572946. 11 pages.	Y
	*	Definition of solvate, The Free Dictionary, http://www.thefreedictionary.com/solvate, accessed online on 21 July 2009, pp. 1-3.	
		The Merck Index, 12th Ed. Merck & Co., Inc. Whitehouse Station, NJ. 1996. Entries 5683, 9094.	
	*	Physician's Desk Reference, 56th Ed., pp. 1800-1804, 2002.	
	*	Physician's Desk Reference, 56th Ed., pp. 2590-2595, 2002.	
	*	Press Release. "Clinical Development of Topiramate for Obesity Extended to Simplify Dosing, Improve Tolerability". http://www.orthomcneil.com/news/article020402.html (February 4, 2002), New Jersey, 2 pages.	
	*	The United States Pharmacopoeia, 23rd Edition, U.S. Pharmacopoeia Convention, Inc. Rockville, MD, 1995, pp. 1843.	
	*	[NO AUTHOR LISTED], Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances Q6A. ICH Harmonised Tripartite Guideline. 1999 Oct 6; 4:46.	

EXAMINER: /NOBLE E JARRELL/	DATE CONSIDERED: 02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	9	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	[NO AUTHOR LISTED], X-ray Diffraction. In: The United States Pharmacopeia – The National Formulary (USP #24 NF19). 2000 Jan. Chapter 941: 2005-7	
	*	AAKERÖY, C. et al. "A high-yielding supramolecular reaction" *J. Am. Chem. Soc.*, 2002, 14425-14432, Vol. 124.	
	*	AAKERÖY, C. et al. "A structural study of 2-amino-5-nitropyridine and 2-amino-3-nitropyridine: intermolecular forces and polymorphism" *J. Mater. Chem.*, 1998, pp. 1385- 1389, Vol. 8, No. 6.	
	*	AAKERÖY, C. et al. "A versatile route to porous solids: organic-inorganic hybrid materials assembled through hydrogen bonds" *Angew. Chem. Int. Ed.*, 1999, pp. 1815-1819, Vol. 38, No. 12.	
	*	AAKERÖY, C. et al. "Aromatic dicarboxylic acids as building blocks of extended hydrogen-bonded architectures" *Supramolecular Chemistry*, 1998, pp. 127-135, Vol. 9.	
	*	AAKERÖY, C. et al. "Assembly of 2-D inorganic/organic lamellar structures through a combination of copper (I) coordination polymers and self-complimentary hydrogen bonds" *J. Chem. Soc., Dalton Trans.*, 2000, pp. 3869-3872.	
	*	AAKERÖY, C. et al. "Building organic assemblies with 2-pyridone and dicarboxylic acids: relating molecular conformation and synthon stability to crystal structure" *Crystal Engineering*, 1998, pp. 225-241, Vol. 1, No. 3-4.	
	*	AAKERÖY, C. et al. "Charge-assisted hydrogen bonds and halogen-halogen interactions in organic salts: benzylammonium benzoates and pentaflourobenzoates" *Structural Chemistry*, 1999, pp. 229-242, Vol. 10, No. 3.	
	*	AAKERÖY, C. et al. "Crystal engineering of hydrogen-bonded assemblies- a progress report" *Aust. J. Chem.*, 2001, pp. 409-421, Vol. 54.	
	*	AAKERÖY, C. et al. "Crystal engineering of ionic solids" Modular Chemistry (ed. by Michl, J.), 1997, pp. 153-162, Kluwer Academic Publishers, The Netherlands.	
	*	AAKERÖY, C. et al. "Crystal engineering using intermolecular hydrogen-bonded connectors and classic coordination chemistry" *Transactions ACA*, 1998, pp. 97-103, Vol. 33.	
	*	AAKERÖY, C. et al. "Crystal engineering: strategies and architectures" *Acta Cryst.*, 1997, pp. 569-586, Vol. B53.	
	*	AAKERÖY, C. et al. "Deliberate combination of coordination polymers and hydrogen bonds in a supramolecular design strategy for inorganic/organic hybrid networks" *Chem. Commun.*, 2000, pp. 935-936.	
	*	AAKERÖY, C. et al. "Di-hydroxy malonic acid as a building block of hydrogen-bonded 3-dimensional architectures" *Journal of Chemical Crystallography*, 1998, pp. 111-117, Vol. 28, No. 2.	
	*	AAKERÖY, C. et al. "Do polymorphic compounds make good cocrystallizing agents? A structural case study that demonstrates the importance of synthon flexibility" *Crystal Growth & Design*, 2003, 159-165, Vol. 3, No. 2.	
	*	AAKERÖY, C. et al. "Hydrogen-bonded layers of hydrogentartrate anions: two-dimensional building blocks for crystal engineering" *J. Mater. Chem.*, 1993, 1129-1135, Vol. 3, No. 11.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	10	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	AAKERÖY, C. et al. "Hydrogen-bonding in solids" Crystal Engineering (ed. by Seddon, K. R. et al.), 1999, pp. 303-324, Kluwer Academic Publishers, The Netherlands.	
	*	AAKERÖY, C. et al. "Low-dimensional architectures of silver coordination compounds assembled *via* amide-amide hydrogen bonds" *Crystal Engineering*, 1998, pp. 39-49, Vol. 1, No. 1.	
	*	AAKERÖY, C. et al. "Modular supramolecular synthesis based on a dominance hierarchy of intermolecular interactions (Abstract)" 223rd ACS National Meeting in Orlando, FL., April 7-11, 2002, published by the American Chemical Society, Washington, D.C.	
	*	AAKERÖY, C. et al. "Molecular mechanics and crystal engineering" " Crystal Engineering (ed. by Seddon, K. R. et al.), 1999, pp. 69-82, Kluwer Academic Publishers, The Netherlands.	
	*	AAKERÖY, C. et al. "New building blocks for crystal engineering. Syntheses and crystal structures of oxime-substituted pyridines" *Cryst Eng. Comm.*, 2000, pp. 1-6, Vol. 27.	
	*	AAKERÖY, C. et al. "Novel colorless composite materials for nonlinear optics" *Adv. Mater*, 1993, pp. 364-367, Vol. 5, No. 5.	
	*	AAKERÖY, C. et al. "Organic assemblies of 2-pyridones with dicarboxylic acids" *Tetrahedron*, 2000, pp. 6693-6699, Vol. 56.	
	*	AAKERÖY, C. et al. "Pitfalls in the supramolecular assembly of silver(I) coordination compounds" *Journal of Molecular Structure*, 1999, pp. 91-101, Vol. 474.	
	*	AAKERÖY, C. et al. "Solid state, crystal engineering and hydrogen bonds" Comprehensive Coordination Chemistry II (ed. by McCleverty, J. et al.), pp. 679-688, Elsevier Ltd., Oxford, UK.	
	*	AAKERÖY, C. et al. "Supramolecular assembly of low-dimensional silver (I) architectures *via* amide-amide hydrogen bonds" *Chem. Commun.*, 1998, pp. 1067-1068.	
	*	AAKERÖY, C. et al. "The C-H•••C1 hydrogen bond: does it exist?" *New J. Chem.*, 1999, pp. 145-152.	
	*	AAKERÖY, C. et al. "The crystal structure of the molecular cocristal *L*-malic acid *L*-tartaric acid (1/1)" *Supramolecular Chemistry*, 1996, pp. 153-156, Vol. 7.	
	*	AAKERÖY, C. et al. "The hydrogen bond and crystal engineering" *Chemical Society Reviews*, 1993, pp. 397-407.	
	*	AAKERÖY, C. et al. "Total synthesis' supramolecular style: design and hydrogen-bond-directed assembly of ternary supermolecules" *Angew. Chem. Int Ed.*, 2001, pp. 3240- 3242, Vol. 40, No. 17.	
	*	AAKERÖY, C. et al. "Two-fold interpenetration of 3-D nets assembled via three-co-ordinate silver(I) ions and amide-amide hydrogen bonds" *J. Chem. Soc., Dalton Trans.*, 1998, pp. 1943-1945.	
	*	AAKERÖY, C. et at "Heteromeric intermolecular interactions as synthetic tools for the formation of binary co-crystals" *Cryst. Eng. Comm.*, 2004, pp. 19-24, Vol. 6, No. 5.	
	*	AAKERÖY, C. et at "Hydrogen-bond assisted assembly of organic and organic-inorganic solids" Crystal Enoineerino: From Molecules and Crystals to Materials, 1999, pp. 89-106, Kluwer Academic Publishers, The Netherlands.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	11	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	AAKERÖY, C.B. et al. "Do Polymorphic Compounds Make Good Cocrystalizing Agents? A Structural Case Study that Demonstrates the Importance of Synthon Flexibility" *Crystal Growth & Design*, 2003, 3(2):159-165.	
	*	ABOURAHMA et al., Network Hydrogen Bonding in Two New Cocrystals Sustained by [Mn(CO)3(OH)]4, a tetrahedral hydrogen bond donor. J Chem Crystallogr. 1995 Nov; 25:731-736.	
	*	AHN, S. et al. "Polymorphs of a 1:1 cocrystal with tunnel and layer structures: *p,p'*-biphenol/dimethyl sulfoxide" *Crystal Growth & Design*, 2001, pp. 107-111, Vol. 1, No. 2.	
	*	AKAZOME, M. et al. "Enantioselective inclusion of methyl phenyl sulfoxides and benzyl methyl sulfoxides by (*R*)-phenylglycyl-(*R*)-phenylglycine and the crystal structures of the inclusion cavities" *J. Org. Chem.*, 2000, pp. 68-76, Vol. 65.	
	*	AKHTARUZZAMAN, M.D. et al. "One-dimensional hydrogen-bonded molecular tapes in 1, 4-bis[(4-pyridinio) ethynyl]benzene chloranilate" *Acta. Cryst.*, 2001, pp. o353-o355, Vol. E57.	
	*	ALBEROLA, S. et al. "Crystalline and Molecular Structure of Sulfanilimide-Antipyrine" *Acta Cryst.*, 1977, pp. 3337-3341, Vol. B33.	
	*	ALLEN, F. et al. "Systematic analysis of structural data as a research technique in organic chemistry" *Acc. Chem. Res.*, 1983, pp. 146-153, Vol. 16.	
	*	ALMARSSON et al., The A to Z of pharmaceutical cocrystals: a decade of fast-moving new science and patents. Pharm Pat Anal. 2012 Jul;1(3):313-27. doi: 10.4155/ppa.12.29.	
	*	ALMARSSON, Ö. et al. "Crystal engineering of the composition of pharmaceutical phases. Do pharmaceutical co-crystals represent a new path to improved medicines?" *Chem. Commun.*, 2004, pp. 1889-1896.	
	*	AMAI, M. et al. "1:1 complex of octadecanoic acid and 3-pyridinecarboxamide" *Acta Cryst.*, 1998, pp. 1367-1369, Vol. C54.	
	*	AMMAR et al., Effects of Aromatic Hydtotropes on the Solubility of Carbamazepine. Part II: Effect of Nicotinamide, Sodium Salts of Benzoic, Naphthoic and Nicotinic Acids. Egypt J Pharmacol Sci. 1994;35(1-6):209-23.	
	*	ANDERSON, J. "Constitution of aurous compounds: Gold mirrors" *Nature*, October 2, 1937, pp. 583-584, Letters to the Editor.	
	*	ANDERSON, N. et al. "Sulfonation with inversion by mitsunobu reaction: an improvement on the original conditions" *J. Org. Chem.*, 1996, pp. 7955-7958, Vol. 61.	
	*	AOKI, K. et al. "A 1:1 complex of theophylline and p-nitrophenol" *Acta Cryst.*, 1978, pp. 2333-2336, Vol. B34.	
	*	ARONHIME, J. et al. "Crystalline forms of pharmaceuticals and characterization thereof", Oral Presentation, March 8, 2005, USPTO, Alexandria, VA.	
	*	ASHTON, P. et al. "Combining different hydrogen-bonding motifs to self-assemble interwoven superstructures" *Chem. Eur. J.*, 1998, pp. 577-589, Vol. 4, No. 4.	
	*	BALL, P. "Materials Chemistry - Scandal of Crystal Design ...", *Nature*, June 20, 1996, pp. 648-650, Vol. 381.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	12	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	BARKER, P. A. et al. "Effect of crystallization temperature on the cocrystallization temperature on the cocrystallization of hydroxybutyrate/ hydroxyvalerate copolymers" *Polymer*, pp. 913-919, Vol. 38, No. 4.	
	*	BASTIN, R.J. et al. "Salt Selection and Optimisation Procedures for Pharmaceutical New Chemical Entities" *Organic Process Research & Development*, 2000, 4:427-435.	
	*	BEDU-ADDO, Understanding Lyophilization Formulation Development. Pharmaceutical Technology. 2004 Mar: 10-18.	
	*	BEERGES, P. et al. "Phenothiazine tetracyanoethylene" *Private Communication*, 1994.	
	*	BERGE et al., Pharmaceutical salts. J Pharm Sci. 1977 Jan;66(1):1-19.	
	*	BERKOVITCH-YELLIN, Z. et al. "Electron density distribution in cumulenes: an x-ray study of the complex allenedicarboxylic acid- acetamide (1:1) at -150°C" *Acta Cryst.*, 1977, pp. 3670-3677, Vol. B33.	
	*	BERKOVITCH-YELLIN, Z. et al. "The role played by C-H•••O and C-H•••N interactions in determining molecular packing and conformation" *Acta Cryst.*, 1984, pp. 159-165, Vol. B40.	
	*	BERL, V. et al. "Induced fit selection of a barbiturate receptor from a dynamic structural and conformational/configurational library" *Eur. J. Org. Chem.*, 1999, pp. 3089-3094.	
	*	BERNSTEIN, J. et al. "Concomitant Polymorphs", *Angew. Chem., Int. Ed.*, 1999, pp. 3440-3461, Vol. 38.	
	*	BERTOLASI, V. et al. "Competition between hydrogen bonding and donor-acceptor interactions in co-crystals of 1,3-dimethylbarbituric acid with aromatic amines" *New J. Chem.*, 2001, pp. 408-415, Vol. 25.	
	*	BERTOLASI, V. et al. "General rules for the packing of hydrogen-bonded crystals as derived from the analysis of squaric acid anions: aminoaromatic nitrogen base co-crystals" *Acta Cryst.*, 2001, pp. 591-598, Vol. B57.	
	*	BETTINETT1, G. et al. "Structure and solid-state chemistry of anhydrous and hydrated crystal forms of the trimethoprim-sulfamethoxypyridazine 1:1 molecular complex" *Journal of Pharmaceutical Sciences*, April 2000, pp. 478-489, Vol. 89, No. 4.	
	*	BETTINETTI, G. et al. "Thermal analysis of binary systems of the pharmaceuticals trimethoprim and benzoic acid" *Journal of Thermal Analysis*, 1983, pp. 285-294, Vol. 28.	
	*	BETTIS, J. et al. "Biopharmaceutics and dosage form design" *Amer. J. Hosp. Pharm.*, March 1973, pp. 240-243, Vol. 30.	
	*	BINGHAM, A. et al. "Over one hundred solvates of sulfathiazole" *Chem. Commun.*, 2001, pp. 603-604.	
	*	BOLTON, S. et al. "Complexes formed in solution by homologs of caffeine" *Journal of the American Pharmaceutical Association*, January 1957, pp. 38-41, Vol. XLVI, No. 1.	
	*	BOND, A. "*In situ* co-crystallisation as a tool for low-temperature crystal engineering" *Chem. Commun.*, 2003, pp. 250-251, Vol. 2.	
	*	BOND, A.D. et al. "On the Polymorphism of Aspirin" *Angew. Chem. Int Ed.*, 2007, 46:615-617.	
	*	BOND, A.D. et al. "On the Polymorphism of Aspirin: Crystalline Aspirin as Intergrowths of Two "Polymorphic" Domains" *Angew. Chem. Int. Ed.*, 2007, 46:618-622.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	13	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	BONIN, M. et al. "Urotropin azelate: a rather unwilling co-crystal" *Acta Cryst.*, 2003, pp. 72-86, Vol. B59.	
	*	BOSSHARD, C. et al. "Microscopic nonlinearities of two-component organic crystals" *J. Opt. Soc. Am. B*, November 2001, pp. 1620-1626, Vol. 18, No. 11.	
	*	BOUCHER, E. et al. "Use of Hydrogen-Bonds to Control Molecular Aggregation. Behavior of Dipyridones and Pyridone-Pyrimidones Designed to Form Cyclic Triplexes", *J. Org. Chem.*, 1995, pp. 1408-1412, Vol. 60.	
	*	BRADER, M.L. et al. "Hybrid insulin cocrystals for controlled release delivery" *Nature Biotechnology*, August 2002, 20:800-804.	
	*	BRAGA, D. et al. "Hydrogen bonding interactions between ions: a powerful tool in molecular crystal engineering" *Structure and Bonding*, 2004, pp. 1-32, Vol. 111.	
	*	BRIERLEY, C. et al. "Preparation and structure of the 1:2 π-molecular complex of phenothiazine with pyromellitic dianhydride" *J. Chem. Phys.*, February 1, 1985, pp. 1522- 1528, Vol. 82, No. 1.	
	*	BRITTAIN, H.G. et al. "Polymorphism in Pharmaceutical Solids" 1999, New York: Marcel Dekker, pp. 183, 202-208, 219.	
	*	BUCZAK, G. et al. "Crystal structure and vibrational spectra of the 1:1 and 1:2 complexes of pyridine betaine with pentachlorophenol" *Journal of Molecular Structure*, 1997, pp. 143- 151, Vol. 436-437.	
	*	BUNICK, G. et al. "The crystal and molecular structure of the complex 2,6-diamino-9-ethylpurine 5,5-diethylbarbituric acid" *American Crystallographic Association, Abstract Papers*" Winter 1976, p. 30.	
	*	BURGI, H. et al. "Crystallisation of supramolecular materials" *Current Opinion in Solid State & Materials Science*, 1998, pp. 425-430, Vol. 3.	
	*	BYRIEL, K., et al. "Molecular cocrystals of carboxylic acids. IX Carboxylic acid interactions with organic heterocyclic bases. The crystal structures of the adducts of (2,4-dichlorophenoxy) acetic acid with 3-hydroxypyridine, 2,4,6,-trinitrobenzoic acid with 2-aminopyrimidine, and 4-nitrobenzoic acid with 3-amino-1,2,4-triazole" *Aust. J. Chem.*, 1992, pp. 969-981, Vol. 45, No. 6.	
	*	BYRN et al., Pharmaceutical solids: a strategic approach to regulatory considerations. Pharm Res. 1995 Jul;12(7):945-54.	
	*	BYRN, S. R. et al. "Solid-state pharmaceutical chemistry" *Chem. Mater.*, 1994, pp. 1148- 1158, Vol. 6.	
	*	CACCIAPUOTI, A. et al. "In vitro and in vivo activities of SCH 56592 (Posaconazole), a new triazole antifungal agent, against *Aspergillus* and *Candida*" *Antimicrobial Agents and Chemotherapy*, August 2000, pp. 2017-2022, Vol. 44, No. 8.	
	*	CAIRA, M. "Molecular complexes of sulfonamides. Part 1. 1:1 complexes between sulfadimidine [4-amino-N-(4,6-dimethyl-2-pyrimidinyl) benzenesulfonamide] and 2- and 4-aminobenzoic acids" *Journal of Crystallographic and Spectroscopic Research*, 1991, pp. 641-648, Vol. 21, No. 5.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	14	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	CAIRA, M. "Molecular complexes of sulfonamides. Part 2. 1:1 complexes between drug molecules: sulfadimidine —acetylsalicylic acid and sulfadimidine-4-aminosalicylic acid" *Journal of Crystallographic and Spectroscopic Research*, 1992, pp. 193-200, Vol. 22, No. 2.	
	*	CAIRA, M. "Molecular complexes of sulfonamides. Part 3. Structure of 5-methoxysulfadiazine (Form II) and its 1:1 complex with acetylsalicylic acid" *Journal of Chemical Crystallography*, 1994, pp. 695-701, Vol. 24, No. 10.	
	*	CAIRA, M. et al. "Order-disorder enantiotropy, monotropy, and isostructurality in a tetroxoprim-sulfametrole 1:1 molecular complex: crystallographic and thermal studies" *Journal of Pharmaceutical Sciences*, November 2003, pp. 2164-2176, Vol. 92, No. 11.	
	*	CAIRA, M. et al. "Selective formation of hydrogen bonded cocrystals between a sulfonamide and aromatic carboxylic acids in the solid state" *J. Chem. Soc. Perkin Trans. 2*, 1995, pp. 2213-2216.	
	*	CAIRA, M. et al. "Structure of a 1:1 complex between the anthelmintic drug mebendazole and propionic acid" *Journal of Chemical Crystallography*, 1998, Vol. 28, No. 1.	
	*	CAIRA, M. et al. "X-ray structure and thermal analysis of a 1:1 complex between (*S*)-naproxen and heptakis (2,3,6-tri-*O*-methyl)-β-cyclodextrin" *Journal of Inclusion Phenomena and Molecular Recognition in Chemistry*, 1995, pp. 277-290, Vol. 20.	
	*	CALLAHAN, J.C. et al. "Equilibrium moisture content of pharmaceutical excipients" *Drug Development and Industrial Pharmacy*, 1982, pp. 355-369, Vol. 8, No. 3.	
	*	CAMERMAN, A. et al. "Hydrogen bonding interaction of diphenylbarbituric acid and 9-ethyladenine. Crystal structure of a 1:1 complex" *Can. J. Chem.*, 2000, pp. 1045-1051, Vol. 78.	
	*	CAMERMAN, A. et al. "Molecular structure of acetylacetone. A crystallographic determination" *J. Am. Chem. Soc.*, 1983, pp. 1584-1586, Vol. 105, No. 6.	
	*	CANNON, A. et al. "Noncovalent derivatization: green chemistry applications of crystal engineering" *Crystal Growth & Design*, 2002, pp. 255-257, Vol. 2. No. 4.	
	*	CARONNA, T. et al. "Halogen bonding and π•••π stacking control reactivity in the solid state" *J. Am. Chem. Soc.*, 2004, pp. 4500-4501, Vol. 126.	
	*	CHANG, Y. L. et al. "An Approach to the Design of Molecular-Solids. Strategies for Controlling the Assembly of Molecules Into Two-Dimensional Layered Structures", *J. Am. Chem. Soc.*, 1993, pp. 5991-6000, Vol. 115.	
	*	CHILDS, S. et al. "Crystal engineering approach to forming cocrystals of amine hydrochlorides with organic acids. Molecular complexes of fluoxetine hydrochloride with benzoic, succinic, and fumaric acids" *J. Am. Chem. Soc.*, 2004, pp. 13335-13342, Vol. 126.	
	*	CHINNAKALI, K. et al. "2-aminopyrimidine and *p*-phenylene-diacetic acid (1:1) co-crystal" *Acta Cryst.*, 1999, pp. 399-401, Vol. C55.	
	*	CHOI, C. et al. "Cocrystallization of melaminium levulinate monohydrate" *Acta Cryst.*, 2004, pp. o295-o296, Vol. C60.	
	*	CHOW, Y. P. et al. "Complexation of acetaminophen with methyl xanthines" *Journal of Pharmaceutical Sciences*, 1972, pp. 1454-1458, Vol. 61.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	15	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	CHRISTIAN, S. et al. "Activity coefficient effects in spectral and solubility studies of molecular complex equilibria" *Journal of the American Chemical Society*, September 20, 1972, pp. 6861-6862, Vol. 94, No. 19, Communications to the editor.	
	*	COLL, M. et al. "Molecular structure of the complex formed between the anticancer drug cisplatin and d(pGpG): $C222_1$ crystal form" *Journal of Biomolecular Structure & Dynamics*, 1990, pp. 315-330, Vol. 8, No. 2.	
	*	COPP, S. et al. "Supramolecular chemistry of $[Mn(CO)_3(\mu 3\text{-}OH)]_4$: Assembly of a cubic hydrogen-bonded diamondoid network with 1,2-diamineothane" *J. Am. Chem. Soc.*, 1992, pp. 8719-8720, Vol. 114.	
	*	CORDI, A. et al. "(*S*)-Spiro [(1, 3-diazacyclopent-1-ene)-5, 2' -(7'-methyl-1,2',3',4'-tetrahydronaphthalene)]: resolution, stereospecific synthesis, and preliminary pharmacological characterization as a partial α-adrenergic agonist" *J. Med. Chem.*, 1997, pp. 2931-2935, Vol. 40.	
	*	COWAN, J.A. et al. "Neutron diffraction studies of the 1:1 and 2:1 cocrystals of benzene-1,2,4,5-tetracarboxylic acid and 4,4'-bipyridine" *Acta Crystallographica Section C: Crystal Structure Communications*, 2006, C62:o157-o161.	
	*	COX, J.R. et al., "Selective Crystal Growth of the Anhydrous and Monohydrate Forms of Theophylline on Self-Assembled Monolayers," *Angew, Chem. Int. Ed.*, 2007, pp. 1988-1991, Vo. 46.	
	*	CRAVEN, M. et al. "The 2:1 crystal complex of 5, 5-diethylbarbituric acid (barbital) and caffeine" *Acta Cryst.*, 1974, pp. 1191-1195, Vol. B30.	
	*	CRAVEN, M. et al. "The crystal structures of two polymorphs of 5,5'-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1969, pp. 1978-1993, Vol. 825.	
	*	CRIHFIELD, A. et al. "Crystal engineering through halogen bonding. 2. Complexes of diacetylene-linked heterocycles with organic iodides" *Crystal Growth & Design*, 2003, pp. 313-320, Vol. 3, No. 3.	
	*	CUDNEY, B. et al. "Screening and optimization strategies for macromolecular crystal growth" *Acta Cryst.*, 1994, pp. 414-423, Vol. D50.	
	*	CUTSEM, J. V. et al. "Oral and parenteral therapy with saperconazole (R 66905) of invasive aspergillosis in normal and immunocompromised animals" *Antimicrobial Agents and Chemotheraphy*, December 1989, pp. 2063-2068, Vol. 33, No. 12.	
	*	DANNAOUI, E. et al. "Acquired itraconazole resistance in *Aspergillus fumigatus*" *Journal of Antimicrobial Chemotherapy*, 2001, pp. 333-340, Vol. 47.	
	*	DATABASE WPI, Section Ch, Week 197936, Derwent Publishing Ltd., London, Great Britain, Class B02, AN 1979-65538B, XP002282989 and JP 54 095589A (Sumitomo) 1979 Abstract.	
	*	DATTA, S. et al. "Crystal structures of drugs: advances in determination, prediction and engineering" *Nature*, January 2004, pp. 42-57, Vol. 3.	
	*	DATTA, S. et al. "Molecular complex formation between riboflavin and salicylate in an aqueous medium" *Bult Chem. Soc. Jpn.*, 2003, pp. 1729-1734, Vol. 76.	
	*	DAVEY, R. J. et al. "Crystal engineering- nucleation, the key step" *Cryst Eng. Comm.*, 2002, pp. 257-264, Vol. 4, No. 47.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	16	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	DAVEY, R. J. et al. "Crystallisation in polymer films: control of morphology and kinetics of an organic dye in a polysilicone matrix" *J. Mater. Chem.*, 1997, pp. 237-241, Vol. 7, No. 2.	
	*	DAVIDOVICH, M. et al. "Detection of Polymorphism by Powder X-Ray Diffraction Interference by Preferred Orientation" *American Pharmaceutical Review*, 2004, pp. 10, 12, 14, 16, 100, Vol. 7, No. 1.	
	*	DAVIES, N.M. ef al. "Clinical Pharmacokinetics and Pharmacodynamics of Celecoxib: A Selective Cyclo-Oxygenase-2 Inhibitor" *Clin Pharmacokinet*, March 2000, 38(3):225-242.	
	*	DE JONG, E.M.G.J. et al. "Dystrophic Psoriatic Fingernails Treated with 1% 5-Fluorouracil in a Nail Penetration-Enhancing Vehicle: A Double-Blind Study" *Dermatology*, 1999, 199:313-318.	
	*	DEAN, J.A. "Analytical Chemistry Handbook" 1995, New York: McGraw-Hill, Inc., pp. 10.24-10.26.	
	*	DEBERNARDIS, J. et al. "Conformationally defined adrenergic agents. 5. Resolution, absolute configuration, and pharmacological characterization of the enantiomers of 2-(5,6-dihydroxy-1,2,3,4-tetrahydro-1-naphthyl) imidazoline: a potent agonist at α-adrenoceptors" *J. Med. Chem.*, 1987, pp. 1011-1017, Vol. 30.	
	*	DENNING, D. W. et al. "In vitro activity of Saperconazole (R66 905) compared with Amphotericin B and ltraconazole against *Aspergillus* species" *Eur. J. Clin. MicrobiaL Infect. Dis.*, 1990, pp. 693-697, Vol. 9.	
	*	DESIRAJU, G. "Supramolecular synthons in crystal engineering- A new organic synthesis" *Angew. Chem. Int. Ed. Engl*, 1995, pp. 2311-2327, Vol. 34.	
	*	DESIRAJU, G. et al. "Crystal and co-crystal" *Cryst. Eng. Comm.*, 2003, pp. 466-467, Vol. 5, No. 82.	
	*	DESIRAJU, G. et al. "Crystal engineering: outlook and prospects" *Current Science*, October 25, 2001, pp. 1038-1042, Vol. 81, No. 8.	
	*	DESIRAJU, G. R. "Chemistry beyond the molecule" *Nature*, July 26, 2001, pp. 397-400, Vol. 412.	
	*	DESIRAJU, G. R. "Crystal Gazing: Structure Prediction and Polymorphism", *Science*, October 17, 1997, pp. 404-405, Vol. 278, No 5337.	
	*	DESIRAJU, G. R. "The C--H•••O Hydrogen Bond in Crystals: What Is It?" *Acc. Chem. Res.*, 1991, pp. 24:290-296.	
	*	DESIRAJU, G. R., "Crystal engineering: A brief overview," *J. Chem. Sci.*, September 2010, pp. 667-675, Vol. 122, No. 5.	
	*	DOELKER, E. "Crystalline Modifications and Polymorphism changes during drug manufacturing" *Annales Pharmaceutiques Francaises*, 2002, 60(3):161-176.	
	*	DOELKER, E. "Physicochemical behavior of active substances. Consequences for the feasibility and stability of pharmaceutical forms" *S.T.P. Pharma Practiques*, 1999, 9(5):399- 409.	
	*	DOI, M. et al. "Conformational study of a potent human renin inhibitor: x-ray crystal structure of isopropyl (2*R*, 3*S*) -4-cyclohexyl-2-hydroxy-3-{*N*-[(2R)-2-morpholinocarbonylmethyl-3-(1-naphthyl) propionyl] -L-histidylamino}butyrate (KRI-1314), a pentapeptide analogue with amino acid sequence corresponding to the cleavage site of angiotensinogen" *J. Chem. Soc. Perkin Trans. 1*, 1991, pp. 1153-1158.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	17	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	DRESSMAN, J. B. et al. "Dissolution testing as a prognostic tool for oral drug absorption: immediate release dosage forms" *Pharmaceutical Research*, 1998, pp. 11-22, Vol. 15, No. 1.	
	*	DUAX, W. et al. "The structure of the crystalline complex estradiol. Urea (1:1)" *Acta Cryst.*, 1972, pp. 1864-1871, Vol. B28.	
	*	DUKE, Handbook of Phytochemical Constituents of GRAS Herbs and Other Economic Plants, 2001, CRC Press LLC, page 419.	
	*	DUNITZ, J. "Crystal and co-crystal: a second opinion" *Cryst. Eng. Comm.*, 2003, pp. 506, Vol. 5, No. 91.	
	*	DUNITZ, J. "New light on an old story: the solid-state transformation on ammonium cyanate into urea" *J. Am. Chem. Soc.*, 1998, pp. 13274-13275, Vol. 120.	
	*	DUNITZ, J. D. "Are crystal structures predictable" *Chem Commun.*, 2003, pp. 545-548.	
	*	DVORKIN et al. "Crystal and Molecular Structure of a Complex 18-crown-6 with 6-chloro-7-sulfamido-3,4-dihydro-1,2,4-benzothiadiazine-1, 1-dioxide (hypothiazide) of 1:1 Composition" *Kristallagrafiya*, 1990, 35(3):682-686.	
	*	EBERT, W. R. "Soft elastic gelatin capsules: a unique dosage form" *Pharmaceutical Technology*, October 1977, pp. 44-50, Vol. 1, No. 5.	
	*	EL-NAHHAS, S.A. "Physico-Chemical characteristics of Carbamazepine-beta-cyclodextrin inclusion compounds and carbamazepine-peg solid dispersions" *Pharmazie,* 1996, 51(12):960-963.	
	*	ENRIGHT, G. et al. "Thermally programmable gas storage and release in single crystals of an organic van der Waals host" *J. Am. Chem. Soc.*, 2003, pp. 9896-9897, Vol. 125.	
	*	EPSTEIN, R. et al. "The x-ray crystal structure of the molecular complex 8-bromo-9-ethyladenine-5-allyl-5-isobutylbarbituric acid" *Acta Cryst.*, 1976, pp. 2180-2188, Vol. B32.	
	*	ERMER, O. et al. "Molecular recognition among alcohols and amines: super-tetrahedral crystal architectures of linear diphenol-diamine complexes and aminophenols" *J. Chem. Soc. Perkins Trans. 2*, 1994, pp. 925-944.	
	*	ETTER, M. "Encoding and decoding hydrogen-bond patterns of organic compounds" *Acc. Chem. Res.*, 1990, pp. 120-126, Vol. 23.	
	*	ETTER, M. "Hydrogen bonds as design elements in organic chemistry" *J. Phys. Chem.*, 1991, pp. 4601-4610, Vol. 95.	
	*	ETTER, M. et al. "Graph-set analysis of hydrogen-bond patterns in organic crystals" *Acta Cryst.*, 1990, pp. 256-262, Vol. B46.	
	*	ETTER, M. et al. "Hydrogen bond directed cocrystallization and molecular recognition properties of acyclic imides" *J. Am. Chem. Soc.*, 1991, pp. 2586-2598, Vol. 113.	
	*	EVGEN'EV et al., Selective determination of 4-aminobenzoic and 4-aminosalicylic acid derivatives in mixtures by flow-injection analysis. J Anal Chem. 2000 July;55(7):696-702.	
	*	FABIAN, L. et al. "Volumetric measure of isostructurality" *Acta Cryst.*, 1999, pp. 1099- 1108, Vol. B55.	
	*	FALLON III, L. "The crystal and molecular structure of 5-fluorouracil" *Acta Cryst.*, pp. 2549-2556, Vol. B29.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	18	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	FAUGHT, E. et al. "Topiramate Dose-Ranging Trial in Refractory Partial Epilepsy" *Amer. Epilepsy Soc. Proc.*, 1995,pg. 33, Vol. 36, Supp. 4.	
	*	FEIBUSH, B. et al. "Chiral separation of heterocyclic drugs by HPLC: solute-stationary phase base-pair interactions" *J. Am. Chem. Soc.*, 1986, pp. 3310-3318, Vol. 108.	
	*	FELTHOUSE et al., Maleic Anhydride, Maleic Acid, And Fumaric Acid. 2001. http://www.huntsman.com/performance_products/media/komaleic.pdf	
	*	FEYNMAN, R. "There's Plenty of Room at the Bottom", *Engineering and Science*, February 1960, pp. 22-36.	
	*	FIFER, E. et al. "Fentanyl analogues 3. 2-(1,2,3,4-tetrahydro)-naphthyl substituted 4-anilidopiperidines" *Eur. J. Med. Chem.- Chim. Ther.*, 1984, pp. 519-524, Vol. 19, No. 6.	
	*	FITZGERALD, G.A. et aL "The Coxibs, Selective Inhibitors of Cyclooxygenase-2", *New England Journal of Medicine*, August 9, 2001, 345(6):433-442.	
	*	FLEISCHMAN, S.G. et al. "Crystal Engineering of the Composition of Pharmaceutical Phases: Multiple-Component Crystalline Solids Involving Carbamazepine" *Crystal Growth & Design.*, 2003, 3(6):909-919.	
	*	FLEISCHMAN, Scott et al. , "Crystal engineering of binary crystals that contain pharmaceutical molecules, Abstracts of Papers, 23rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002, IEC-076.	
	*	FOXMAN, B. M. et al. "Environmentally benign synthesis using crystal engineering: steric accommodation in non-covalent derivatives of hydroquinones" *Crystal Engineering*, 1998, pp. 109-118, Vol. 1, No. 1.	
	*	FOXMAN, B. M. et al. "Noncovalent derivatives of hydroquinone: *BIS*- (*N,N*-dialkyl) bicyclo[2.2.2]octane-1,4-dicarboxamide complexes" *Crystal Engineering*, 1999, pp. 55-64, Vol. 2. No. 1.	
	*	FREEMONT, Cocrystal structure of an editing complex of Klenow fragment with DNA. PNAS. 1988 Dec;85(23):8924-8.	
	*	FRITCHIE, C. et al. "The configuration of phenothiazine in various molecular complexes" *Chem. Commun.*, 1968, pp. 833-834.	
	*	FUJII, S. et al. "Crystal and molecular structure of a 1:1 molecular complex of adenine and riboflavin" *Archives of Biochemistry and Biophysics*, 1977, pp. 363-370, Vol. 181.	
	*	FUNG, H.L. et al. "Solvent Effects on Comparative Dissolution of Pharmaceutical Solvates" *Chemical and Pharmaceutical Bulletin*, 1974, 22(2):454-458.	
	*	GAO, X et al. "Supramolecular construction of molecular ladders in the solid state" *Angew. Chem. Int. Ed.*, 2004, pp. 232-236, Vol. 43.	
	*	GARTLAND, G. L. et al. "Hydrogen bonding NH•••O=C of barbiturates: the (1:1) crystal complex of urea and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 980-987, Vol. B30.	
	*	GASCON, M. -P. et al. "In vitro forecasting of drugs which may interfere with the biotransformation of midazolam" *Eur. J. Clin. Pharmacol.*, 1991, pp. 573-578, Vol. 41.	
	*	GAVEZZOTTI, A. "Are crystal structures predictable?" *Acc. Chem. Res.*, 1994, pp. 309- 314, Vol. 27.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	19	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	GHOSH, M. "Structure and conformation of the 1:1 molecular complex sulfaproxyline-caffeine" *Acta Cryst.*, 1991, pp. 577-580, Vol. C47.	
	*	GIUSEPPETTI, G. P. et al. "The crystal structure of a sulfamethoxazole-trimethoprim 1:1 molecular compound" *II Farmaco- Ed. Sc.*, pp. 138-151, Vol. 35.	
	*	GLUZMAN, M. Kh. et al. "Investigation of Eutectic Melting in Systems Composed of Organic Salts and Acids" *Journal of Physical Chemistry*, 1960, pp. 2742-2747, Vol. 34.	
	*	GOSWAMI, S. et al. "1:1 Hetero-assembly of 2-amino-pyramidine and (+)-camphoric acid" *Acta Cryst.*, 2000, pp. 477-478, Vol. C56.	
	*	GOSWAMI, S. et al. "2-aminopyrimidine-fumaric acid cocrystal" *Acta Cryst.*, 1999, pp. 583-585, Vol. C55.	
	*	GOSWAMI, S. et al. "Molecular recognition induced supramolecular array of 2-aminopyrimidine with terephthalic acid, 1,4-phenylenediacetic acid and furmaric acid in solid state *via* H-bonding and π-stacking interactions" *Supramolecular Chemistry*, 1999, pp. 25-33, Vol. 11.	
	*	GRAJA, A. et al. "Interplay of acceptor molecule shape, crystal structure and physical properties of a new molecular complex C_{70} • 2[(Ph_3P) AuCl]" *Chemical Physics Letters*, November 19, 1999, pp. 725-732. Vol. 313.	
	*	GROTH, P. "*d*-Glucose-sodium chloride-monohydrate (glucose-sodium chloride) = $2C_6H_{12}O_6.NaCl.H_2O$" *Chemische Krystallographie*, 1910, pp. 438-439.	
	*	GUARRERA, D. et al. "Molecular self-assembly in the solid state. The combined use of solid state NMR and differential scanning calorimetry for the determination of phase constitution" *Chem. Mater.*, 1994, pp. 1293-1296, Vol. 6.	
	*	HAIXIN, L. et at "Structure of the 1:1 complex of 6,6'-diquinolyl ether with 5,5-diethylbarbituric acid" *Acta Cryst.*, 1992, pp. 2096-2098, Vol. C48.	
	*	HARKEMA, S. et al. "The crystal structure of urea oxalic acid (2:1)" *Acta Cryst.*, 1972, pp. 1646-1648, Vol. B28.	
	*	HAYNES, D. "Supramolecular synthon competition in organic sulfonates: A CSD survey" *Cryst Eng. Comm.*, 2004, pp. 584-588, Vol. 6, No. 95.	
	*	HEERES, J. et al. "Antimycotic azoles. 7. Synthesis and antifungal properties of a series of novel triazol-3-ones" *J. Med. Chem.*, 1984, pp. 894-900, Vol. 27.	
	*	HELFRICH, B. et al. "Polymorphism as an indication of structural versatility (Abstract)" 223rd ACS National Meeting in Orlando, FL., April 7-11, 2002, published by the American Chemical Society, Washington, D.C.	
	*	HENCK, J. et al. "Disappearing and reappearing polymorphs. The benzocaine:picric acid system" *J. Am. Chem. Soc.*, 2001, pp. 1834-1841, Vol. 123.	
	*	HEPPERLE, M. et al. "Mono *N*-arylation of piperazine(III): metal-catalyzed *N*-arylation and its application to the novel preparations of the antifungal posaconazole and its advanced intermediate" *Tetrahedron Letters*, 2002, pp. 3359-3363, Vol. 43.	
	*	HIGUCHI, T. et al. "Complexation of organic substances in aqueous solution by hydroxyaromatic acids and their salts" *J. Pharm. Sci.*, 1961, pp. 905-909, Vol. 50.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	20	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	HINO, T. et al. "Assessment of nicotinamide polymorphs by differential scanning calorimetry" *Thermochimica Acta*, 2001, pp. 85-92, Vol. 374.	
	*	HÖGBERG, T. et al. "Crystallographic, theoretical and molecular modelling studies on the conformations of the salicylamide, raclopride, a selective dopamine-D_2 antagonist" *J. Pharm. Pharmacol.*, 1987, pp. 787-796, Vol. 39.	
	*	HONIG, P. K. et al. "Itraconazole affects single-dose Terfenadine pharmacokinetics and cardiac repolarization pharmacodynamics" *J. Clin. Pharmacol.*, 1993, pp. 1201-1206, Vol. 33.	
	*	HSU, I. et al. "Hydrogen bonding NH...N of barbiturates: The 1:1 crystal complex of imidazole and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 988-993, Vol. 830.	
	*	HSU, I. et al. "The 1:1 crystal complex of *N*-methyl-2-pyridone and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 998-1001, Vol. B30.	
	*	HSU, I. et al. "The 2:1 crystal complex of 2-aminopyridine and 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 994-997, Vol. B30.	
	*	HSU, I. et al. "The crystal structure of the 1:1 complex of acetamide with 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 974-979, Vol. B30.	
	*	HSU, I. et al. "The crystal structure of the triclinic 1:2 complex of hexamethylphosphoramide with 5,5-diethylbarbituric acid (barbital)" *Acta Cryst.*, 1974, pp. 1299-1304, Vol. B30.	
	*	HSU, I. et al. "The crystalline complex (1:1) of salicylamide and 5-ethyl-5-isoamylbarbituric acid (amobarbital)" *Acta Cryst.*, 1974, pp. 843-846, Vol. B30.	
	*	HU, Z. et al. "Separation of 4-aminobenzoic acid by cocrystallization: Crystal structure of the complex of 4-aminobenzoic acid with (2*R*,3*R*)-tartaric acid" *Journal of Chemical Crystallography*, December 2002, pp. 525-529, Vol. 32, No. 12.	
	*	HUANG, C.-M. et al. "Molecular packing modes. Part XI. Crystal structures of the 2:1 complexes of benzamide with succinic acid and furamide with oxalic acid" *J. Chem. Soc. Perkins Trans. 2: Physical Organic Chemistry*, 1973, pp. 503-508, Vol. 5.	
	*	IBRAGIMOV, B. "A simple correlation between the structures of different crystal modifications of a given host-guest complex and their crystallization temperatures" *Journal of Inclusion of Phenomena and Macrocyclic Chemistry*, 1999, pp. 345-353, Vol. 34.	
	*	IMAI, T. et al. "Successful treatment of cerebral Aspergillosis with a high oral dose of Itraconazole after excisional surgery" *Internal Medicine*, October 1999, pp. 829-832, Vol. 38, No. 10.	
	*	ISHIDA, T. et al. "Structural study of histamine H_2-receptor antagonists. Five 3-[2-(diaminomethyleneamino)-4-thiazolymethylthio] propionamidine and -amide derivatives" *Acta Cryst.*, 1989, pp. 505-512, Vol. 645.	
		ITO et al., Compelled Orientational Control of the Solid-State Photodimerization of *trans*-Cinnamamides: Dicarboxylic Acid as a Non-covalent Linker. Tetrahedron. 2000;56:6833-44.	
		IWAMOTO et al., Structure of Cinnamamide. Acta Cryst. 1989;C45:1110-2.	
	*	JACKISCH, M. et al. 'Structures of three related biphenyl compounds: 4,4'-biphenyldiol, 3, 3',5,5'-tetra-*tert*-butyl-4,4'-biphenyldiol, and 3,3',5,5'- tetra-*tert*-butyl-1,1'-bicyclohexa-2,5-dienylidene-4,4'-dione" *Acta Cryst.*, 1990, pp. 919-922, Vol. C46.	
	*	JAIN, N.K. et al. "Polymorphism in Pharmacy" *Indian Drugs*, 1986, 23(6):315-329.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	21	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

		JIANG et al., Cinnamamide, an antitumor agent with low cytotoxicity acting on matrix metalloproteinase. Anti-Cancer Drugs. 2000 Jan;11(1):49-54.	
	*	KATAKAI, R. et al. "Stepwise synthesis of oligopeptides with N-carboxy-α-amino acid anhydrides. IV. Glycine NCA" *J. Org. Chem.*, 1972, pp. 327-329, Vol. 37, No. 2.	
	*	KAWAKAMI, Y. et al. "The rationale for E2020 as a potent acetylcholinesterase inhibitor" *Bioorganic & Medicinal Chemistry*, 1996, pp. 1429-1446, Vol. 4, No. 9.	
	*	KELDERS, H. et al. "Automated protein crystallization and a new crystal form of a subtilisin: eglin complex" *Protein Engineering*, 1987, pp. 301-303, Vol. 1, No. 4.	
	*	KHALIL, R. M. "Complexation of paracetamol with xanthine derivatives" *Egypt. J. Pharm. Sol.*, 1992, pp. 757-769, Vol. 33, No. 5-6.	
	*	KIM, H. et al. "High-performance liquid chromatographic analysis of the anti-fungal agent SCH 56592 in dog serum" *Journal of Chromatography B*, 2000, pp. 93-98, Vol. 738.	
	*	KIM, S. "Crystal structure of the 1:1 complex of 5-fluorouracil and 9-ethylhypoxanthine" *Science*, November 24, 1967, pp. 1046-1048, Vol. 158, No. 3804.	
	*	KIM, S. et al. "The structure of a crystalline complex containing one phenobarbital molecule and two adenine derivatives" P*roc. Natl. Acad. Sci. USA*, 1968, pp. 402-408, Vol. 60.	
	*	KIRCHNER, M.T. et al. "Co-crystals with Acetylene: Small Is not Simple" *Chem. Eur J.*, 2010, 16:2131-2146.	
	*	KIRYU, S. et al. "Crystal structure of a 1:1 aminopyrine-barbital complex" *Journal of Pharmaceutical Sciences*, May 1971, pp. 699-703, Vol. 60, No. 5.	
	*	KIRYU, S. et al. "Crystal structure of a 1:1 aminopyrine-cyclobarbital complex" *Chem. Pham. Bull.*, 1974, pp. 1588-1592, Vol. 22.	
	*	KLEIN, C.L. et al. "Molecular Structure of Two Conformationally Restrained Fentanyl Analogues: cis- and trans-Isomers of *N*-{3-Methyl-1-[2-(1,2,3,4-tetrahydro)naphthyl]-4-piperidinyl}-*N*-phenylpropanamide" *Journal of Pharmaceutical Sciences*, November 1985, 74(11):1147-1151.	
	*	KOBAYASHI, H. et al. "Sinusoidal structure of the 1:1 complex of phenothiazine and 7,7,8,8-tetracyanoquinodimethane, PTZ-TCNQ" *Acta Cryst.*, 1974, pp. 1010-1017, Vol. B30.	
	*	KOFLER, L. et al., Thermal micromethods for the study of organic compounds and their mixtures, pp. 1-145, 148-351, 354-386, Innsbruck, Austria, 1980.	
	*	KOSHIMA, H. et al. "Photoreactivities of two kinds of bimolecular crystals formed from acridine and phenothiazine" *J. Chem. Soc., Perkins Trans. 2*, 1997, pp. 2033-2038.	
	*	KOSHIMA, H. et al. "Polymorphs of a cocrystal with achiral and chiral structures prepared by pseudoseeding: tryptamine/hydrocinnamic acid" *Crystal Growth & Design*, 2001, pp. 355-357, Vol. 1, No. 5.	
	*	KOVACS, J. et al. "New type of bridged monoamino-β-cyclodextrins" *Journal of Inclusion Phenomena and Molecular Recognition in Chemistry*, 1996, pp. 53-56, Vol. 25.	
	*	KRANTZ, J. et al. "Sodium theophylline glycinate" *Journal of the American Pharmaceutical Association*, 1946, pp. 248-250.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	22	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	KRISHNAMOHAN SHARMA, C. V. et al. "X-ray crystal structure of C_6H_3 $(CO_2H)_3$-1,3,5•1.5(4,4'-bipy): a 'super trimesic acid' chicken-wire grid" *Chem. Commun.*, 1996, pp. 2655-2656.	
	*	KURODA, R. et al. "Generation of a co-crystal phase with coloristic properties *via* solid state grinding procedures" *Chem. Commun.*, 2002, pp. 2848-2849.	
	*	LAVRIJSEN, A. P. M. et al. "Hepatic injury associated with itraconazole" *The Lancet*, July 25, 1992, pp. 251-252, Vol. 340.	
	*	LE JEUNNE, C. et al. "Comparative efficacy and safety of calcium carbasalate plus metoclopramide versus ergotamine tartrate plus caffeine in the treatment of acute migraine attacks" *Eur. Neurol.*, 1999, pp. 37-43, Vol. 41.	
	*	LEGER, J.M. et al. "Crystal Structure of the 1:1 Sulfacetamide-Caffeine Complex" *Acta Cryst.*, 1977, pp. 1455-1459, Vol. 633.	
	*	LEHN, J.-M. et al. "Molecular recognition directed self-assembly of ordered supramolecular strands by cocrystallization of complementary molecular components" *Chem. Soc., Chem. Commun.*, 1990, pp. 479-481.	
	*	LEISEROWITZ, L. "Molecular packing modes. Carboxylic acids" *Acta Cryst.*, 1976, pp. 775-802, Vol. B32.	
	*	LEISEROWITZ, L. et al. "The molecular packing modes and hydrogen-bonding properties of amide: dicarboxylic acid complexes" *Acta Cryst.*, 1977, pp. 2719-2733, Vol. B33.	
	*	LEVIN, B. et al. "The not-so-trivial synthesis and characterization of heterocyclic boronic acids (Abstract)" 38th Midwest Regional Meeting of the American Chemical Society in Columbia, MO., November 5-7, 2003, published by the American Chemical Society, Washington, D.C.	
	*	LYNCH, D. et al. "1:1 Molecular complexes of 4-amino-N-(4,6-dimethylpyrimidin-2-yl) benzene-sulfonamide (sulfamethazine) with indole-2-carboxylic acid and 2,4-dinitrobenzoic acid" *Aust. J. Chem.*, 2000, pp. 383-387, Vol. 53.	
	*	LYNCH, D. et al. "Molecular cocrystals of carboxylic acids. XV Preparation and characterization of heterocyclic base adducts with a series of carboxylic acids, and the crystal structures of the adducts of 2-aminopyrimidine with 2,6-dihydroxybenzoic acid, 4-aminobenzoic acid, phenoxyacetic acid, (2,4-dichlorophenoxy) acetic acid, (3,4-dichlorophenoxy)- acetic acid and salicylic acid, and 2-aminopyridmine with 2,6-dihydroxybenzoic acid" *Aust. J. Chem.*, 1994, pp. 1097-1115, Vol. 47.	
	*	LYNCH, D. et al. "Molecular cocrystals of carboxylic acids. XXXI adducts of 2-aminopyrimidine and 3-amino-1,2,4-triazole with heterocyclic carboxylic acids" *Aust. J. Chem.*, 1998, pp. 403-408, Vol. 51.	
	*	MACGILLIVRAY, L. et al. "Supramolecular control of reactivity in the solid state using linear molecular templates" *J. Am. Chem. Soc.*, 2000, pp. 7817-7818, Vol. 122.	
	*	MADARASZ, J. et al. "Thermal, ftir and xrd study on some 1:1 molecular compounds of theophylline" *Journal of Thermal Analysis and Calorimetry*, 2002, pp. 281-290, Vol. 69.	
	*	MARTIN, R. et al. "Polyphenal-caffeine complexation" *J. Chem. Soc., Chem. Commun.*, 1986, pp. 105-106.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	23	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	MARTIN, R. et al. 'The caffeine-potassium chlorogenate molecular complex" *Phytochemistry*, 1987, pp. 273-279, Vol. 26, No. 1.	
	*	MARTINS, F.T. et al., "Intermolecular Contacts Influencing the Conformational and Geometric Features of the Pharmaceutically Preferred Mebendazole Polymorph C," *Journal of Pharmaceutical Sciences*, July 2009, pp. 2336-2344, Vol. 98, No. 7.	
	*	MARYANOFF, B. "Stereochemistry in a medium-sized ring. Highly diastereoselective N-oxidation of a substituted 3-benzazonine. X-ray crystal structure of an unusual complex between an amine *N*-oxide and saccharin" *J. Org. Chem.*, 1990, pp. 760-764, Vol. 55.	
	*	MASTROPAOLO, D. et al. "Hydrogen bonding interaction of diphenylhydantoin and 9-ethyladenine" *Molecular Pharmacology*, 1983, pp. 273-277, Vol. 23.	
	*	MATHIAS, J. et al. "Structural preferences of hydrogen-bonded networks in organic solution-the cyclic $CA_3{\bullet}M_3$ 'rosette'" *J. Am. Chem. Soc.*, 1994, pp. 4316-4325, Vol. 116.	
	*	MCCRONE, W. C. "Polymorphism", In: The Physics and Chemistry of the Organic Solid State, Vol. II, FOX, D. et al. (eds.), 1965, pp. 725-767, Interscience, New York.	
	*	MCINTOSH, J. et al. "Chemotherapeutic drugs in anaerobic infections of wounds" *The Lancet*, June 26, 1943, pp. 793-795.	
	*	MCINTOSH, J. et al. "Further observations on the chemotherapy of experimental gas gangrene: flavazole, marfanil, V187 and V335" *British Journal of Experimental Pathology*, 1946, pp. 46-54, Vol. 27.	
	*	MCINTOSH, J. et al. "Zinc peroxide, proflavine and penicillin in experimental *cl. welchii* infections" *The Lancet*, December 26, 1942, pp. 750-752.	
	*	MCMAHON, J. et al. "Crystal engineering of the composition of pharmaceutical phases. 3^1. Primary amide supramolecular heterosynthons and their role in the design of pharmaceutical co-crystals" *Z. Kristallogr.*, 2005, pp. 340-350, Vol. 220.	
	*	MEEJOO, S. et al. "The interplay of aryl-perfluoroaryl stacking interactions and interstack hydrogen bonding in controlling the structure of a molecular cocrystal" *Chemphyschem*, 2003, pp. 766-769, Vol. 4.	
	*	MIRMEHRABI, M. et al. "Improving the filterability and solid density of ranitidine hydrochloride form 1" *Journal of Pharmaceutical Sciences*, July 2004, pp. 1692-1700, Vol. 93, No. 7.	
	*	MORRIS, K. et al. "Theoretical approaches to physical transformations of active pharmaceutical ingredients during manufacturing processes" *Advanced Drug Delivery Reviews*, 2001, pp. 91-114, Vol. 48.	
	*	MOULTON, B. et al. "From Molecules to Crystal Engineering: Supramolecular Isomerism and Polymorphism in Network Solids", *Chem. Rev.*, 2001, pp. 1629-1658, Vol. 101.	
	*	MUNN, R. et al. "A Model for resonance-assisted hydrogen bonding in crystals and its graph set analysis" *J. Phys. Chem. A*, 2001, pp. 6938-6942, Vol. 105.	
	*	MUZAFFAR, N.A. et al. "Polymorphism and Drug Availability" *Journal of Pharmacy (Lahore)*, 1997, 1(1):59-66.	
	*	NAKANISHI, I. et aL "X-ray structural studies on two forms of β-cyclodextrin barbital complexes" *Journal of Inclusion Phenomena*, 1984, pp. 689-699, Vol. 2.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	24	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	NAKAO, S. et al. "The crystal and molecular structure of the 2:1 molecular complex of theophylline with phenobarbital" *Acta Cryst.*, 1977, pp. 1373-1378, Vol. B33.	
	*	NATARAJAN, S. et al. "Reinvestigation of the crystal structure of diglycine hydrochloride" *Zeitschrift für Kristallographic*, 1992, pp. 265-270, Vol. 198.	
	*	NEUVONEN, P. J. et al. "Itraconazole drastically increases plasma concentrations of lovastatin and lovastatin acid" *Clinical Pharmacology & Therapeutics*, 1996, pp. 54-61, Vol. 60, No. 1	
	*	NOMEIR, A. A. et al. "Pharmacokinetics of SCH 56592, a new azole broad-spectrum antifungal agent, in mice, rats, rabbits, dogs, and cynomolgus monkeys" *Antimicrobial Agents and Chemotherapy*, March 2000, pp. 727-731, Vol. 44, No. 3.	
	*	ODDS, F. C. "Antifungal activity of saperconazole (R 66 905) *in vitro*" *Journal of Antimicrobial Chemotherapy*, 1989, pp. 533-537, Vol. 24.	
	*	OLENIK, B. et al. "Cooperative and anticooperative effects in the cocrystals of mono- and diazanaphthalenes with *meso*-1, 2-diphenyl-1,2-ethanediol" *Crystal Growth & Design*, 2003, pp. 175-181, Vol. 3, No. 2.	
	*	OLENIK, B. et al. "Supramolecular synthesis by cocrystallization of oxalic and fumaric acid with diazanaphthalenes" *Crystal Growth & Design*, 2003, pp. 183-188, Vol. 3, No. 2.	
	*	OSORIO-LOZADA, A. et al. "Synthesis and determination of the absolute stereochemistry of the enantiomers of adrafinil and modafinil" *Tetrahedron: Asymmetry*, 2004, 15:3811-3815.	
	*	OSWALD, I. et al. "Rationalisation of co-crystal formation through knowledge-mining" *Crystallography Reviews*, 2004, pp. 57-66, Vol. 10, No. 1.	
	*	OSWALD, I.D.H. et al. "The formation of paracetamol (acetaminophen) adducts with hydrogen-bond acceptors" *Acta Crystallographica Section B*, 2002, B58:1057-1066.	
	*	OTSUKA, M. et al. "Effect of Polymorphic Forms of Bulk Powders on Pharmaceutical Properties of Carbamazepine Granules" *Chem Pharm Bull*, 1999, 47(6):852-856.	
	*	OUYANG, X. et al. "Single-crystal-to-single-crystal topochemical polymerizations of a terminal diacetylene: two remarkable transformations give the same conjugated polymer" *J. Am. Chem. Soc.*, 2003, pp. 12400-12401, Vol. 125.	
	*	PATEL, U. et al. "Structure of the 1:1 complex between 4-amino-*N*-(4,6-dimethyl-2-pyrimidinyl)- benzenesulfonamide (sulfadimidine) and 2-hydroxybenzoic acid (salicylic acid)" *Acta Cryst.*, 1988, pp. 1264-1267, Vol. C44.	
	*	PEDIREDDI, V.R. et al. "Layered Structures Formed by Dinitrobenzoic Acids" *Tetrahedron Letters*, 1998, 39:9831-9834.	
	*	PRIVITERA, M. et al. "Dose-Ranging Trial with Higher Doses of Topiramate in Patients with Resistant Partial Seizures", *Amer. Epilepsy Soc. Proc.*, 1995, pg. 33, Vol. 36, Supp. 4.	
	*	QUEHENBERGER, H. "Concerning organic molecular compounds and their polymorphism" Monatshefte für Chemie, 1949, pp. 595-606, Vol. 80, No. 5.	
	*	RASENACK, N. et al. "Dissolution Rate Enhancement by *in Situ* Micronization of Poorly Water-Soluble Drugs" *Pharmaceutical Research*, December 2002, 19(12):1894-1900.	
	*	RECK, G. et al. "Crystal structures of the carbamazepine/ammonium chloride and carbamazepine/ammonium bromide adducts and their transformation into carbamazepine dihydrate" *Pharmazie*, 1991, pp. 509-512, Vol. 46, No. 7.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	25	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	REDDY, L. et al. "Phenyl-perfluorophenyl synthon mediated cocrystallization of carboxylic acids and amides" *Crystal Growth & Design*, 2004, pp. 89-94, Vol. 4., No. 1.	
	*	REMENAR, J. F. et al. "Celecoxib sodium salt: engineering crystal forms for performance" *CrystEngComm*, 2011, 13:1081-1089.	
	*	REMENAR, J. F. et al. "Crystal engineering of novel cocrystals of a triazole drug with 1,4-dicarboxylic acids" *J. Am. Chem. Soc.*, 2003, pp. 8456-8457, Vol. 125.	
	*	REYNOLDS, J. E. F. (ed). Martindale, The Extra Pharmacopoeia, 1993, The Pharmaceutical Press, London, England, 13th Edition, pp. 1431 (e.g., Acetaminophen, Aspirin, and Caffeine Tablets), 1465 (e.g., Aspirin plus C), 1521 (Codafen Continus), 1610 (Gaboril Complex).	
	*	ROBBINS, A. H. et al. "The crystal structure of the 1:2 adduct of potassium triiodide and 5,5-diethylbarbituric acid (barbital)" *American Crystallographic Association- Series 2 Papers and Abstracts*, 1973, p. 87.	
	*	ROSENFELD, W. E. "Topiramate: A Review of Preclinical, Pharmacokinetic, and Clinical Data" *Clinical Therapeutics*, 1997, 1916):1294-1308.	
	*	RUBINO, J.T. et al. "Influence of solvent composition on the solubilities and solid-state properties of the sodium salts of some drugs" *International Journal of Pharmaceutics*, 1990, 65:141-145.	
	*	SACHDEO, S.K. et al. "Topiramate: Double-Blind Trial as Monotherapy", *Amer. Epilepsy Soc. Proc.*, 1995, pg. 33, Vol. 36, Supp. 4.	
	*	SAKSENA, A. K. et al. "Advances in the chemistry of novel broad-spectrum orally active azole antifungals: recent studies leading to the discovery of SCH 56592" in Advances in the Chemistry of Novel Broad-Spectrum Orally Active Azole Antifunoals (Royal Soc. Chem., Cambridge), 1997, pp. 180-199.	
	*	SAKSENA, A. K. et al. "Concise asymmetric routes to 2,2,4-trisubstituted tetrahydrofurans via chiral titanium imide enolates: key intermediates towards synthesis of highly active azole antifungals SCH 51048 and SCH 56592" *Tetrahedron Letters*, 1996, pp. 5657-5660, Vol. 37, No. 32.	
	*	SALEM, M.S. et al. "Preparation, characterisation and transformation of terfenadine polymorphic forms" *International Journal of Pharmaceutics,* 1996, 141:257-259.	
	*	SALMON, J. et al. "Supramolecular chemistry of boronic acids (Abstract)" 38th Midwest Regional Meeting of the American Chemical Society in Columbia, MO., November 5-7, 2003, published by the American Chemical Society, Washington, D.C.	
	*	SCARBROUGH, F. et al. "Crystal structure of a complex between lumiflavin and 2,6-diamino-9-ethylpurine: a flavin adenine dinucleotide model exhibiting charge-transfer interactions" *Proc. Natl. Acad. Sci. USA*, November 1976, pp. 3807-3811, Vol. 73, No. 11.	
	*	SCHMIDT, G. "Photodimerization in the solid state" *Pure Appl. Chem.*, 1971, pp. 647-678, Vol. 27.	
	*	SHAN, N. et al. "Co-crystal of 4,7-phenanthroline and carboxylic acids: synthon competition and prediction" *Tetrahedron Letters*, 2002, pp. 8721-8725, Vol. 43.	
	*	SHAN, N. et al. "Crystal engineering using 4,4'-bipyridyl with di- and tricarboxylic acids" *Crystal Engineering*, 2002, pp. 9-24, Vol. 5.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	26	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	SHAN, N. et al. "Mechanochemistry and co-crystal formation: effect of solvent on reaction kinetics" *Chem. Commun.*, 2002, pp. 2372-2373.	
	*	SHAN, N. et al. "Supramolecular synthons in the co-crystal structures of 2-aminopyrimdine with diols and carboxylic acids" *Tetrahedron Letters*, 2002, pp. 3101-3104, Vol. 43.	
	*	SHATTOCK, T. R. et al. "Hierarchy of Supramolecular Synthons: Persistent Carboxylic Acid ••• Pyridine Hydrogen Bonds in Cocrystals that also contain a Hydroxyl Moiety" *Crystal Growth 7 Design*, 2008, pp. 4533-4545, Vol. 8, No. 12.	
	*	SHAVIV, R. et al. "Magnetochemistry of the tetrahaloferrate (III) ions 6. Crystal structure and magnetic ordering in $[(pyH)_3Cl]$ $[FeCl_4]_2$" *Inorganica Chimica Acta*, 1992, pp. 613-621, Vol. 198-200.	
	*	SHEFTER, E. "Structural studies on complexes IV: Crystal structure of a 1:1 5-chlorosalicylic acid and theophylline complex" *Journal of Pharmaceutical Sciences*, 1969, pp. 710-714, Vol. 58.	
	*	SHEFTER, E. et al., ACS, Abstr. Papers (Summer), 1970, 35, compound name: sulfathiazole-theophylline complex.	
	*	SHIMIZU, N. et al. "Structure of 2,4-diamino-5-(3,4,5-trimethoxybenzyl) pyrimidine-5,5-diethylbarbituric acid (1:1)" *Acta Cryst.*, 1982, pp. 2309-2311, Vol. B38.	
	*	SIMONOV, Y. et al. "Structure of the caffeine-copper(II) acetate additional compound", *Izvestiya Akademii Nauk Moldavskoi SSR, Seriya Fiziko-Tekhnicheskikh i Matematicheskikh Nauk*, 1972, Vol. 3, pp. 83-84, abstract only.	
	*	SINGH, N. B. et al. "Solid state reaction between 8-hydroxyquinoline and *p*-nitrobenzoic acid" *Indian Journal of Chemistry*, May 1988, pp. 429-432, Vol. 37B.	
		SMITH et al., The Determination of the Crystal Structure of Anhydrous Theophylline by X-ray Powder Diffraction with a Systematic Search Algorithm, Lattice Energy Calculations, and ^{13}C and ^{15}N Solid-State NMR: A Question of Polymorphism in a Given Unit Cell. J Phys Chem B. 2001;105(24):5818-26.	
	*	SMITH et al., The utility of 4-aminobenzoic acid in promotion of hydrogen bonding in crystallization processes: the structures of the cocrystals with halo and nitro subsituted aromatic compounds, and the crystal structures of the adducts with 4-nitroaniline (1:1), 4-(4-nitrobenzyl)pyridine (1:2), and (4-nitrophenyl)acetic acid (1:1). J Chem Crystallogr. 1997 May; 27(5):307-317.	
	*	SMITH, D. et al. "Structure confirmation by single crystal X-ray diffraction of a series of new schiff bases and theoretical computations on 3-(N-2-α, α, α-triflourotoluylidene amino) tetrahydrothiophene-1, 1-dioxide (Abstract)" 216th ACS National Meeting in Boston, MA., August 23-27, 1998, published by the American Chemical Society, Washington, D.C.	
	*	SMITH, G. et al. "Interactions of aromatic carboxylic acids with quinolin-8-ol (oxine): Synthesis and the crystal structures of the proton-transfer compounds with the nitro-substituted benzoic acids" *Aust. J. Chem.*, 2001, pp. 171-175, Vol. 54.	

EXAMINER: /NOBLE E JARRELL/	DATE CONSIDERED: 02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	27	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	SMITH, G. et al. "Molecular cocrystals of carboxylic acids. XXI The role of secondary group interactions in adduct formation between 2-aminopyramidine and substituted benzoic acids: the crystal structures of the adducts with *o*-phthalic acid, *o*-nitrobenzoic acid, *o*-aminobenzoic acid and *m*-aminobenzoic acid" *Aust. J. Chem.*, 1995, pp. 1151- 1166, Vol. 48.	
	*	SMITH, G. et al. "The 1:1 adduct of 4-aminobenzoic acid with 4-aminobenzonitrile" *Acta Cryst.*, 2000, pp. 1155-1156, Vol. C56.	
	*	STAHL, P.H. *The Practice of Medicinal Chemistry*; "Chapter 35: Preparation of water-soluble compounds through salt formation" 1 January 2003, Elsevier, NL, pp. 601-615, XP002566271.	
	*	STAHLY, G. P. "A Survey of Cocrystals Reported prior to 2000" *Crystal Growth & Design*, 2009, 9:4212-4229.	
	*	STALKER, R. et al. "Asymmetric synthesis of two new conformationally constrained lysine derivatives" *Tetrahedron*, 2002, pp. 4837-4849, Vol. 58.	
	*	STEINER, T. "Donor and acceptor strengths in C-H•••0 hydrogen bonds quantified from crystallographic data of small solvent molecules" *New. J. Chem.*, 1998, pp. 1099-1103.	
	*	STEZOWSKI, J. J. et al. "Characterization of a 1:1 complex of an unusual structure in the phenothiazine/phenazine binary phase diagram" *Zeitschrift fur Kristallographie* in International Journal for Structural, Physical, Chemical Aspects of Crystalline Materials, 1983, pp. 213-215, Vol. 162, No. 1-4.	
	*	STOREY, R. et al. "Automation of solid form screening procedures in the pharmaceutical industry- how to avoid the bottlenecks" *Crystallography Reviews*, 2004, pp. 45-56, Vol. 10, No. 1.	
	*	SUMMERS, M.P. et al. "The polymorphism of aspirin" *J. Pharm. Pharmac.*, 1970, 22:615-616.	
	*	SZAFRAN, M. et al. "Molecular structures and hydrogen bonding in the 1:1 and 1:2 complexes of pyridine betaine with 2,6-dichloro-4-nitrophenol; an example of strongly coupled hydrogen bonds, 0-H•••O=C-0-H•••0-" *Journal of Molecular Structure*, 1997, pp. 145-160, Vol. 416.	
	*	TAKEUCHI, M. et al. "Synchrotron radiation SAXS/WAXS study of polymorph-dependent phase behavior of binary mixtures of saturated monoacid triacylglycerols" *Crystal Growth & Design*, 2003, pp. 369-374, Vol. 3, No. 3.	
	*	TANG, C. P. et al. "Reaction pathways in crystalline host-guest inclusion complexes: rotation by a net 180° of the acetyl group on photoaddition of guest- acetophenone and —*m*-Chloroacetophenone to the atom C5 of host deoxycholic acid" *J. Am. Chem. Soc.*, 1985, pp. 4058-4070, Vol. 107.	
	*	TAYLOR, R. et aL "Rules governing the crystal packing of mono- and dialcohols" *Acta Crystallographica Section B, Structural Science*, 2001, pp. 815-827, Vol. B57.	
	*	THALLAPALLY, P. et al. "Polymorphism of 1,3,5-trinitrobenzene induced by a trisindane additive" *Angew. Chem. Mt. Ed.*, 2004, pp. 1149-1155, Vol. 43.	
	*	THAYER, A.M. et al. "Form and Function" *Chemical & Engineering News*, June 18, 2007, 85(25):17-30 (8 pages).	
	*	TIMMERMAN, P. et al. "Noncovalent Assembly of functional groups on calix[4]arene molecular boxes" *Chem. Eur. J.*, 1997, pp. 1823-1832, Vol. 3., No. 11.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	28	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	TOMURA, M. et al. "One-dimensional zigzag chain structures with intermolecular C-H•••π and C-H•••O interactions consisted of phthalic acid and pyridine derivatives" *Chemistry Letters*, 2001, pp. 532-533.	
	*	TRASK, A. et al. "Crystal engineering of organic cocrystals by the solid-state grinding approach" *Top Curr. Chem.*, 2005, pp. 41-70, Vol. 254.	
	*	TRASK, A. et al. "Pharmaceutical cocrystallization: engineering a remedy for caffeine hydration" *Crystal Growth & Design*, 2005, pp. 1013-1021, Vol. 5, No. 3.	
	*	TRASK, A. et al. "Solvent-drop grinding: green polymorph control of cocrystallisation" *Chem. Commun.*, 2004, pp. 890-891 in addition to supplemental materials.	
	*	TROWBRIDGE, L. et al. "Composites for nonlinear optics: Crystal growth and polymorphism" *University of Sussex, Falmer Brighton UK, School of Chemistry and Molecular Sciences*, pp. 272.	
	*	UNO, T. et al. "Structure of 5,5-diphenylhydantoin-1- (4-bromophenyl)-4-dimethylamino-2,3-dimethyl-3-pyrazolin-5-one (1:1)" *Acta Cryst.*, 1980, pp. 2794-2796, Vol. B36.	
	*	URBINA, J. et al. "Supramolecular design of inorganic/organic networks using flexible ligands with self-complementary hydrogen bonds (Abstract)" 38th Midwest Regional Meeting of the American Chemical Society in Columbia, MO., November 5-7, 2003, published by the American Chemical Society, Washington, D.C.	
	*	VAN ROEY, P. et al. "Structure of *cis*-1-{[4-(1-imidazolylmethyl) cyclohexyl] methyl} imidazole- succinic acid complex" *Acta Cryst.*, 1991, pp. 1015-1018, Vol. C47.	
	*	VAN ROEY, P. et al. "Structure-activity studies of non-steroidal aromatase inhibitors: the crystal and molecular structures of CGS 16949A and CGS 18320B" *J. Enzyme Inhibition*, 1991, pp. 119-132, Vol. 5.	
	*	VILLA, L. A. et al. "Central nervous system paracoccidioidomycosis. Report of a case successfully treated with itraconazol" *Rev. Inst. Med. Trop. S. Paulo*, July-August, 2000, pp. 231-234, Vol. 42, No. 4.	
	*	VIPPAGUNTA, S. R. et al. "Crystalline solids" *Advanced Drug Delivery Reviews*, 2001, pp. 3-26, Vol. 48.	
	*	VISHWESHWAR, P. et al. "Crystal engineering of pharmaceutical co-crystals from polymorphic active pharmaceutical ingredients" *Chem. Commun.*, 2005, pp. 4601-4603.	
	*	VISHWESHWAR, P. et al. "Molecular complexes of homologous alkanedicarboxylic acids with isonicotinamide: X-ray crystal structures, hydrogen bond synthons, and melting point alternation" *Dotal Growth & Design*, 2003, pp. 783-790, Vol. 3, No. 5.	
	*	VISHWESHWAR, P. et al. "Recurrence of carboxylic acid- pyridine supramolecular synthon in the crystal structures of some pyrazinecarboxylic acids" *J. Org. Chem.*, 2002, pp. 556-565, Vol. 67.	
	*	VISHWESHWAR, P. et al. "Supramolecular synthons based on N-H•••N and C-H•••0 hydrogen bonds. Crystal engineering of a helical structure with 5,5-diethylbarbituric acid" *Chem. Commun.*, 2002, pp. 1830-1831.	
	*	VISHWESHWAR, P. et al. "Supramolecular synthons in phenol-isonicotinamide adducts" *Cryst Eng. Comm.* 2003, pp. 164-168, Vol. 5, No. 31.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	29	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	VOET, D. et al. "Barbiturates and adenine derivatives. Molecular structure of a hydrogen-bonded complex" *Joumal of the American Chemical Society*, August 9, 1972, pp. 5888- 5891, Vol. 94, No. 16.	
	*	VOET, D. et al. "The crystal and molecular structure of the intermolecular complex 9-ethyladenine-5, 5-diethylbarbituric acid" *Journal of the American Chemical Society*, November 15, 1972, pp. 8213-8222, Vol. 94, No. 23.	
	*	VOET, D. et al. "The structure of an intermolecular complex between cytosine and 5-fluorouracil" *Journal of the American Chemical Society*, May 21, 1969, pp. 3069-3075, Vol. 91, No. 11.	
	*	WALSH, R.D.B. et al. " Crystal Engineering of the composition of pharmaceutical phases". *Chem. Commun.*, 2003, pp. 186-187.	
	*	WANG, A. et al. "Crystal structure of 1:1 complex of barbital with 1-methylimidazole" *Journal of Pharmaceutical Sciences*, March 1979, pp. 361-363, Vol. 68, No. 3.	
	*	WEBER, E. et al. "Synthesis of new Schiff bases: reaction of monofluorobenzaldehydes with 3-aminosulfolane hydrochloride (Abstract)" 216th ACS National Meeting in Boston, MA., August 23-27, 1998, published by the American Chemical Society, Washington, D.C.	
	*	WEISSBUCH, I. et al. "Crystal morphology control with tailor-made additives; a stereochemical approach" *Advances in Crystal Growth Research*, 2001, pp. 381-400.	
	*	WEISSBUCH, I. et al. "Understanding and Control of Nucleation, Growth, Habit, Dissolution and Structure of Two- and Three-Dimensional Crystals Using 'Tailor-Made' Auxiliaries" *Acta Cryst.*, 1995, B51:115-148.	
	*	WEST, A. R., "Solid Solutions" In: Solid State Chemistry and its Applications, 1988, p. 358, p. 365, Wiley, NY.	
	*	WHEATLEY, P.J., "The Crystal and Molecular Structure of Aspirin," *J. Chem. Soc.*, 1964, pp. 6036- 6048.	
	*	WIEDENFELD, H. et al. "Solubilization of aminophenazone" *Arch. Pharm.*, 1982, pp. 633- 641, Vol. 315.	
	*	WIEDENFELD, H. et al. "The crystal structure of the theophylline-urea complex" *Arch. Pharm.*, 1986, pp. 654-659, Vol. 319.	
	*	WOOD, R. A. et at "2,5-O-methylene-D-mannitol sodium-chloride, $C_7 H_{14} O_6$. NaCl" *Cryst. Struct. Comm.*, 1976, 207-210, Vol. 5.	
	*	WUNDERLICH, H.F. et al. " The Derivatives of carbamazepine with ammonium halogenides and formamide" *Pharmazie*, 1991,46(7):507-509.	
	*	XU, J. et al. "Effect of composition distribution on miscibility and co-crystallization phenomena in the blends of low density polyethylene with conventional and metallocene-based ethylene-butene copolymers" *Polymer*, 2001, pp. 3867-3874, Vol. 42.	
	*	YADAV, A.V. et al. "Co-crystals: A novel approach to modify physicochemical properties of active pharmaceutical ingredients" *Indian Journal of Pharmaceutical Sciences*" 2009, 71(4):359-370.	
	*	YOO, J. et at "Cocrystallization of a dinuclear platinum complex as a monomer and a one-dimensional polymer" *Polyhedron*, 2002, pp. 715-719, Vol. 21.	

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08) **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	30	of	30	GROUP ART UNIT:1625	EXAMINER: Not Yet Assigned

	*	ZAITU, S. et al. "1:1 Molecular complex of theophylline and *p*-nitroaniline" *Acta Cryst.*, 1995, pp. 2390-2392, Vol. C51.	
	*	ZAITU, S. et al. "A 2:1 molecular complex of theophylline and 5-fluorouracil as the monohydrate" *Acta Cryst.*, 1995, pp. 1857-1859, Vol. C51.	
	*	ZAMAN, M. B. et al. "Crystal Engineering Using Anilic Acids and Dipyridyl Compounds through a New Supramolecular Synthon" *J. Org. Chem.*, 2001, pp. 5987-5995, Vol. 66.	
	*	ZAMAN, M. B. et at "Linear hydrogen-bonded molecular tapes in the cocrystals of squaric acid with 4,4'-dipyridylacetylene and 1,2-bis(4-pyridyl) ethylene" *Acta Cryst.*, 2001, pp. 621-624, Vol. C57.	
	*	ZAMAN, M.B. et al. "Crystal Engineering Using Anilic Acids and Dipyridyl Compounds through a New Supramolecular Synthon" *J. Org. Chem.*, 2001, 66:5987-5995.	
	*	ZAWOROTKO, M. J. "Crystal Engineering of Diamondoid Networks", *Chem. Soc. Rev.*, 1994, pp. 283-288, Vol. 23.	
	*	ZAWOROTKO, Michael J., "Binary Crystals by Design," Abstracts of Papers, 23rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002, IEC-030.	
	*	ZERKOWSKI, J. et al. "Design of organic structures in the solid state: hydrogen-bonded molecular "tapes"[1]" *J. Am. Chem. Soc.*, 1990, pp. 9025-9026, Vol. 112.	
	*	ZERKOWSKI, J. et al. "Design of organic structures in the solid state: molecular tapes based on the network of hydrogen bonds present in the cyanuric acid•melamine complex" *J. Am. Chem. Soc.*, 1994, pp. 2382-2391, Vol. 116.	
	*	ZERKOWSKI, J. et al. "Investigations into the robustness of secondary and tertiary architecture of hydrogen-bonded crystalline tapes" *Chem. Mater*, 1994, pp. 1250-1257, Vol. 6.	
	*	ZERKOWSKI, J. et al. "New varieties of crystalline architecture produced by small changes in molecular structure in tape complexes of melamines and barbiturates" *J. Am. Chem. Soc.*, 1994, pp. 4305-4315, Vol. 116.	
	*	ZERKOWSKI, J. et al. "Polymorphic packing arrangements in a class of engineered organic crystals" Chem. Mater., 1997, pp. 1933-1941, Vol. 9.	
	*	ZERKOWSKI, J. et al. "Solid-state structures of "Rosette" and "Crinkled Tape" motifs derived from the cyanuric acid-melamine lattice" *J. Am. Chem. Soc.*, 1992, pp. 5473-5475, Vol. 114.	
	*	ZERKOWSKI, J. et al. "Steric control of secondary, solid-state architecture in 1:1 complexes of melamines and barbiturates that crystallize as crinkled tapes" *J. Am. Chem. Soc.*, 1994, pp. 4298-4304, Vol. 116.	
	*	ZHANG, R. et al. "Atmospheric new particle formation enhanced by organic acids" *Science*, June 4, 2004, pp. 1487-1490 with additional supporting online material, Vol. 304.	
	*	ZHU, H. et al. "Influence of water activity in organic solvent + water mixtures on the nature of the crystallizing drug phase. 1. theophylline" *International Journal of Pharmaceutics*, 1996, pp. 151-160, Vol. 135.	

[NOTE – No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR § 1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR § 1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR § 1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. § 120.]

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	02/19/2019

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. 10/378956 , filed March 3, 2003, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

BIB DATA SHEET

CONFIRMATION NO. 8089

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
15/639,223	06/30/2017	424	1625	U0157.70023US03

APPLICANTS

University of South Florida, Tampa, FL;
The Regents of the University of Michigan, Ann Arbor, MI;

INVENTORS

Michael J. Zaworotko, Tampa, FL;
Nair Rodriguez-Hornedo, Ann Arbor, MI;
Brian Moulton, Temple Terrace, FL;

**** CONTINUING DATA ***************************

This application is a CON of 10/378,956 03/03/2003 ABN
which claims benefit of 60/360,768 03/01/2002

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **
07/10/2017

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /NOBLE E JARRELL/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		FL	22	20	4

ADDRESS

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206
UNITED STATES

TITLE

MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

FILING FEE RECEIVED		
1010	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

DOCKET NO.: U0157.70023US03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1625

Certificate of Electronic Filing under 37 CFR §1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 8, 2018 Electronic Signature for Chelsie Bailey: /Chelsie Bailey/

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF DISCLOSURE UNDER 37 C.F.R. §§ 1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, the undersigned requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. § 1.97

This Information Disclosure Statement has been filed before the mailing of a first Office Action on the merits in the above-identified case.

No fee or certification is required.

PART II: Information Cited

The undersigned hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified PTO/SB/08). The order of presentation of the references should not be construed as an indication of the importance of the references.

6224463.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

The undersigned hereby makes the following additional information of record in the above-identified application.

The undersigned would like to bring to the Examiner's attention the following co-pending applications that may contain subject matter related to this application:

Serial No.	Filing Date	Inventor(s)	Docket No.
*10/378,956	March 3, 2003	Zaworotko et al.	U0157.70023US01
*14/179,862	February 13, 2014	Zaworotko et al.	U0157.70023US02

*A copy of this reference is not provided as the Office has waived the requirement under 37 C.F.R. § 1.98(a)(2)(iii) for submitting a copy of a cited U.S. patent application if it is scanned to the Image File Wrapper system and is available on Private PAIR .

The undersigned would like to bring to the Examiner's attention the enclosed search report or other communication from a corresponding or related International or Foreign National Application:

Serial No.	Date of Mailing	Type(s) of Communication	Docket No.
EP 03711407.1	11-22-2006	European Search Report	U0157.70023EP00
PCT/US2003/06662	10-24-2003	International Search Report	U0157.70023WO00

PART III: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;

2. The enclosed form PTO-1449 (modified PTO/SB/08) be signed by the Examiner to evidence that the cited information has been fully considered by the United States Patent and Trademark Office during the examination of this application;

3. The citations for the information be printed on any patent which issues from this application.

/NOBLE E JARRELL/ 02/20/2019

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

By submitting this Information Disclosure Statement, the undersigned makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. § 102.

Notwithstanding any statements by the undersigned, the Examiner is urged to form his or her own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

The Director is hereby authorized to charge any deficiency or credit any overpayment in the fees occasioned by the filing of this Information Disclosure Statement to our Deposit Account No. 23/2825 under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Respectfully submitted,

By: /David F. Cauble/

David F. Cauble, PhD, JD, Reg. No. 73,490
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
Telephone: (617) 646-8000

Docket No.: U0157.70023US03
Date: November 8, 2018

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

```
=> d his full

     (FILE 'HOME' ENTERED AT 08:50:33 ON 19 FEB 2019)

     FILE 'HCAPLUS' ENTERED AT 08:50:41 ON 19 FEB 2019
L1             4 SEA SPE=ON  ABB=ON  PLU=ON  US20170362182/PN
                 E CRYSTALLIZATION/CT
                 E E3+ALL
L2               QUE SPE=ON  ABB=ON  PLU=ON  CRYSTALLIZATION+PFT,NT/CT
                 E E84+ALL
L3               QUE SPE=ON  ABB=ON  PLU=ON  CRYSTALLINITY+OLD/CT
                 D SCA L1
                 E CRYSTAL STRUCTURE/CT
                 E E3+ALL
L4               QUE SPE=ON  ABB=ON  PLU=ON  "CRYSTAL STRUCTURE"+PFT,NT/CT
                 E CRYSTAL STRUCTURE/CT
                 E E3+ALL
L5               QUE SPE=ON  ABB=ON  PLU=ON  "CRYSTAL STRUCTURE"+PFT,NT/CT
                 E ACTIVE PHARMACEUTICAL INGREDIENT/CT
                 E PHARMACEUTICAL/CT
                 E E3+ALL
                 E E2
                 E E3+OLD,NT1
L6               QUE SPE=ON  ABB=ON  PLU=ON  DRUGS+PFT,NT1/CT
L7         16288 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND (L2 OR L3 OR L4 OR L5)
L8               QUE SPE=ON  ABB=ON  PLU=ON  PRD<=20020301 OR AD<=20020301 OR
                 PD<=20020301
L9               QUE SPE=ON  ABB=ON  PLU=ON  PD<=20010301
L10              QUE SPE=ON  ABB=ON  PLU=ON  PY<=2002
L11         1160 SEA SPE=ON  ABB=ON  PLU=ON  L7 AND (L8 OR L9 OR L10)
L12            0 SEA SPE=ON  ABB=ON  PLU=ON  L11 AND L1
L13            4 SEA SPE=ON  ABB=ON  PLU=ON  L11 AND L6 (L) (COCRYSTAL? OR CO
                 (2A) CRYSTAL?)

     FILE HOME

     FILE HCAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.

     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
     strictly prohibited.

     FILE COVERS 1907 - 19 Feb 2019 VOL 170 ISS 10
     FILE LAST UPDATED: 18 Feb 2019 (20190218/ED)
     REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Dec 2015
     USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Dec 2015

     HCAplus now includes the comprehensive Cooperative Patent Classification
     (CPC).  See HELP CPC for details.

     CAS Information Use Policies apply and are available at:
```


NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 221 of 415

http://www.cas.org/legal/infopolicy

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 18 FEB 2019 HIGHEST RN 2271062-41-8
DICTIONARY FILE UPDATES: 18 FEB 2019 HIGHEST RN 2271062-41-8

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

TSCA INFORMATION NOW CURRENT THROUGH April 2018.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/training/stn/database-specific

=>

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 222 of 415

EAST Search History

EAST Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	12384	(Zaworotko rodriguez (2a) hornedo moulton).in.	US-PGPUB; USPAT	OR	OFF	2019/02/19 17:38
L2	128	c07d223/26.cpc.	US-PGPUB; USPAT	OR	OFF	2019/02/19 17:38
L3	5	l1 and l2	US-PGPUB; USPAT	OR	OFF	2019/02/19 17:39
L4	9	l2 and (cocrystal co NEAR crystal cocrystals co near crystals).clm.	US-PGPUB; USPAT	OR	OFF	2019/02/19 17:44
L5	5	l4 and l3	US-PGPUB; USPAT	OR	OFF	2019/02/19 17:44
L6	4	l4 not l5	US-PGPUB; USPAT	OR	OFF	2019/02/19 17:45

2/19/2019 5:46:14 PM
C:\Users\njarrell\Documents\EAST\Workspaces\white_dwarf.wsp

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 223 of 415

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1625

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 23, 2019 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

RESPONSE TO NON-FINAL OFFICE ACTION UNDER 37 C.F.R. § 1.111

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Office Action dated February 26, 2019, the time being extended to the present by the attached Petition for Extension of Time, Applicant respectfully requests entrance of the following Amendments and consideration of the following Remarks.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 5 of this paper.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 224 of 415

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, and listings, of claims in the Application:

Listing of Claims

1 – 36. (Canceled)

37. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-crystal former,

wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form,

wherein the co-crystal former has a second chemical functionality complimentary to the first chemical functionality via non-covalent hydrogen bonding,

wherein supramolecular synthons comprise non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-crystal former.

38. (Previously presented) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, a GRAS compound, a food additive, a low toxicity organic, and a metal-organic complex.

39. (Previously presented) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 225 of 415

40. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and one co-crystal former.

41. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of one active pharmaceutical ingredient (API) and one co-crystal former.

42. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a group selected from acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases, amines, alcohols, halogens, sulfones, and nitro groups.

43. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an acid.

44. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amine.

45. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amide.

46. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an alcohol.

47. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 226 of 415

48. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a heterosynthon.

49. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon and a heterosynthon.

50. (Previously presented) The pharmaceutical composition of claim 48, wherein the heterosynthon comprises an alcohol/amine interaction.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 227 of 415

REMARKS

Prior to entry of the instant amendments, claims 37-50 were pending in the Application. No claims have been amended in this response. Each of the rejections levied by the Examiner is addressed in turn below.

Claim Rejections under 35 U.S.C. § 112

Claims 37-50 are rejected under 35 U.S.C. 112(a), first paragraph, because the specification, while being enabling for the preparation of co-crystals of examples 1-17 in the specification, allegedly does not enable preparation of the scope of co-crystals as claimed. Applicant respectfully disagrees, and as a preliminary matter notes that the Application discloses 19 working examples.

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (*United States v. Telectronics, Inc.,* 857 F.2d 778, 785 (Fed. Cir. 1988)) This standard is satisfied by the present application.

In paragraph [0043], the present application discloses a method of preparing a multiple-component solid phase composition composed of an API and at least one co-crystal former involving techniques such as such as crystallization from solution, cooling the melt, sublimation and grinding. A "multiple-component phase" is defined in paragraph [0047] as any solid material (phase) that is sustained by intermolecular interactions between at least two independent molecular entities, in any stoichiometric ratio, wherein at least one of the independent molecular entities is a pharmaceutical entity. "Pharmaceutical entities" are defined in paragraph [0048] and numerous examples of chemical functional groups that are capable of forming supramolecular synthons are provided.

Paragraphs [0040]-[0042] disclose methods for identifying complementary chemical functional groups with which to form the desired supramolecular synthons. The methods involve

- evaluating the structure of an API, which can include determining its crystal structure;

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 228 of 415

- determining whether the API contains chemical functionalities capable of forming supramolecular synthons with different molecules;
- identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular synthons with the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the API; and
- identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

In paragraphs [0057]-[0178], the Applicant discloses the application of the preceding method to the discovery of 19 different co-crystals. MPEP 2164.02(III) states that:

> For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art…would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus ***only where adequate reasons are advanced*** by the examiner ***to establish that a person skilled in the art could not use the genus as a whole without undue experimentation***. (Emphasis added)

In the Office Action, no adequate reasons have been advanced to support the rejection of the claimed genus. For example, page 3 of the Office Action references Kumar et al. for allegedly teaching that "many steps are required to make a cocrystal…and that different methods of making cocrystals are known…" Applicant respectfully notes that the present Application itself discloses a method having several steps, and discloses different methods of making cocrystals. In this regard, Kumar et al. merely reiterates the teachings of the present Application. Kumar et al. allegedly teaches that "the formation of cocrystals has challenges: selection of a suitable conformer…" In this regard, Applicant notes that the present Application discloses a method of selecting a suitable conformer on the basis of complementary chemical functionality. Kumar et al. neither teaches nor suggests the inoperability of the methods disclosed in the present Application. Kumar et al. allegedly teaches that the "development, screening, and evaluation of new cocrystals of drugs [requires a] lot of time due to the steps required…" Even assuming, arguendo, that this statement is

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 229 of 415

accurate, it is not evidence that undue experimentation is required to make and use the claimed invention. MPEP 2164.01 states that "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." In fact, Kumar et al. itself discloses that the art engages in such experimentation, as described below.

Page 3 of the Office Action states that although the relative skill of those in the art is high, "their…skill and knowledge is insufficient to overcome the lack of understanding as to how cocrystal formation occurs." Applicant disagrees. The Office has not identified any teaching of Kuman et al. that indicates a lack of understanding. In fact, Kuman et al. makes no such statement.

Page 4 of the Office Action states that the "specification does not provide guidance for the scope of the stoichiometric crystals claimed." In response, Applicant refers the Office to MPEP 2164.02(III), quoted above, and maintains that no adequate reasons have been advanced to support the rejection of the claimed genus.

On page 4, the Office Action refers to "the high unpredictability" evidenced by Kumar et al, and the "lack of guidance" provided by the specification. As discussed above, the specification provides abundant guidance, and there is no evidence that the guidance provided is insufficient to enable the full scope of the claimed invention. Furthermore, Applicant notes that nowhere in Kumar et al. is there a teaching that cocrystal formation is unpredictable. To the contrary, Kumar et al. teaches that:

- "A ***prediction can be made*** by ΔpKa value whether cocrystals are formed or not." (page 859, second column, first paragraph);
- "***Cocrystals…formation can be predicted*** by proton transfer between acid and base. The formation of…cocrystals can be predicted by determining the ΔpKa=[pKa (base)-pKa (acid)]" (page 863, first column, third paragraph);
- "The miscibility of the components in the solid state ***could predict the cocrystal formation***." (page 863, second column, fourth paragraph); and
- "FTIR spectroscopy is ***used to predict*** the intermolecular interactions and compatibility study between drug and coformers." (page 866, first column, fifth paragraph)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 230 of 415

At least for the foregoing reasons, Applicant requests withdrawal of the rejection of the claims under 35 U.S.C. 112(a), first paragraph.

Claim Rejections under 35 U.S.C. § 102

Claims 37-42, 45, 46, and 48 are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by Hsu (*Acta Crystallographica*, 1974, B30, 843-846, cited in IDS), hereinafter referred to as "Hsu". Applicant respectfully traverses this rejection.

Hsu allegedly teaches a 1:1 cocrystal of salicylamide and 5-ethyl-5-isoamylbarbituric acid. However, Hsu does not teach a pharmaceutical composition, as claimed. As such, Hsu does not teach all elements of claim 37, and therefore does not anticipate claim 37, or claims depending therefrom. Accordingly, Applicant requests withdrawal of this rejection.

Double Patenting

Claims 37-50 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37 and 45 of copending Application No. 14/179862. Applicant requests that the Examiner hold this rejection in abeyance until the claims are otherwise held to be in condition for allowance.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 231 of 415

CONCLUSION

In view of the foregoing, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this response, the application is not in condition for allowance, the Examiner is requested to call the undersigned at the telephone number indicated below to discuss any outstanding issues.

All fees due in connection with the filing of this paper are being paid by credit card. However, if additional fees are due with this filing, please charge our Deposit Account No. 23/2825, under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Dated: July 23, 2019

Respectfully submitted,

By /David F. Cauble/_____
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 232 of 415

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Cathy Nicholson
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 2 months with $0 paid	2252	1	300	300
Miscellaneous:				
		Total in USD ($)		**300**

Electronic Acknowledgement Receipt	
EFS ID:	36667043
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Cathy Nicholson
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	23-JUL-2019
Filing Date:	30-JUN-2017
Time Stamp:	16:10:14
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$300
RAM confirmation Number	072419INTEFSW16104700
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	U015770023US03-TRN-DFC.pdf	26316 b5814897e69d7bb05a3f89423ea21d4bb0c5dd66	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	32833 02eb296b0ee01e6aac8197b8673719200190e773	no	1
Warnings:					
Information:					
3	Extension of Time	U015770023US03-EXT-DFC.pdf	25045 4194c8df8ed07aaf003c2ed3d4a396c3bc7941f2	no	1
Warnings:					
Information:					
4		U015770023US03-AMN-DFC.pdf	65365 71b704dab0a5ab9579222eb07b2a82e4dfd868f6	yes	9

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment/Req. Reconsideration-After Non-Final Reject	1	1
Claims	2	4
Applicant Arguments/Remarks Made in an Amendment	5	9

Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	30758 f4d54997a41da37b931e05ae082e89412bc8151a	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	180317

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/AIA/22 (03-13)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) U0157.70023US03
Application Number 15/639,223-Conf. #8089	Filed June 30, 2017
For MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT	
Art Unit 1625	Examiner N. E. Jarrell

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
☐ One month (37 CFR 1.17(a)(1))	$200	$100	$50	$
☒ Two months (37 CFR 1.17(a)(2))	$600	$300	$150	$ 300.00
☐ Three months (37 CFR 1.17(a)(3))	$1,400	$700	$350	$
☐ Four months (37 CFR 1.17(a)(4))	$2,200	$1,100	$550	$
☐ Five months (37 CFR 1.17(a)(5))	$3,000	$1,500	$750	$

☒ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

☐ A check in the amount of the fee is enclosed.

☒ Payment by credit card. ~~Form PTO-2038 is attached~~.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 23/2825 .

☒ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant.

☒ attorney or agent of record. Registration number 73,490 .

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____ .

/David F. Cauble/	July 23, 2019
Signature	Date
David F. Cauble, PhD, JD	617.646.8000
Typed or printed name	Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ * Total of 1 forms are submitted.

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 23, 2019 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

7399581.1

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Art Unit	1625
Examiner Name	N. E. Jarrell
Total Number of Pages in This Submission	
Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

- [X] Fee Transmittal Form
- [ ] Fee Attached
- [X] Amendment/Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [X] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
- [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	July 23, 2019	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 23, 2019 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

7399576.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1625
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)300.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	300	150*	75	660	330	165	760	380	190	
Design	200	100	50	160	80	40	600	300	150	
Plant	200	100	50	420	210	105	620	310	155	
Reissue	300	150	75	660	330	165	2,200	1,100	550	
Provisional	280	140	70	0	0	0	0	0	0	

* The $150 small entity status filing fee for a utility application is further reduced to $75 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	460	230	115
Multiple dependent claims	820	410	205

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
20	- or HP =	_____	x _____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Multiple Dependent Claims	
Fee ($)	**Fee Paid ($)**
_____	_____

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- or HP =	_____	x _____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $400 ($200 for small entity) ($100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**		**Fee ($)**		**Fee Paid ($)**
_____	- 100 =	_____	/50 =	_____	(round **up** to a whole number) x	_____	=	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2252 Extension for response within second month	300.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	July 23, 2019

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 23, 2019 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

7399574.1

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/639,223	Filing Date 06/30/2017	☐ To be Mailed

ENTITY: ☐ LARGE ☑ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $40 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $210 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT	07/23/2019	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 14	Minus	** 36	= 0		x $50 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 9	= 0		x $230 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/TINA J BARDEN/
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".	
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.	

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 11/05/2019

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
11/05/2019	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Office Action Summary	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.	
	Examiner NOBLE E JARRELL	**Art Unit** 1625	**AIA (FITF) Status** No

-- 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 23 July 2019.

☐ 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) 37-50 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 37-50 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 _____.

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

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Response to Amendment

The rejections of 26 February 2019 are overcome by the amendment filed 23 July 2019.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, 365(c), or 386(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of 35 U.S.C. 112(a) or the first paragraph of pre-AIA 35 U.S.C. 112, except for the best mode requirement. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994)

The disclosure of the prior-filed application, Application No. 10/378956 fails to provide adequate support or enablement in the manner provided by 35 U.S.C. 112(a) or pre-AIA 35 U.S.C. 112, first paragraph for one or more claims of this application. Application 10/378956 does not disclose pharmaceutical composition comprising a co-crystal. Original claims of 3 March 2003 recite a multiple-component phase composition of with no mention of a pharmaceutically acceptable carrier. The specification provides no discussion of a pharmaceutical composition win a co-crystal. Examples 1-19 (page 17, paragraph [0056] to page 33, paragraph [00177]) describe co-crystals only. There is no discussion of a pharmaceutical composition comprising a co-crystal and a separate pharmaceutical acceptable carrier. Example 1 of 10/378956 is drawn to a crystalline complex of acetaminoiphen, 4,4'-bipyidine, and water. This co-crystal has no additional pharmaceutically acceptable carrier which is required by the instant claims set. Based on this analysis the effective filing of the instant application is 30 April 2017.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

> (a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-50 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, because the specification, while being enabling for preparation of cocrystals of examples 1-17 in specification, does not reasonably provide enablement for preparation of the scope of cocrystals claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a stoichiometric cocrystal of an active pharmaceutical ingredient and a co-former. Thus, the claims taken together with the specification imply a stoichiometric cocrystal can be formed.

The state of the prior art and (4) the predictability or unpredictability of the art:

MIRSOSHNYK (*Expert Opinion in Drug Delivery*, **2009**, *6(4)*, 333-341) describes that translational challenges are present in cocrystal design (page 334, section 2; sections 3 and 4, pages 337-340). The challenges include the following: stability of an active pharmacological ingredient; seeing studies that follow the development cycle all the way to the end product; systematically investigating the applicability of agglomeration techniques; and regulatory issues.

The relative skill of those in the art:

While the artisan generally would have an advanced degree in cocrystal formation and analysis, their high level of skill and knowledge is insufficient to overcome the lack of understanding as to how cocrystal formation occurs.

The amount of direction or guidance presented and the presence or absence of working examples:

The specification has provided guidance for preparation of the following cocrystals (examples 1-17 in specification):acetaminophen: 4,4'-bipyridine:water (1:1:1); phenytoin/pyridine (1:1); aspirin and 4,4'-bipyridine (2:1); ibuprofen and 4,4'-bipyridine (2:1); flurbiprofen and [4,4'-bipyridine or trans-1,2-bis(4-pyridyl)ethylene] (2:1); carbamazepine and [one of *p*-phthalaldehyde, nicotinamide, saccharin, 5-nitroisophthalic acid, acetic acid, 1,3,5,7-adamantanetetracarboxylic acid, benzoquinone, butyric acid, DMSO, or formamide] (1:1); carbamazepine and 2,6-pyridinecarboxylic acid (2:3)

The specification does not provide guidance for the scope of stoichiometric cocrystals claimed.

The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to cocrystal formation and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Response to Arguments

This rejection is maintained because the art shows that pharmaceutical cocrystal deign presently has challenges that need to be overcome. Applicants argue that the MPEP 21264.10 states that although experimentation may be complex, it is not considered undue. In light of Mirshnyk, these challenges still need to be overcome.

Claim Rejections - 35 USC § 102

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

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 37-49 is/are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by MCMAHON (WO2006007448, published 19 January 2006). McMahon describes co-crystals of examples 1-11 (page 55, paragraph [00189] to page 63, paragraph [00235]). In these co-crystals, hydrogen bonding is used to bond the compounds of the co-crystals (pages 27-34, paragraph [00110]; page 57, table XXI). Different method of making the co-crystals are described (page 49, paragraph [00159] to page 52, paragraph [00174]). Pharmaceutical compositions comprising these co-crystals are described (page 35, paragraph [00113] to page 48, paragraph [00157]).

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 conflicting claims 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 re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *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 nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) 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 www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 37-50 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37and 45 of copending Application No. 14/179862 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of 14/179862. Claim 37 of '862 overlaps with instant claims 37 and 39. Claim 45 of '862 is embraced by instant claims 37 and 40.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Arguments

This rejection is maintained because applicants have decided to keep this rejection in abeyance.

Conclusion

Claims 37-50 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE E JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on 9:00 AM to 5:00 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Kosar can be reached on 571-372-0913. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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.

/NOBLE E JARRELL/
Primary Examiner, Art Unit 1625

Notice of References Cited	Application/Control No. 15/639,223	Applicant(s)/Patent Under Reexamination Zaworotko et al.	
	Examiner NOBLE E JARRELL	Art Unit 1625	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
	A					
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	MIRSOSHNYK. Expert Opinion in Drug Delivery, 2009, 6(4), 333-341 (Year: 2009)
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 250 of 415

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/639,223	Zaworotko et al.
	Examiner	Art Unit
	NOBLE E JARRELL	1625

CPC - Searched*		
Symbol	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystal cocrystals co near crystals).clm.	02/19/2019	NJ

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystalcocrystals co near crystals).clm.	02/19/2019	NJ
stn registry and hcaplus	02/19/2019	NJ
inventor search in PALM and EAST	02/19/2019	NJ
stn registry and hcaplus	10/30/2019	NJ

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
C07D	223/26	02/19/2019	NJ

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1625	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 251 of 415

```
=> d his full

     (FILE 'HOME' ENTERED AT 12:49:59 ON 30 OCT 2019)

     FILE 'HCAPLUS' ENTERED AT 12:50:10 ON 30 OCT 2019
L1             4 SEA SPE=ON  ABB=ON  PLU=ON  US20170362182 /PN
                 D SCA
                 E HYDROGEN BOND/CT
                 E E3+ALL
L2               QUE SPE=ON  ABB=ON  PLU=ON  "HYDROGEN BOND"+OLD,NT/CT
                 E E26+ALL
L3               QUE SPE=ON  ABB=ON  PLU=ON  "MOLECULAR ASSOCIATION"+NT/CT
                 E SELF-ASSEMBLY/CT
                 E E3+ALL
L4               QUE SPE=ON  ABB=ON  PLU=ON  SELF-ASSEMBLY+OLD,NT/CT
                 E SUPRAMOLECULAR STRUCTURE/CT
                 E E3+ALL
L5               QUE SPE=ON  ABB=ON  PLU=ON  "SUPRAMOLECULAR STRUCTURE"+OLD/CT
L6           475 SEA SPE=ON  ABB=ON  PLU=ON  (L2 OR L3 OR L4 OR L5) (L)
                 (COCRSYTAL? OR CO (1A) CRYSTAL?)
L7             1 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L1
                 D SCA
                 E DRUG DELIVERY SYSTEMS/CT
                 E E3+ALL
L8               QUE SPE=ON  ABB=ON  PLU=ON  "DRUG DELIVERY SYSTEMS"+OLD,NT/CT
L9            29 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L8
                 E COCRYSTALLIZATION/CT
                 E E3+ALL
                 E E6+ALL
L10              QUE SPE=ON  ABB=ON  PLU=ON  CRYSTALLIZATION+NT/CT
L11          249 SEA SPE=ON  ABB=ON  PLU=ON  L6 AND L10
L12           25 SEA SPE=ON  ABB=ON  PLU=ON  L9 AND L11

     FILE 'STNGUIDE' ENTERED AT 12:59:04 ON 30 OCT 2019

     FILE 'HCAPLUS' ENTERED AT 13:02:06 ON 30 OCT 2019
L13          21 SEA SPE=ON  ABB=ON  PLU=ON  L12 AND PY<=2017
L14           4 SEA SPE=ON  ABB=ON  PLU=ON  L12 NOT L13
L15          25 SEA SPE=ON  ABB=ON  PLU=ON  (L13 OR L14)

     FILE HOME

     FILE HCAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.

     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
     strictly prohibited.

     FILE COVERS 1907 - 30 Oct 2019 VOL 171 ISS 20
     FILE LAST UPDATED: 29 Oct 2019 (20191029/ED)
     REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Dec 2015
     USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Dec 2015
```


NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 252 of 415

HCAplus now includes the comprehensive Cooperative Patent Classification (CPC). See HELP CPC for details.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 11, 2019 (20191011/UP).

FILE HCA

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 24 Oct 2019 VOL 171 ISS 20
FILE LAST UPDATED: 24 Oct 2019 (20191024/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2015
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2015

HCA now includes the comprehensive Cooperative Patent Classification (CPC). See HELP CPC for details.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 253 of 415

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/639,223	Filing Date 06/30/2017	☐ To be Mailed

ENTITY: ☐ LARGE ☑ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $40 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $210 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT	04/03/2020	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 14	Minus	** 36	= 0		x $50 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 9	= 0		x $230 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/CHRISTINE V MOORE/
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".	
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.	

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1625

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated:April 3, 2020 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

RESPONSE TO NON-FINAL OFFICE ACTION UNDER 37 C.F.R. § 1.111

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Office Action dated November 5, 2019, the time for response being extended by the attached Petition for Extension of Time, please amend the above-identified U.S. patent application as follows:

Listing of the Claims begins on page 2 of this paper.

Remarks/Arguments begin on page 5 of this paper.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 255 of 415

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Cathy Nicholson
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 2 months with $0 paid	2252	1	300	300
Miscellaneous:				
		Total in USD ($)		**300**

Electronic Acknowledgement Receipt

EFS ID:	39059413
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Cathy Nicholson
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	03-APR-2020
Filing Date:	30-JUN-2017
Time Stamp:	15:35:35
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$300
RAM confirmation Number	E202043F36016860
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	U015770023US03-TRN-DFC.pdf	26171 8c2704835642f9f979c157d9cc9da6e10418c891	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	32968 167cbd3c3b3ccbbfaf73b5f467b715d75e5279e8	no	1
Warnings:					
Information:					
3	Extension of Time	U015770023US03-EXT-DFC.pdf	24988 e4c9ad809c051b1fecdbdb05323380b4eacd3d81	no	1
Warnings:					
Information:					
4		U015770023US03-RESP-DFC.pdf	57424 2bf918cca95e87ccb5b8acf5b010e4bf19b6a7a2	yes	9

Multipart Description/PDF files in .zip description

Document Description	Start	End
Applicant Arguments/Remarks Made in an Amendment	5	9
Claims	2	4
Amendment/Req. Reconsideration-After Non-Final Reject	1	1

Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	30756 686cdcdbc7065564925f67558b013797319ca298	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	172307

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/AIA/22 (03-13)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) U0157.70023US03
Application Number 15/639,223-Conf. #8089	Filed June 30, 2017
For MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT	
Art Unit 1625	Examiner N. E. Jarrell

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
☐ One month (37 CFR 1.17(a)(1))	$200	$100	$50	$
☒ Two months (37 CFR 1.17(a)(2))	$600	$300	$150	$ 300.00
☐ Three months (37 CFR 1.17(a)(3))	$1,400	$700	$350	$
☐ Four months (37 CFR 1.17(a)(4))	$2,200	$1,100	$550	$
☐ Five months (37 CFR 1.17(a)(5))	$3,000	$1,500	$750	$

☒ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

☐ A check in the amount of the fee is enclosed.

☒ Payment by credit card. ~~Form PTO-2038 is attached~~.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 23/2825 .

☒ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant.

☒ attorney or agent of record. Registration number 73,490 .

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____ .

/David F. Cauble/	April 3, 2020
Signature	Date
David F. Cauble, PhD, JD	617.646.8000
Typed or printed name	Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ * Total of 1 forms are submitted.

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 3, 2020 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

8096340.1

REMARKS

Prior to entry of the instant amendments, claims 37-50 were pending in the Application. No claims have been amended.

PRIORITY

The office action states that U.S. Patent Application No. 10/378,956 (the '956 application) fails to provide adequate support or enablement for one or more claims of the application but it allegedly does not disclose a pharmaceutical composition comprising a co-crystal, stating "Original claims of 3 March 2003 recite a multiple-component phase composition [with] no mention of a pharmaceutically acceptable carrier. The specification provides no discussion of a pharmaceutical composition [with] a co-crystal." Applicant disagrees.

In the '956 application as filed, paragraph [0037] discloses that "Figure 24 shows an exemplified scheme for preparing ***multiple-component phase compositions*** of the subject invention." Figure 24 describes the preparation of "***multiple-component crystals***" from an API and one or more co-crystal formers. Examples 1-19 describe "***Multi-component crystals***" and refer to each such crystal as a "***co-crystal***." Accordingly, it is clear that the applicant of the '956 application equates the term "multiple-component phase compositions" with the term "multiple component crystals" and that the latter term is equivalent to the term "co-crystal." As such, the term "multiple-component phase composition" is equivalent to the term "co-crystal."

Paragraph [0049] discloses that "[t]he ***multiple-component phase compositions*** can be formulated according to known methods for preparing pharmaceutically useful compositions," that "[s]uch ***pharmaceutical compositions*** can be adapted for various forms of administration…" and that "the pharmaceutical compositions can include a ***pharmaceutically acceptable carrier*** or diluent." Accordingly, it is clear that the '956 application contemplates the preparation of pharmaceutical compositions comprising co-crystals, and that such pharmaceutical compositions may comprise a pharmaceutically acceptable carrier.

As such, the instant application has a valid claim of priority to the '956 application, which was filed on March 3, 2003.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 262 of 415

CLAIM REJECTIONS – 35 USC § 112

Claims 37-50 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, because the specification, while being enabling for preparation of cocrystals of examples 1-17 in the specification, allegedly does not reasonably provide enablement for preparation of the scope of cocrystals claimed. Applicant disagrees.

As a preliminary matter, Applicant notes that the previous office action (non-final rejection dated February 26, 2019) included a rejection of claims 37-50 under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, which was supported by a single publication (Kumar et al.) This rejection was overcome by Applicant's response under 37 CFR § 1.111, dated July 23, 2019. The present rejection is also supported by a single publication (Miroshnyk et al.), and therefore the Applicant traverses the rejection for the reasons stated in its response of July 23, 2019, with further remarks specifically in response to the Office's characterization of Miroshnyk et al.

On page 4 of the present non-final rejection, the Office states that "This rejection is maintained because the art shows that pharmaceutical cocrystal [design] presently has challenges that need to be overcome… In light of [Miroshnyk], these challenges still need to be overcome." On page 3 of the non-final rejection, the Office states that those challenges include:

1. stability of an active pharmacological ingredient;
2. seeing studies that follow the development cycle all the way to the end product;
3. systematically investigating the applicability of agglomeration techniques; and
4. regulatory issues.

These alleged challenges are addressed in turn below:

(1) Miroshnyk et al. does not characterize "stability of an active pharmaceutical ingredient" as a challenge to pharmaceutical co-crystal design. To the contrary, Miroshnyk et al. teaches that pharmaceutical co-crystals are a ***solution*** to the problem of poor API stability:

> *The stability of a solid API when exposed a wide range of relative humidities is another essential property… It is often the case that moisture promotes unwanted solid-phase transformation of an API…One approach proposed to inhibit such moisture-induced phase transformations is rational co-former selection for a specific formulation. In this context,* ***co-crystallization of an API with a co-former***

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 263 of 415

> ***can be thought as a more-radical strategy to address the poor physical stability of moisture-sensitive pharmaceutical materials***. *For instance, caffeine/oxalic acid co-crystals have been demonstrated to be superior to caffeine anhydrate in terms of physical stability to humidity.* (Page 338, left column, last paragraph; emphasis added)

(2) Miroshnyk et al. does not characterize "seeing studies that follow the development cycle all the way to the end product" as a challenge to pharmaceutical co-crystal design. Miroshnyk et al. states that it "would be desirable" to see such studies, but in no way suggests that this is a "challenge to pharmaceutical co-crystal design," as stated on page 4 of the office action. The fact that Miroshnyk is not aware of any such studies, or the fact that such studies may not have been published, cannot be understood to mean that such studies have not taken place, or that the skilled person is not capable of performing such studies without undue experimentation. To the contrary, the fact that such studies have taken place can be inferred from the regulatory approval in Japan of the ipragliflozin/L-proline co-crystal Suglat (see, e.g., Astellas press release dated December 21, 2018, made of record in the IDS submitted concurrently herewith). Here, Applicant notes MPEP 2164.01, which states that "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." As evidenced, at least, by the regulatory approval described above, the art does engage in such experimentation, i.e., studies that follow the development cycle of a co-crystalline drug product all the way to the end product.

(3) Miroshnyk et al. states that "there is a need for studies that systematically investigate the applicability of agglomeration techniques…" but goes on to say that such studies "***could*** provide valuable information for ***commercial-scale manufacture*** of co-crystal systems." (Page 338, right column, third paragraph; emphasis added) Miroshnyk et al.'s statement regarding studies related to ***commercial-scale manufacture*** does not teach or suggest that the skilled person would be unable to make and use the claimed pharmaceutical compositions. Even, arguendo, if the statement were understood to represent such a teaching, the regulatory approval and commercial availability of Suglat tablets, discussed above, proves that the art is equipped to engage in experimentation required to commercially manufacture solid formulations of pharmaceutical co-crystals.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 264 of 415

(4) Miroshnyk et al. states that "Regulatory issues are also of ***great interest***," for example, "whether a new co-crystal of a marketed API is eligible for regulatory approval via the abbreviated new drug approval mechanism…" These statements of Miroshnyk et al. clearly relate to commercial considerations, and are irrelevant to the question of enablement.

At least for the foregoing reasons, Applicant requests withdrawal of the rejection of the claims under 35 U.S.C. 112(a), first paragraph.

CLAIM REJECTIONS – 35 USC § 102

Claims 37-49 are rejected under pre AIA 35 U.S.C. 102(b) as being anticipated by McMahon (WO2006007448), hereinafter referred to as "McMahon". Applicant disagrees. As described above, instant application has a valid claim of priority to U.S. Patent Application No. 10/378,956, which was filed on March 3, 2003. McMahon claims priority to June 17, 2004. Accordingly, the instant application is not anticipated by McMahon, and Applicant requests withdrawal of the rejection of the claims under 35 U.S.C. 102(b).

DOUBLE PATENTING

Claims 37-50 are provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 37 and 45 of co-pending Application No. 14/179,862. Applicant requests that the Examiner hold this rejection in abeyance until the claims are otherwise held to be in condition for allowance.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 265 of 415

CONCLUSION

In view of the foregoing, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this response, the application is not in condition for allowance, the Examiner is requested to call the undersigned at the telephone number indicated below to discuss any outstanding issues.

All fees due in connection with this filing are being paid by Credit Card. However, should additional fees be due with this filing, please charge our Deposit Account No. 23/2825, under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Dated: April 3, 2020

Respectfully submitted,

By /David F. Cauble/_____
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 266 of 415

LISTING OF THE CLAIMS

1 – 36. (Canceled)

37. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-crystal former,

wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form,

wherein the co-crystal former has a second chemical functionality complimentary to the first chemical functionality via non-covalent hydrogen bonding,

wherein supramolecular synthons comprise non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-crystal former.

38. (Previously presented) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, a GRAS compound, a food additive, a low toxicity organic, and a metal-organic complex.

39. (Previously presented) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form.

40. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and one co-crystal former.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 267 of 415

41. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of one active pharmaceutical ingredient (API) and one co-crystal former.

42. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a group selected from acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases, amines, alcohols, halogens, sulfones, and nitro groups.

43. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an acid.

44. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amine.

45. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amide.

46. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an alcohol.

47. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon.

48. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a heterosynthon.

49. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon and a heterosynthon.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 268 of 415

50. (Previously presented) The pharmaceutical composition of claim 48, wherein the heterosynthon comprises an alcohol/amine interaction.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 269 of 415

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM *(to be used for all correspondence after initial filing)*		Application Number	15/639,223-Conf. #8089
		Filing Date	June 30, 2017
		First Named Inventor	Michael J. Zaworotko
		Art Unit	1625
		Examiner Name	N. E. Jarrell
Total Number of Pages in This Submission		Attorney Docket Number	U0157.70023US03

ENCLOSURES (***Check all that apply***)

[X] Fee Transmittal Form	[ ] Drawing(s)	[ ] After Allowance Communication to TC
[ ] Fee Attached	[ ] Licensing-related Papers	[ ] Appeal Communication to Board of Appeals and Interferences
[X] Amendment/Reply	[ ] Petition	[ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
[ ] After Final	[ ] Petition to Convert to a Provisional Application	[ ] Proprietary Information
[ ] Affidavits/declaration(s)	[ ] Power of Attorney, Revocation Change of Correspondence Address	[ ] Status Letter
[X] Extension of Time Request	[ ] Terminal Disclaimer	[ ] Other Enclosure(s) (please Identify below):
[ ] Express Abandonment Request	[ ] Request for Refund	
[ ] Information Disclosure Statement	[ ] CD, Number of CD(s) _____	
[ ] Certified Copy of Priority Document(s)	[ ] Landscape Table on CD	
[ ] Reply to Missing Parts/ Incomplete Application	Remarks	
[ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	April 3, 2020	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 3, 2020 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

8096339.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1625
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)300.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	300	150*	75	660	330	165	760	380	190	
Design	200	100	50	160	80	40	600	300	150	
Plant	200	100	50	420	210	105	620	310	155	
Reissue	300	150	75	660	330	165	2,200	1,100	550	
Provisional	280	140	70	0	0	0	0	0	0	

* The $150 small entity status filing fee for a utility application is further reduced to $75 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	460	230	115
Multiple dependent claims	820	410	205

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- or HP =	_____	x _____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Multiple Dependent Claims	
Fee ($)	**Fee Paid ($)**
_____	_____

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- or HP =	_____	x _____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $400 ($200 for small entity) ($100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**		**Fee ($)**		**Fee Paid ($)**
_____	- 100 =	_____	/50 =	_____	(round **up** to a whole number) x	_____	=	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2252 Extension for response within second month	300.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	April 3, 2020

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 3, 2020 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

8096338.1

FORM PTO-1449/A and B (modified PTO/SB/08)	APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
	FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet 1 of 1	GROUP ART UNIT: 1699	EXAMINER: N. E. Jarrell

U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite No.	U.S. Patent Document Number	Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY
		2019-0169130	A1	Zaworotko et al.	06-06-2019

FOREIGN PATENT DOCUMENTS

Examiner's Initials #	Cite No.	Foreign Patent Document Office/ Country	Number	Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)

OTHER ART – NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
		[NO AUTHOR LISTED], Approval of Suglat Tablets, Selective SGLT2 Inhibitor, for Additional Indication of type 1 diabetes mellitus and Additional dosage and administration in Japan. Astellas Pharma Inc., 12 Dec 2018, https://www.astellas.com/en/news/14481. Accessed 22 Mar 2020. 2 pages.	

[NOTE – No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR § 1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR § 1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR § 1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. § 120.]

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.**8097831.1**

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Katherine Wade
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	2806	1	120	120
		Total in USD ($)		**120**

Electronic Acknowledgement Receipt

EFS ID:	39061362
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Katherine Wade
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	03-APR-2020
Filing Date:	30-JUN-2017
Time Stamp:	17:01:17
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$120
RAM confirmation Number	E202043H02268613
Deposit Account	232825
Authorized User	Katherine Wade

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

37 CFR 1.17 (Patent application and reexamination processing fees)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	U015770023US03-TRN-DFC.pdf	26184 d8792def09905f79ed90eb55b8986bdfca3e6bfd	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	32819 96b464bc3eddb826dc2e264450ecdc5266e708d5	no	1
Warnings:					
Information:					
3	Transmittal Letter	U015770023US03-IDSBODY-DFC.pdf	30332 75a248a1083d2ea8fbff12676293979dc7c1924c	no	3
Warnings:					
Information:					
4	Information Disclosure Statement (IDS) Form (SB08)	U015770023US03-IDS1449-DFC.pdf	23207 bd77b0a7ca4e4d645c8e9892798adc7b38521e18	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
5	Non Patent Literature	Suglat_Approval_Announcement_2018.pdf	1088637 05f60f8c09306a16f6ed343ae56be20468b4d2ee	no	2
Warnings:					
Information:					
6	Fee Worksheet (SB06)	fee-info.pdf	30874 52fd76847f40b4e8e7b64b5d7ce2e47c72f726b6	no	2
Warnings:					

Information:	
Total Files Size (in bytes):	1232053

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

DOCKET NO.: U0157.70023US03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1699

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 3, 2020 Electronic Signature for Katherine T. Wade: /Katherine T. Wade/

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF DISCLOSURE UNDER 37 C.F.R. §§ 1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, the undersigned requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. § 1.97

This Information Disclosure Statement has been filed more than three months after the filing date of this application and after the mailing date of a first Office Action, but before the mailing date of any of a Final Action under 37 C.F.R. § 1.113, a Notice of Allowance under 37 C.F.R. § 1.311, or an action that otherwise closes prosecution in this application.

Please charge our Credit Card in the amount of $120.00 covering the fee set forth in 37 C.F.R. § 1.17(p).

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 278 of 415

PART II: Information Cited

The undersigned hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified PTO/SB/08). The order of presentation of the references should not be construed as an indication of the importance of the references.

The undersigned hereby makes the following additional information of record in the above-identified application.

The undersigned would like to bring to the Examiner's attention the following co-pending applications that may contain subject matter related to this application:

Serial No.	Filing Date	Inventor(s)	Docket No.
*16/270,981	02-08-2019	Zaworotko et al.	U0157.70023US04

*A copy of this reference is not provided as the Office has waived the requirement under 37 C.F.R. § 1.98(a)(2)(iii) for submitting a copy of a cited U.S. patent application if it is scanned to the Image File Wrapper system and is available on Private PAIR .

PART III: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;

2. The enclosed form PTO-1449 (modified PTO/SB/08) be signed by the Examiner to evidence that the cited information has been fully considered by the United States Patent and Trademark Office during the examination of this application;

3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the undersigned makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. § 102.

Notwithstanding any statements by the undersigned, the Examiner is urged to form his or her own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

The Director is hereby authorized to charge any deficiency or credit any overpayment in the fees occasioned by the filing of this Information Disclosure Statement to our Deposit Account No. 23/2825 under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Respectfully submitted,

By: /David F. Cauble/
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

Docket No.: U0157.70023US03
Date: April 3, 2020

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Art Unit	1699
Examiner Name	N. E. Jarrell
Total Number of Pages in This Submission	
Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

- [X] Fee Transmittal Form
- [ ] Fee Attached
- [ ] Amendment/Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [X] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
- [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [X] Other Enclosure(s) (please Identify below):

Form PTO-1449
Copy of cited reference

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	April 3, 2020	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 3, 2020 Electronic Signature for Katherine T. Wade: /Katherine T. Wade/

8097830.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1699
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)120.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	300	150*	75	660	330	165	760	380	190	
Design	200	100	50	160	80	40	600	300	150	
Plant	200	100	50	420	210	105	620	310	155	
Reissue	300	150	75	660	330	165	2,200	1,100	550	
Provisional	280	140	70	0	0	0	0	0	0	

* The $150 small entity status filing fee for a utility application is further reduced to $75 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	460	230	115
Multiple dependent claims	820	410	205

Total Claims	**Extra Claims**	**Fee ($)**	**Fee Paid ($)**
20 - 20 or HP =	_____	x _____	= _____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims	**Extra Claims**	**Fee ($)**	**Fee Paid ($)**
4 - 4 or HP =	_____	x _____	= _____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	
Fee ($)	**Fee Paid ($)**
_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $400 ($200 for small entity) ($100 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	**Extra Sheets**	**Number of each additional 50 or fraction thereof**	**Fee ($)**	**Fee Paid ($)**
_____ - 100 =	_____ /50 =	_____ (round **up** to a whole number) x	_____ =	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2806 Submission of an Information Disclosure Statement	120.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	April 3, 2020

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 3, 2020 Electronic Signature for Katherine T. Wade: /Katherine T. Wade/

8097829.1

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 07/10/2020
WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
07/10/2020	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Office Action Summary	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.	
	Examiner NOBLE E JARRELL	**Art Unit** 1699	**AIA (FITF) Status** No

-- 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 03 April 2020.

☐ 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) 37-50 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 37-50 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 3 April 2020.

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

4) ☐ Other: _____.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 284 of 415

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Response to Amendment

Claims 37-50 are pending and examined on the merits. The rejection under 35 U.S.C. 102 is overcome by the arguments filed 3 April 2020. Based on the priority arguments, the priority date of the instant application is 3 March 2003 (based on paragraph [0049] of the specification).

Information Disclosure Statement

The information disclosure statements filed 3 April 2020 are acknowledged and considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

> (a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37-50 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, because the specification, while being enabling for preparation of cocrystals of examples 1-17 in specification, does not reasonably provide enablement for preparation of the scope of cocrystals claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a stoichiometric cocrystal of an active pharmaceutical ingredient and a co-former. Thus, the claims taken together with the specification imply a stoichiometric cocrystal can be formed.

The state of the prior art and (4) the predictability or unpredictability of the art:

MIRSOSHNYK (*Expert Opinion in Drug Delivery*, **2009**, *6(4)*, 333-341) describes that translational challenges are present in cocrystal design (page 334, section 2; sections 3 and 4, pages 337-340). The challenges include the following: stability of an active pharmacological ingredient; seeing studies that follow the development cycle all the way to the end product; systematically investigating the applicability of agglomeration techniques; and regulatory issues.

The relative skill of those in the art:

While the artisan generally would have an advanced degree in cocrystal formation and analysis, their high level of skill and knowledge is insufficient to overcome the lack of understanding as to how cocrystal formation occurs.

The amount of direction or guidance presented and the presence or absence of working examples:

The specification has provided guidance for preparation of the following cocrystals (examples 1-17 in specification):acetaminophen: 4,4'-bipyridine:water (1:1:1); phenytoin/pyridine (1:1); aspirin and 4,4'-bipyridine (2:1); ibuprofen and 4,4'-bipyridine (2:1); flurbiprofen and [4,4'-bipyridine or trans-1,2-bis(4-pyridyl)ethylene] (2:1); carbamazepine and [one of *p*-phthalaldehyde, nicotinamide, saccharin, 5-nitroisophthalic acid, acetic acid, 1,3,5,7-adamantanetetracarboxylic acid, benzoquinone, butyric acid, DMSO, or formamide] (1:1); carbamazepine and 2,6-pyridinecarboxylic acid (2:3)

The specification does not provide guidance for the scope of stoichiometric cocrystals claimed.

The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to cocrystal formation and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the

specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Response to Arguments

This rejection is maintained because the state of the art shows that pharmaceutical cocrystal deign presently has challenges that need to be overcome. Applicants argue that the MPEP 21264.10 states that although experimentation may be complex, it is not considered undue. Applicants argues that the reference shows the studies relating to co-crystal can (or should be) done. The reference teaches both that this type of research can be done and more challenges are present that need to be dealt with ("Expert opinion" section, pages 337-338; "Conclusions" section, pages 338-340).

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 conflicting claims 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 re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *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 nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) 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 www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 37-50 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37 and 45 of copending Application No. 14/179862 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of 14/179862. Claim 37 of '862 overlaps with instant claims 37 and 39. Claim 45 of '862 is embraced by instant claims 37 and 40.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Claims 37, 38 and 42 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37, 38, and 42 of copending Application No. 16/270981 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of 16/270981. Claims 37, 38, and 42 of '981 overlap with instant claims 37, 38, and 42. Example 1 (page 16, paragraph [0056] to page 17, paragraph [0059]) shows a co-crystal of acetaminophen, bipyridine, and water.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Arguments

This double patenting rejection against 14/179682 is maintained because applicants have decided to keep this rejection in abeyance.

Conclusion

Claims 37-50 are not allowed.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 3 April 2020 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and

the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE E JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on 9:00 AM to 5:00 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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 https://ppair-my.uspto.gov/pair/PrivatePair. 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.

/NOBLE E JARRELL/
Primary Examiner, Art Unit 1699

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/639,223	Zaworotko et al.
	Examiner	Art Unit
	NOBLE E JARRELL	1699

CPC - Searched*		
Symbol	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystal cocrystals co near crystals).clm.	02/19/2019	NJ

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystalcocrystals co near crystals).clm.	02/19/2019	NJ
stn registry and hcaplus	02/19/2019	NJ
inventor search in PALM and EAST	02/19/2019	NJ
stn registry and hcaplus	10/30/2019	NJ

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
C07D	223/26	02/19/2019	NJ

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1625	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 290 of 415

DOCKET NO.: U0157.70023US03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1699

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: April 3, 2020 Electronic Signature for Katherine T. Wade: /Katherine T. Wade/

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF DISCLOSURE UNDER 37 C.F.R. §§ 1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, the undersigned requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. § 1.97

This Information Disclosure Statement has been filed more than three months after the filing date of this application and after the mailing date of a first Office Action, but before the mailing date of any of a Final Action under 37 C.F.R. § 1.113, a Notice of Allowance under 37 C.F.R. § 1.311, or an action that otherwise closes prosecution in this application.

Please charge our Credit Card in the amount of $120.00 covering the fee set forth in 37 C.F.R. § 1.17(p).

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 291 of 415

PART II: Information Cited

The undersigned hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified PTO/SB/08). The order of presentation of the references should not be construed as an indication of the importance of the references.

The undersigned hereby makes the following additional information of record in the above-identified application.

The undersigned would like to bring to the Examiner's attention the following co-pending applications that may contain subject matter related to this application:

Serial No.	Filing Date	Inventor(s)	Docket No.
*16/270,981	02-08-2019	Zaworotko et al.	U0157.70023US04

*A copy of this reference is not provided as the Office has waived the requirement under 37 C.F.R. § 1.98(a)(2)(iii) for submitting a copy of a cited U.S. patent application if it is scanned to the Image File Wrapper system and is available on Private PAIR .

PART III: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;

2. The enclosed form PTO-1449 (modified PTO/SB/08) be signed by the Examiner to evidence that the cited information has been fully considered by the United States Patent and Trademark Office during the examination of this application;

3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the undersigned makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

/NOBLE E JARRELL/ 07/06/2020

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. § 102.

Notwithstanding any statements by the undersigned, the Examiner is urged to form his or her own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

The Director is hereby authorized to charge any deficiency or credit any overpayment in the fees occasioned by the filing of this Information Disclosure Statement to our Deposit Account No. 23/2825 under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Respectfully submitted,

By: /David F. Cauble/

David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

Docket No.: U0157.70023US03
Date: April 3, 2020

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	1	of	1	GROUP ART UNIT: 1699	EXAMINER: N. E. Jarrell

U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite No.	U.S. Patent Document Number	Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY
		2019-0169130	A1	Zaworotko et al.	06-06-2019

FOREIGN PATENT DOCUMENTS

Examiner's Initials #	Cite No.	Foreign Patent Document Office/ Country	Number	Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)

OTHER ART – NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
		[NO AUTHOR LISTED], Approval of Suglat Tablets, Selective SGLT2 Inhibitor, for Additional Indication of type 1 diabetes mellitus and Additional dosage and administration in Japan. Astellas Pharma Inc., 12 Dec 2018, https://www.astellas.com/en/news/14481. Accessed 22 Mar 2020. 2 pages.	

[NOTE – No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR § 1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR § 1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR § 1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. § 120.]

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	07/06/2020

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.**8097831.1**

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

PTO/AIA/25 (04-13)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TERMINAL DISCLAIMER TO OBVIATE A PROVISIONAL DOUBLE PATENTING REJECTION OVER A PENDING "REFERENCE" APPLICATION	Docket Number (Optional) U0157.70023US03

In re Application of: Michael J. Zaworotko et al.

Application No.: 15/639,223-Conf. #8089

Filed: June 30, 2017

For: MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

The applicant, University of South Florida and The Regents of the University of Michigan, owner of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending **reference** Application Number 16/270,981, filed, Feb. 8, 2019, as the term of any patent granted on said **reference** application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending **reference** application. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on the **reference** application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the applicant does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term of any patent granted on said **reference** application, "as the term of any patent granted on said **reference** application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending **reference** application," in the event that: any such patent granted on the pending **reference** application expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

Check either box 1 or 2 below, if appropriate.

1. ☐ The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee.

I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

2. ☒ The undersigned is an attorney or agent of record. Reg. No. 73,490

/David F. Cauble/ — Signature
October 8, 2020 — Date

David F. Cauble, PhD, JD — Typed or printed name

Attorney for Applicant(s) — Title
617.646.8000 — Telephone Number

☒ Terminal disclaimer fee under 37 CFR 1.20(d) is included.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

8598925.1

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional) U0157.70023US03

In re Application of: Michael J. Zaworotko et al.

Application No.: 15/639,223-Conf. #8089

Filed: June 30, 2017

For: MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

The applicant, University of South Florida and The Regents of the University of Michigan, owner of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of **prior patent** No. 10,633,344 as the term of said **prior patent** is presently shortened by any terminal disclaimer. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the **prior patent** are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the applicant does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the **prior patent**, "as the term of said **prior patent** is presently shortened by any terminal disclaimer," in the event that said **prior patent** later:

expires for failure to pay a maintenance fee;
is held unenforceable;
is found invalid by a court of competent jurisdiction;
is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
has all claims canceled by a reexamination certificate;
is reissued; or
is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

1. ☐ The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee.

I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

2. ☒ The undersigned is an attorney or agent of record. Reg. No. 73,490

/David F. Cauble/ — Signature
October 8, 2020 — Date

David F. Cauble, PhD, JD — Typed or printed name

Attorney for Applicant(s) — Title
617.646.8000 — Telephone Number

☒ Terminal disclaimer fee under 37 CFR 1.20(d) included.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Cathy Nicholson
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
NOTICE OF APPEAL	2401	1	420	420
Post-Allowance-and-Post-Issuance:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
STATUTORY OR TERMINAL DISCLAIMER	2814	2	170	340
		Total in USD ($)		**760**

Electronic Acknowledgement Receipt	
EFS ID:	40791820
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Cathy Nicholson
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	08-OCT-2020
Filing Date:	30-JUN-2017
Time Stamp:	12:18:43
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$760
RAM confirmation Number	E202008C19041470
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	U015770023US03-TRN-DFC.pdf	26479 e90e0663671254a03cd3c449e11b2d7563e96a34	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	37480 27bb0a4ad74b407ae185c2376eadcfe5ac171ebd	no	1
Warnings:					
Information:					
3	Notice of Appeal Filed	U015770023US03-NAPL-DFC.pdf	20977 e7edc3ab75a8423e5a69832a761a5b6313d3bd2b	no	1
Warnings:					
Information:					
4	Pre-Brief Conference request	U015770023US03-PABRF-DFC.pdf	20346 1ebb38240ffd78f3a705232096eb5469eb5e767c	no	1
Warnings:					
Information:					
5	Miscellaneous Incoming Letter	U015770023US03-PABRF-ARG-DFC.pdf	50882 387c090b76d3a07e889c7350cbf483cfbc32783f	no	5
Warnings:					
Information:					
6	Terminal Disclaimer Filed	U015770023US03-TD-APL-DFC.pdf	20890 e01e650af520b9bd5f1a2ea334d4124be35f9c53	no	1
Warnings:					
Information:					

7	Terminal Disclaimer Filed	U015770023US03-TD-PAT-DFC.pdf	19561 044441d81d41886f9ca799aafa7b1e93cd4dcbe6	no	1
Warnings:					
Information:					
8	Fee Worksheet (SB06)	fee-info.pdf	32423 866ea3ab9c12bc27d2cd1b1db594606450c1c930	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	229038		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM *(to be used for all correspondence after initial filing)*		Application Number	15/639,223-Conf. #8089
		Filing Date	June 30, 2017
		First Named Inventor	Michael J. Zaworotko
		Art Unit	1699
		Examiner Name	N. E. Jarrell
Total Number of Pages in This Submission		Attorney Docket Number	U0157.70023US03

ENCLOSURES (***Check all that apply***)

[X] Fee Transmittal Form	[ ] Drawing(s)	[ ] After Allowance Communication to TC
[ ] Fee Attached	[ ] Licensing-related Papers	[ ] Appeal Communication to Board of Appeals and Interferences
[ ] Amendment/Reply	[ ] Petition	[X] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
[ ] After Final	[ ] Petition to Convert to a Provisional Application	[ ] Proprietary Information
[ ] Affidavits/declaration(s)	[ ] Power of Attorney, Revocation Change of Correspondence Address	[ ] Status Letter
[ ] Extension of Time Request	[X] Terminal Disclaimer (2)	[X] Other Enclosure(s) (please Identify below):
[ ] Express Abandonment Request	[ ] Request for Refund	Pre-Appeal Brief Request For Review Form (PTO/AIA/33; Pre-Appeal Brief Request For Review
[ ] Information Disclosure Statement	[ ] CD, Number of CD(s) _____	
[ ] Certified Copy of Priority Document(s)	[ ] Landscape Table on CD	
[ ] Reply to Missing Parts/ Incomplete Application	Remarks	
[ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	October 8, 2020	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: October 7, 2020 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

8600687.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1699
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)760.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	320	160*	80	700	350	175	800	400	200	
Design	220	110	55	160	80	40	640	320	160	
Plant	220	110	55	440	220	110	660	330	165	
Reissue	320	160	80	700	350	175	2,320	1,160	580	
Provisional	300	150	75	0	0	0	0	0	0	

* The $160 small entity status filing fee for a utility application is further reduced to $80 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	480	240	120
Multiple dependent claims	860	430	215

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- 20 or HP =	_____	x _____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- 4 or HP =	_____	x _____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	
Fee ($)	**Fee Paid ($)**

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $420 ($210 for small entity) ($105 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**	**Fee ($)**		**Fee Paid ($)**
_____	- 100 =	_____	/50 =	_____ (round **up** to a whole number)	x _____	=	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2814 Statutory disclaimer, including terminal ...	340.00
2401 Notice of appeal	420.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	October 8, 2020

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: October 7, 2020 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

8600797.1

NOTICE OF APPEAL FROM THE EXAMINER TO THE PATENT TRIAL AND APPEAL BOARD	Docket Number (Optional) U0157.70023US03

	In re Application of Michael J. Zaworotko et al.	
	Application Number 15/639,223-Conf. #8089	Filed June 30, 2017
	For MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT	
	Art Unit 1699	Examiner N. E. Jarrell

Applicant hereby **appeals** to the Patent Trial and Appeal Board from the last decision of the examiner.

The fee for this Notice of Appeal is (37 CFR 41.20(b)(1)) $ 840.00

[x] Applicant asserts small entity status. See 37 CFR 1.27. Therefore, the fee shown above is reduced by 50%, and the resulting fee is: $ 420.00

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Therefore, the fee shown above is reduced by 75%, and the resulting fee is: $ _____

Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

[ ] A check in the amount of the fee is enclosed.

[x] Payment by credit card. ~~Form PTO-2038 is attached~~.

[x] The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 23/2825 .

[x] Payment made via EFS-Web.

[ ] A petition for an extension of time under 37 CFR 1.136(a) (PTO/AIA/22 or equivalent) is enclosed. For extensions of time in reexamination proceedings, see 37 CFR 1.550.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

[ ] applicant [x] attorney or agent of record Registration number 73,490 [ ] attorney or agent acting under 37 CFR 1.34 Registration number _____

Signature /David F. Cauble/

Typed or printed name David F. Cauble, PhD, JD

Telephone Number 617.646.8000

Date October 8, 2020

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

[ ] * Total of 1 forms are submitted.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 304 of 415

Doc Code: AP.PRE.REQ

PTO/AIA/33 (03-13)
Approved for use through 11/30/2020
OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) U0157.70023US03	
I hereby certify that this correspondence is being facsimile transmitted to the USPTO, EFS-Web transmitted to the USPTO, or deposited with the United States Postal Service with sufficient postage in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on October 7, 2020. Signature /Cathy Nicholson/ Typed or printed name Cathy Nicholson	Application Number 15/639,223-Conf. #8089	Filed June 30, 2017
	First Named Inventor Michael J. Zaworotko et al.	
	Art Unit 1699	Examiner N. E. Jarrell

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

☐ applicant.

☒ attorney or agent of record.
Registration number 73,490.

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

/David F. Cauble/
Signature

David F. Cauble, PhD, JD
Typed or printed name

617.646.8000
Telephone number

Date

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of 1 forms are submitted.

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1699

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: October 7, 2020 Signature: /Cathy Nicholson (Cathy Nicholson)

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicant hereby requests review of the rejection of claims 37-50 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. As a preliminary matter, Applicant notes that the outstanding rejections on grounds of non-statutory double patenting over claims 37 and 45 of Application Number 14/179,862 (now issued as US Patent Number 10,633,344) and claims 37, 38, and 42 of co-pending Application 16/270,981 are moot in view of the terminal disclaimer filed over both of these publications.

The rejection under 35 U.S.C. § 112, first paragraph has been maintained following Applicant's response of April 3, 2020. On page 4 of the Final Rejection dated July 10, 2020, the Office explains that "[t]his rejection has been maintained because the state of the art shows that pharmaceutical co-crystal [design] presently has challenges that need to be overcome." The Office bases this view on the publication of Miroshnyk et al., *Expert Opinion in Drug Delivery*, **2009**, *6(4)*, 333-341 ("Miroshnyk"), noting specifically the "Expert Opinion" section, pages 337-338; and the "Conclusions" section, pages 338-340.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 306 of 415

With regard to the *Wands* factor related to "the state of the prior art and the predictability of unpredictability in the art," Applicant notes as a preliminary matter that the publication of Miroshnyk is not prior art. Nevertheless, the Office maintains that Miroshnyk provides evidence of "high unpredictability in the art" in view of alleged "translational challenges [that] are present in cocrystal design…" (page 3). Such challenges allegedly include:

1. Stability of an active pharmacological ingredient;
2. Seeing studies that follow the development cycle all the way to the end product;
3. Systematically investigating the applicability of agglomeration techniques; and
4. Regulatory issues.

The publication of Miroshnyk does not demonstrate high unpredictability in the art as it pertains to the manufacture and use of the ***claimed invention***, and Applicant submits that the teachings of Miroshnyk have been mischaracterized by the Office. The four alleged teachings of Miroshnyk, listed above, are addressed in turn below.

(1) Miroshnyk does not characterize "stability of an active pharmaceutical ingredient" as a challenge to pharmaceutical co-crystal design. To the contrary, Miroshnyk teaches that pharmaceutical co-crystals are a ***solution*** to the problem of poor API stability:

> *The stability of a solid API when exposed a wide range of relative humidities is another essential property… It is often the case that moisture promotes unwanted solid-phase transformation of an API…One approach proposed to inhibit such moisture-induced phase transformations is rational co-former selection for a specific formulation. In this context,* ***co-crystallization of an API with a co-former can be thought as a more-radical strategy to address the poor physical stability of moisture-sensitive pharmaceutical materials****. For instance, caffeine/oxalic acid co-crystals have been demonstrated to be superior to caffeine anhydrate in terms of physical stability to humidity.* (Page 338, left column, last paragraph; emphasis added).

(2) Miroshnyk does not characterize "seeing studies that follow the development cycle all the way to the end product" as a challenge to pharmaceutical co-crystal design. Miroshnyk states that it "would be desirable" to see such studies, but in no way suggests that this is a "challenge to pharmaceutical co-crystal design," as stated on page 4 of the Non-final Rejection dated November 5, 2019. The fact that Miroshnyk is not aware of any such studies, or the fact that such studies may

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 307 of 415

not have been published, cannot be understood to mean that such studies have not taken place, or that the skilled person is not capable of performing such studies without undue experimentation. To the contrary, the fact that such studies have taken place can be inferred from the regulatory approval in Japan of the ipragliflozin/L-proline co-crystal Suglat (see, *e.g.*, Astellas press release dated December 21, 2018, made of record in the IDS submitted on April 3, 2020). Here, Applicant notes MPEP 2164.01, which states that "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." As evidenced, at least, by the regulatory approval described above, the art does engage in such experimentation, *i.e.*, studies that follow the development cycle of a co-crystalline drug product all the way to the end product.

(3) Miroshnyk states that "there is a need for studies that systematically investigate the applicability of agglomeration techniques…" but goes on to say that such studies "***could*** provide valuable information for ***commercial-scale manufacture*** of co-crystal systems." (page 338, right column, third paragraph; emphasis added) Miroshnyk's statement regarding studies related to ***commercial-scale manufacture*** does not teach or suggest that the skilled person would be unable to make and use the claimed pharmaceutical compositions. Even assuming, *arguendo*, that the statement were understood to represent such a teaching, the regulatory approval and commercial availability of Suglat tablets, discussed above, proves that the art is equipped to engage in experimentation required to commercially manufacture solid formulations of pharmaceutical co-crystals.

(4) Miroshnyk states that "Regulatory issues are also of ***great interest***," for example, "whether a new co-crystal of a marketed API is eligible for regulatory approval via the abbreviated new drug approval mechanism…" These statements of Miroshnyk clearly relate to considerations that are irrelevant to the manufacture and use of the claimed invention, and therefore are irrelevant to the question of enablement.

With regard to the *Wands* factor related to "the relative skill of those in the art," the Office alleges that "the artisan generally would have an advanced degree in cocrystal formation and analysis, [but that] their high level of skill and knowledge is insufficient to overcome the lack of understanding as to how cocrystal formation occurs." Applicant submits that Miroshnyk does not teach or suggest that there is a lack of understanding as to how cocrystal formation occurs. On the contrary, Miroshnyk describes in detail the "General aspects of co-crystal formation" (pages 334-

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 308 of 415

337) and even discloses a "Schematic of steps for co-crystal design" (Figure 2). There is no other evidence of record which supports the presumption of a lack of understanding as to how cocrystal formation occurs, nor is there any evidence of record that the knowledge of a person having ordinary skill in the art (*i.e.*, having an advanced degree in cocrystal formation and analysis) would be insufficient to overcome any lack of understanding.

With regard to the *Wands* factor related to "the quantity of experimentation necessary," the Office refers to the "state of the prior art as discussed by the references above" (*i.e.*, the publication of Miroshnyk). For the reasons described above, Applicant submits that there is no teaching of Miroshnyk which indicates that undue experimentation would be required to make or use the claimed invention, and consequently that there is no evidence of record to support the Office's statements in this regard.

With regard to the *Wands* factor related to "the amount of direction or guidance presented and the presence of absence of working examples," the Office acknowledges the working examples of examples 1-17 but does not acknowledge the considerable guidance provided in addition to these examples. For example, in paragraph [0043], the application discloses a method of preparing a multiple-component solid phase composition composed of an API and at least one co-crystal former involving techniques such as such as crystallization from solution, cooling the melt, sublimation and grinding. A "multiple-component phase" is defined in paragraph [0047] as any solid material (phase) that is sustained by intermolecular interactions between at least two independent molecular entities, in any stoichiometric ratio, wherein at least one of the independent molecular entities is a pharmaceutical entity. "Pharmaceutical entities" are defined in paragraph [0048] and numerous examples of chemical functional groups that are capable of forming supramolecular synthons are provided. Paragraphs [0040]-[0042] disclose methods for identifying complementary chemical functional groups with which to form the desired supramolecular synthons. The methods involve:

- evaluating the structure of an API, which can include determining its crystal structure;
- determining whether the API contains chemical functionalities capable of forming supramolecular synthons with different molecules;
- identifying from a plurality of chemical functionalities that are known to form supramolecular synthons at least one functionality that will form a supramolecular

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 309 of 415

synthons with the API, and wherein the selected chemical functionality is capable of forming a noncovalent bond to a complementary chemical functionality on the API; and

- identifying co-crystal formers having chemical functionalities that are complementary with the active pharmaceutical ingredient.

In paragraphs [0057] through [0178], the methods described above are applied to the preparation of 19 different, exemplary co-crystals. In this regard, Applicant notes that MPEP 2164.02(III) states:

> For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art…would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus ***only where adequate reasons are advanced*** by the examiner ***to establish that a person skilled in the art could not use the genus as a whole without undue experimentation***. (Emphasis added)

The Office has not advanced any reasons or evidence supporting a conclusion that a skilled person would not be able to make and use the claimed genus without undue experimentation.

At least for the foregoing reasons, the Office has not adequately supported the rejection of 37-50 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Accordingly, reversal of this rejection is respectfully requested.

A Notice of Appeal (and associated fees) are submitted herewith. If a further fee is due with this Pre-Appeal Brief Request, please charge our Deposit Account No. 23/2825, under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Dated: October 8, 2020

Respectfully submitted,

By /David F. Cauble/
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

8600666.1

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
* 15/639,223 *	15/639,223	Zaworotko et al.	
	Examiner	**Art Unit**	
	JARRELL, NOBLE E	1699	

Document Code - DISQ	**Internal Document - DO NOT MAIL**

TERMINAL DISCLAIMER	☐ APPROVED	☑ DISAPPROVED
Date Filed: **08 October 2020**	**This patent is subject to a Terminal Disclaimer**	

Approved/Disapproved by:

/CHARRISSA S BROWN/

Technology Center: PLRC

Telephone: (571)272-1558

2 TD'S Disapproved.
The person who signed the terminal disclaimer is not the applicant, patentee or an attorney or agent of record. 37 CFR 1.321(a) and (b). (See FP 14.26.08)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 311 of 415

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 11/17/2020

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
11/17/2020	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 312 of 415

Notice of Panel Decision from Pre-Appeal Brief Review	Application No.	Applicant(s)	
	15/639,223	Zaworotko et al.	
	Examiner	Art Unit	AIA (FITF) Status
	Andrew D Kosar	1625	No

This is in response to the Pre-Appeal Brief Request for Review filed 08 October 2020 .

1. ☐ **Improper Request** - The Request is improper and a conference will not be held for the following reason(s):

☐ The Notice of Appeal has not been filed concurrent with the Pre-Appeal Brief Request.
☐ The request does not include reasons why a review is appropriate.
☐ A proposed amendment is included with the Pre-Appeal Brief request.
☐ Other: _____ .

The time period for filing a response continues to run from the receipt date of the Notice of Appeal or from the mail date of the last Office communication, if no Notice of Appeal has been received.

2. ☐ **Proceed to Board of Patent Appeals and Interferences** - A Pre-Appeal Brief conference has been held. The application remains under appeal because there is at least one actual issue for appeal. Applicant is required to submit an appeal brief in accordance with 37 CFR 41.37. The time period for filing an appeal brief will be reset to be one month from mailing this decision, or the balance of the two-month time period running from the receipt of the notice of appeal, whichever is greater. Further, the time period for filing of the appeal brief is extendible under 37 CFR 1.136 based upon the mail date of this decision or the receipt date of the notice of appeal, as applicable.

☐ The panel has determined the status of the claim(s) is as follows:
Claim(s) allowed: _____ .
Claim(s) objected to: _____ .
Claim(s) rejected: _____ .
Claim(s) withdrawn from consideration: _____ .

3. ☐ **Allowable application** - A conference has been held. The rejection is withdrawn and a Notice of Allowance will be mailed. Prosecution on the merits remains closed. No further action is required by applicant at this time.

4. ☑ **Reopen Prosecution** - A conference has been held. The rejection is withdrawn and a new Office action will be mailed. No further action is required by applicant at this time.

All participants:

(1) ANDREW D KOSAR .	(3) Lora Driscoll .
(2) Noble Jarrell .	(4) _____ .

/Andrew D Kosar/ Supervisory Patent Examiner, Art Unit 1625		

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 313 of 415

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 02/05/2021

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
02/05/2021	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Office Action Summary	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.	
	Examiner NOBLE E JARRELL	**Art Unit** 1699	**AIA (FITF) Status** No

-- 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 08 October 2020.

☐ 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) 37-50 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 37-50 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 _____.

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

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Response to Amendment

This action is in response to the notice of appeal filed 8 October 2020 and pre-appeal brief conference decision of 17 November 2020. Prosecution is being re-opened. The 35 U.S.C. 112 (a) scope of enablement rejection is dropped.

Claim Rejections - 35 USC § 112

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons. Each synthon is formed from a stoichiometric amount of at least one active pharmaceutical ingredient (API) and at least one co-crystal former. The synthons are associated together through non-covalent hydrogen bonding. The universe of pharmaceutical compositions comprising an API and co-crystal former includes any co-crystal comprising an API and co-crystal bound together by noncovalent H-bonding.

(1) Level of skill and knowledge in the art:

HSU (*Acta Crystallographica*, **1974**, *B30*, 843-846, cited in IDS) describes a 1:1 cocrystal of salicylamide and 5-ethylisoamylbarbituric acid (title and abstract). Hydrogen bonding is used to bind the compounds together (abstract; page 845, column 2 to page 846, column 1, paragraph 1).

MIROSHNYK (*Expert Opinion in Drug Delivery*, **2009**, *6(4)*, 333-341, cited previously) describes how cocrystals are bound together and examples of the same (table 1, page 336; table 2, page 339).

(2) Partial structure:

A partial structure encompasses a pharmaceutical composition comprising a cocrystal of an API and a co-crystal former bound together by non-covalent H-bonding.

(3) Physical and/or chemical properties and (4) Functional characteristics:

Examples 1-18 (page 16, paragraph [0056]) to page 33, paragraph [00177]) describe different properties of the compositions selected from crystal data, IR spectroscopy, DSC, TGA, and XRPD. The examples provide a wide range of solid phases having properties such as melting point, solubility, dissolution rate, chemical stability, thermodynamic stability, and/or bioavailability.

(5) Method of making the claimed invention:

Example 1 shows a representative method of making a pharmaceutical composition where 50 mg of acetaminophen and 52 mg of 4,4'-bipyridine were dissolved in hot water and allowed to stand. Slow evaporation lead to colorless needles of 1:1:1 acetaminophen:4,4'-bipyridine:water co-crystal (figure 4B).

The MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 37-50 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any a pharmaceutical composition comprising an API and a co-crystal former that are associated through non-covalent hydrogen binding. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus. While having written description of examples 1-18 and compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention

will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

> 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 37-50 are 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 applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

The concept of a "GRAS compound" (page 12, paragraph [0046]) is unclear because the metes and bounds of what is regarded as safe and requires more guidance (KNUDSEN, *Regulatory Toxicology and Pharmacology*, **1995**, *21*, 365-369).

Claims 37-50 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the required structural components of an API and a co-crystal former and the functional groups that are used for non-covalent hydrogen bonding. None of claims 37-49 fully define the required structural elements of the API or the cocrystal former. Rather, an API and cocrystal former are defined by their properties. Hsu (same reference as above) prepares a complex of salicylamide and 5-ethylisoamylbarbituric acid. Miroshnyk (same reference as above) describes three broad methods of non-covalent H-bonding interactions and various combinations of seven different API's with various cocrystal formers.

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 conflicting claims 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 re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *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 nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) 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 www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 37-50 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37 and 45 of U.S. Patent No. 10633344 (hereinafter '344). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of '344. Claim 37 of '344 overlaps with instant claims 37 and 39. Claim 45 of '344 is embraced by instant claims 37 and 40.

Claims 37, 38 and 42 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37, 38, and 42 of copending Application No. 16/270981 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of 16/270981. Claims 37, 38, and 42 of '981 overlap with instant claims 37, 38, and 42. Example 1 (page 16, paragraph [0056] to page 17, paragraph [0059]) shows a co-crystal of acetaminophen, bipyridine, and water.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Amendment

The terminal disclaimers filed 9 October 2020 are not approved because the person who signed the terminal disclaimer is not the applicant, patentee, or an attorney or agent of record (see 37 CFR 1.321 (a) and (b) and FP 14.26.08). Consequently the double patenting rejections are maintained.

Conclusion

Claims 37-50 are not allowable presently.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE E JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on 9:00 AM to 5:00 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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 https://ppair-my.uspto.gov/pair/PrivatePair. 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.

/NOBLE E JARRELL/
Primary Examiner, Art Unit 1699

Notice of References Cited	Application/Control No. 15/639,223	Applicant(s)/Patent Under Reexamination Zaworotko et al.	
	Examiner NOBLE E JARRELL	Art Unit 1699	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-10633344-B2	04-2020	Zaworotko; Michael J.	A61P29/00	1/1
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 321 of 415

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/639,223	Zaworotko et al.
	Examiner	Art Unit
	NOBLE E JARRELL	1699

CPC - Searched*		
Symbol	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystal cocrystals co near crystals).clm.	02/19/2019	NJ

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystalcocrystals co near crystals).clm.	02/19/2019	NJ
stn registry and hcaplus	02/19/2019	NJ
inventor search in PALM and EAST	02/19/2019	NJ
stn registry and hcaplus	10/30/2019	NJ

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
C07D	223/26	02/19/2019	NJ

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1625	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 322 of 415

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 15/639,223	Filing Date 06/30/2017	☐ To be Mailed

ENTITY: ☐ LARGE ☑ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $40 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $210 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT	05/27/2021	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 14	Minus	** 36	= 0		x $50 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	*** 9	= 0		x $240 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

		(Column 1)		(Column 2)	(Column 3)			
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/CHRISTINE V MOORE/
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".	
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.	

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1625

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: May 27, 2021 Signature: /Cathy Nicholson / (Cathy Nicholson)

RESPONSE TO NON-FINAL OFFICE ACTION UNDER 37 C.F.R. § 1.111

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Office Action dated February 5, 2021, the time being extended to the present by the attached Petition for Extension of Time, please amend the above-identified U.S. patent application as follows:

Listing of the Claims begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 324 of 415

LISTING OF THE CLAIMS

1 – 36. (Canceled)

37. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-crystal former,

wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form,

wherein the co-crystal former has a second chemical functionality complimentary to the first chemical functionality via non-covalent hydrogen bonding,

wherein supramolecular synthons comprise non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-crystal former.

38. (Currently amended) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, ~~a GRAS compound,~~ a food additive, a low toxicity organic, and a metal-organic complex.

39. (Previously presented) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form.

40. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and one co-crystal former.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 325 of 415

41. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of one active pharmaceutical ingredient (API) and one co-crystal former.

42. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a group selected from acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases, amines, alcohols, halogens, sulfones, and nitro groups.

43. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an acid.

44. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amine.

45. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amide.

46. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an alcohol.

47. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon.

48. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a heterosynthon.

49. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon and a heterosynthon.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 326 of 415

50. (Previously presented) The pharmaceutical composition of claim 48, wherein the heterosynthon comprises an alcohol/amine interaction.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 327 of 415

REMARKS

Prior to entry of the instant amendments, claims 37-50 were pending in the Application. Claim 38 has been amended. No new matter is added. Upon entry of the amendments, claims 37-50 will be pending.

CLAIM REJECTIONS – 35 USC § 112

Page 4 of the Office Action states that "it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s)…had possession of the entire scope of the invention." The Office further takes the position that "although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples of the specification."

Applicants respectfully disagree. MPEP 2163 states that "[a]n applicant may…show that an invention is complete by disclosure of…complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Enzo Biochem, 323 F.3d at 964, 63 USPQ2d at 1613 (quoting the Written Description Guidelines, 66 Fed. Reg. at 1106, n. 49, stating that 'if the art has established a strong correlation between structure and function, one skilled in the art would be able to predict with a reasonable degree of confidence the structure of the claimed invention from a recitation of its function'), concluding "[t]hus, ***the written description requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function."*** Emphasis added.

Claim 37 specifies, inter alia, the following structure in relation to the recited co-crystal:

- stoichiometric amounts of an API and a co-crystal former;
- API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form; and
- co-crystal former has a second chemical functionality complimentary to the first chemical functionality via non-covalent hydrogen bonding.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 328 of 415

Claim 37 specifies, inter alia, the function:

- hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-crystal former.

The function recited in claim 37 relates to hydrogen bonding between complimentary functional groups of the API and the co-crystal formula. There is a well-established correlation between structure and function in the context of hydrogen bonding, and the correlation was well-established as of the filing date of the present application. The correlation between structure and function in the context of hydrogen bonding is described in terms of hydrogen bond donors and hydrogen bond acceptors.

The correlation between structure and function, and the associated terminology, is reflected in the Examples and Figures of the instant application. See, e.g., Figure 1 depicts a carboxylic acid moiety comprising a carbonyl (hydrogen bond acceptor) and an acidic hydrogen (hydrogen bond donor). Figure 2 depicts the interaction between hydrogen bond donor and acceptor. Figures 4A-4B depict hydrogen bonding interactions between the H atoms (hydrogen bond donors) of amide moieties and water, with the O and N atoms (hydrogen bond acceptors) of carbonyl moieties, water, and bipyridine. Paragraph [0018] of the application refers to "all hydrogen bonding donors and acceptors interacting" in Figures 4A-4B. Paragraph [0009] of the application refers to certain representative, non-limiting examples of functional groups which may participate in hydrogen bonding: acids, amides, aliphatic nitrogen bases, unsaturated aromatic nitrogen bases (e.g. pyridines, imidazoles), amines, alcohols, halogens, sulfones, nitro groups, S-heterocyles, N-heterocycles (saturated or unsaturated), O-heterocycles, ethers, thioethers, thiols, esters, thioesters, thioketones, epoxides, acetonates, nitrils, oximes, and organohalides.

With reference to the bold/italicized text above, the written description requirement is satisfied in connection with the present application by the disclosure of structure and function, both as noted above, together with a well-established correlation between structure and function. Moreover, the application describes adequate exemplary structures and working examples, i.e., each of Examples 1-19. As such, Applicant requests withdrawal of this rejection.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 329 of 415

Claims 37-50 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as allegedly being indefinite in view of the term "GRAS compound." Applicant respectfully disagrees, and as a preliminary matter notes that independent claim 37, and dependent claims 39-50 do not recite the term "GRAS compound." As such, Applicant understands the rejection to be limited to claim 38. Without conceding the merits of the rejection, and solely to expedite prosecution, claim 38 has been amended to delete the term "GRAS compound." Accordingly, Applicant requests withdrawal of this rejection.

Claims 37-50 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being incomplete for omitting essential elements. Specifically, the Office alleges that the claims omit "the required structural components of an API and co-crystal former and the functional groups that are used for non-covalent hydrogen bonding. Applicant respectfully disagrees.

MPEP 2172.01 states that "[a] claim which omits matter disclosed to be essential to the invention as described in the specification or in other statements of record may be rejected under 35 U.S.C. 112, first paragraph, as not enabling" and that "[i]f a claim fails to interrelate essential elements of the invention as defined by applicant(s) in the specification, the claim may be rejected under… 35 U.S.C. 112, second paragraph, as indefinite.

The present rejection is under 35 U.S.C. 112 (pre-AIA), second paragraph, and therefore the relevant question is whether the rejected claims "fail to interrelate essential elements of the invention as defined by applicant(s) in the specification." Applicant notes that the specification does not define any subject matter as "essential" in relation to the claimed invention, and the Office has not identified any part of the specification that defines "essential" subject matter. The Office has cited the publications of Hsu and Miroshnyk, but the publications of Hsu and Miroschnyk are not part of the specification, and therefore the Office has not met its threshold burden of specifying which essential elements, ***as defined by the applicant in the specification***, have been omitted, or that the applicant has failed to interrelate. Accordingly, Applicant requests withdrawal of this rejection.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 330 of 415

DOUBLE PATENTING

Claims 37-50 are rejected on the ground of non-statutory double patenting as being unpatentable over claims 37 and 45 of U.S. Patent No. 10,633,344.

Claims 37, 38, and 42, are provisionally rejected on the ground of non-statutory double patenting as being unpatentable over claims 37, 38 and 42, of co-pending Application No. 16/270981.

Applicant requests that these rejections be held in abeyance until the claims are held to be in condition for allowance otherwise.

CONCLUSION

In view of the foregoing, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this response, the application is not in condition for allowance, the Examiner is requested to call the undersigned at the telephone number indicated below to discuss any outstanding issues.

All fees due are being paid by Credit Card. However, should additional fees be due with this filing, please charge our Deposit Account No. 23/2825, under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Dated: May 27, 2021

Respectfully submitted,

By /David F. Cauble/_____
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 331 of 415

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Cathy Nicholson
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 1 month with $0 paid	2251	1	110	110
Miscellaneous:				
		Total in USD ($)		**110**

Electronic Acknowledgement Receipt	
EFS ID:	42839449
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Cathy Nicholson
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	27-MAY-2021
Filing Date:	30-JUN-2017
Time Stamp:	15:23:36
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$110
RAM confirmation Number	E20215QF23510314
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	U015770023US03-TRN-DFC.pdf	26208 e26e4e41e44073d0092da717a532577d1d6b9dd5	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	37423 022c6d4e09afc507616a9318c505a7c111f31e84	no	1
Warnings:					
Information:					
3	Extension of Time	U015770023US03-EXT-DFC.pdf	25074 b0119b2a54f4e15a6e13147a92e8fa22808e5396	no	1
Warnings:					
Information:					
4		U015770023US03-AMN-DFC.pdf	52303 e003a70187ec65359dfea4067dba87335a385b90	yes	8

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment/Req. Reconsideration-After Non-Final Reject	1	1
Claims	2	4
Applicant Arguments/Remarks Made in an Amendment	5	8

Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	30756 af3b35954e44d4d33de9437b3d843263c769be04	no	2

Warnings:	
Information:	
Total Files Size (in bytes):	171764

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	

Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Art Unit	1699
Examiner Name	N. E. Jarrell
Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

[X] Fee Transmittal Form	[ ] Drawing(s)	[ ] After Allowance Communication to TC
[ ] Fee Attached	[ ] Licensing-related Papers	[ ] Appeal Communication to Board of Appeals and Interferences
[X] Amendment/Reply	[ ] Petition	[ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
[ ] After Final	[ ] Petition to Convert to a Provisional Application	[ ] Proprietary Information
[ ] Affidavits/declaration(s)	[ ] Power of Attorney, Revocation Change of Correspondence Address	[ ] Status Letter
[X] Extension of Time Request	[ ] Terminal Disclaimer	[ ] Other Enclosure(s) (please Identify below):
[ ] Express Abandonment Request	[ ] Request for Refund	
[ ] Information Disclosure Statement	[ ] CD, Number of CD(s) _____	
[ ] Certified Copy of Priority Document(s)	[ ] Landscape Table on CD	
[ ] Reply to Missing Parts/ Incomplete Application	Remarks	
[ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	May 27, 2021	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: May 27, 2021 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

9274873.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1699
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)110.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	320	160*	80	700	350	175	800	400	200	
Design	220	110	55	160	80	40	640	320	160	
Plant	220	110	55	440	220	110	660	330	165	
Reissue	320	160	80	700	350	175	2,320	1,160	580	
Provisional	300	150	75	0	0	0	0	0	0	

* The $160 small entity status filing fee for a utility application is further reduced to $80 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	480	240	120
Multiple dependent claims	860	430	215

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
20	- or HP =	_____	x _____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
_____	- or HP =	_____	x _____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	**Fee ($)**	**Fee Paid ($)**
	_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $420 ($210 for small entity) ($105 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**	**Fee ($)**	**Fee Paid ($)**
_____	- 100 =	_____	/50 =	_____ (round **up** to a whole number) x	_____	= _____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2251 Extension for response within first month	110.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	May 27, 2021

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: May 27, 2021 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

9274872.1

PTO/AIA/22 (10-20)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional): U0157.70023US03

Application Number	15/639,223-Conf. #8089	Filed	June 30, 2017

For: MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT

Art Unit	1699	Examiner	N. E. Jarrell

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
[x] One month (37 CFR 1.17(a)(1))	$220	$110	$55	$ 110.00
[ ] Two months (37 CFR 1.17(a)(2))	$640	$320	$160	$
[ ] Three months (37 CFR 1.17(a)(3))	$1,480	$740	$370	$
[ ] Four months (37 CFR 1.17(a)(4))	$2,320	$1,160	$580	$
[ ] Five months (37 CFR 1.17(a)(5))	$3,160	$1,580	$790	$

[x] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

[ ] A check in the amount of the fee is enclosed.

[x] Payment by credit card. ~~Form PTO-2038 is attached~~.

[ ] The Director has already been authorized to charge fees in this application to a Deposit Account.

[x] The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 23/2825 .

[x] Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

[ ] applicant.

[ ] attorney or agent of record. Registration number _____ .

[x] attorney or agent acting under 37 CFR 1.34. Registration number 73,490 .

/David F. Cauble/	May 27, 2021
Signature	Date
David F. Cauble, PhD, JD	617.646.8000
Typed or printed name	Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

[ ] * Total of 1 forms are submitted.

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: May 27, 2021 Signature: /Cathy Nicholson/(Cathy T. Nicholson)

9274874.1

FORM PTO-1449/A and B (modified PTO/SB/08)	APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
	FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet 1 of 1	GROUP ART UNIT: 1699	EXAMINER: N. E. Jarrell

U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY
		Number	Kind Code		

FOREIGN PATENT DOCUMENTS

Examiner's Initials #	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
		WO	2006/007448	A2	Transform Pharmaceuticals, Inc.	01-19-2006	

OTHER ART – NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
		KOBAYASHI et al., Supramolecular architecture consisting of an enantiopure amine and an achiral carboxylic acid: application to the enantioseparation of racemic alcohols. Org Lett. 2004 Aug 19;6(17):2941-4. doi: 10.1021/ol048948b.	
		KODAMA et al., Two-component supramolecular helical architectures: creation of tunable dissymmetric cavities for the inclusion and chiral recognition of the third components. Chemistry. 2007;13(7):2144-52. doi: 10.1002/chem.200601295.	

[NOTE – No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR § 1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR § 1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR § 1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. § 120.]

EXAMINER:	DATE CONSIDERED:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

9372490.1

PATENT TERM ADJUSTMENT STATEMENT UNDER 37 CFR 1.704(d)		
	Application Number	15/639,223-Conf. #8089
	Filing Date	June 30, 2017
	First Named Inventor	Michael J. Zaworotko
	Art Unit	1699
	Examiner Name	N. E. Jarrell
	Practitioner Docket No.	U0157.70023US03

APPLICANT HEREBY STATES THE FOLLOWING (please review 37 CFR 1.704(d) before filing this form):

[x] Each item of information contained in the information disclosure statement was first cited in any communication from a patent office in a counterpart foreign or international application or from the Office, and this communication was not received by any individual designated in 37 CFR 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

AND/OR

[ ] Each item of information contained in the information disclosure statement is a communication that was issued by a patent office in a counterpart foreign or international application or by the Office, and this communication was not received by any individual designated in 37 CFR 1.56(c) more than thirty days prior to the filing of the information disclosure statement.

INSTRUCTIONS:

- **This form will not satisfy the requirement of 37 CFR 1.97(e).** The present statement is filed under 37 CFR 1.704(d) and will not substitute for compliance with any of the requirements of 37 CFR 1.97 and 1.98. For an information disclosure statement to comply with 37 CFR 1.97(c) or (d), the information disclosure statement must be accompanied by a statement under 37 CFR 1.97(e) notwithstanding any statement filed under 37 CFR 1.704(d).
- The present form (PTO/SB/133) should be filed concurrently with the information disclosure statement to derive benefit under 37 CFR 1.704(d).

Signature	/David F. Cauble/	Date	July 2, 2021
Typed or printed name	David F. Cauble, PhD, JD	Practitioner Registration Number	73,490

***Note**: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required in accordance with 37 CFR 1.33 and 11.18. Please see 37 CFR 1.4(d) for the form of the signature. If necessary, submit multiple forms for more than one signature, see below*.*

[ ] *Total of 1 forms are submitted.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 2, 2021 Signature: /Jessica O. Valli/ (Jessica O. Valli)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 341 of 415

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Jessica Valli
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	2806	1	130	130
		Total in USD ($)		**130**

Electronic Acknowledgement Receipt

EFS ID:	43159890
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Jessica Valli
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	02-JUL-2021
Filing Date:	30-JUN-2017
Time Stamp:	12:38:15
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$130
RAM confirmation Number	E202172C39174342
Deposit Account	232825
Authorized User	Jessica Valli

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

37 CFR 1.17 (Patent application and reexamination processing fees)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Miscellaneous Incoming Letter	U015770023US03-TRN-DFC.pdf	26440 58e02104c44761da16ce7ea5445c918b5a94dcde	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	32801 e5ad306079dac5d0e9bb63440a92ab845e8974bd	no	1
Warnings:					
Information:					
3	Letter specifying the conditions for filing under 37CFR1.97	U015770023US03-IDSBODY-DFC.pdf	28916 3fc638454205c545493667861c8ded1bcb585f48	no	3
Warnings:					
Information:					
4	Information Disclosure Statement (IDS) Form (SB08)	U015770023US03-IDS1449-DFC.pdf	22847 f86b6fecfee542f24de894dc79b6a8b48ae9b3a6	no	1
Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
5	Patent Term Adjustment Stmt Under 37CFR1.704(d)	U015770023US03-IDSPTA-DFC.pdf	62936 a4b4c72c72afdb7825889d43f4f053b2998818a2	no	1
Warnings:					
Information:					
6	Non Patent Literature	Kobayashi_et_al_Org_Lett_2004_v6_p2941.pdf	476619 e6c52cb690cc78f67220df2bd21fe69a77bcbe41	no	4
Warnings:					

Information:					
7	Non Patent Literature	Kodama_et_al_Chemistry_2007_v13_p2144.pdf	746708 bafb9e5d56d07ffdac47f2248ce4373466a35273	no	9
Warnings:					
Information:					
8	Foreign Reference	WO2006007448A2.pdf	7168462 286d37bb43a17e09a24a1e1baa7a2fbb111ddea4	no	149
Warnings:					
Information:					
9	Fee Worksheet (SB06)	fee-info.pdf	30649 0387790e799083cebaf44989e1fd2787d67a374d	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	8596378	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	

Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Art Unit	1699
Examiner Name	N. E. Jarrell
Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

- [X] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [X] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [X] Other Enclosure(s) (please Identify below):
  - Patent Term Adjustment Statement Under 37 CFR 1.704(d)
  - Form PTO-1449
  - Copies of cited references

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	July 2, 2021	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 2, 2021 Signature: /Jessica O. Valli/ (Jessica O. Valli)

9372487.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1699
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)130.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	320	160*	80	700	350	175	800	400	200	
Design	220	110	55	160	80	40	640	320	160	
Plant	220	110	55	440	220	110	660	330	165	
Reissue	320	160	80	700	350	175	2,320	1,160	580	
Provisional	300	150	75	0	0	0	0	0	0	

* The $160 small entity status filing fee for a utility application is further reduced to $80 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	480	240	120
Multiple dependent claims	860	430	215

Total Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
20	- 20 or HP =	_____	x _____	=	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims		**Extra Claims**	**Fee ($)**		**Fee Paid ($)**
4	- 4 or HP =	_____	x _____	=	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	**Fee ($)**	**Fee Paid ($)**
	_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $420 ($210 for small entity) ($105 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets		**Extra Sheets**		**Number of each additional 50 or fraction thereof**		**Fee ($)**		**Fee Paid ($)**
_____	- 100 =	_____	/50 =	_____	(round **up** to a whole number) x	_____	=	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2806 Submission of an Information Disclosure Statement	130.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	July 2, 2021

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 2, 2021 Signature: /Jessica O. Valli/ (Jessica O. Valli)

9372592.1

DOCKET NO.: U0157.70023US03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1699

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: July 2, 2021 Signature: /Jessica O. Valli/ (Jessica O. Valli)

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF DISCLOSURE UNDER 37 C.F.R. §§ 1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, the undersigned requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. § 1.97

This Information Disclosure Statement has been filed more than three months after the filing date of this application and after the mailing date of a first Office Action, but before the mailing date of any of a Final Action under 37 C.F.R. § 1.113, a Notice of Allowance under 37 C.F.R. § 1.311, or an action that otherwise closes prosecution in this application.

Please charge our Credit Card in the amount of $130.00 covering the fee set forth in 37 C.F.R. § 1.17(p).

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 349 of 415

PART II: Compliance with 37 C.F.R. § 1.704(d)

Each item of information contained in this Information Disclosure Statement

(i) was first cited in any communication from a patent office in a counterpart foreign or international application or from the United States Patent and Trademark Office, and this communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty (30) days prior to the filing of the Information Disclosure Statement; or

(ii) is a communication that was issued by a patent office in a counterpart foreign or international application or by the United States Patent and Trademark Office, and this communication was not received by any individual designated in 37 C.F.R. § 1.56(c) more than thirty (30) days prior to the filing of the Information Disclosure Statement.

PART III: Information Cited

The undersigned hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified PTO/SB/08). The order of presentation of the references should not be construed as an indication of the importance of the references.

PART III: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;

2. The enclosed form PTO-1449 (modified PTO/SB/08) be signed by the Examiner to evidence that the cited information has been fully considered by the United States Patent and Trademark Office during the examination of this application;

3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the undersigned makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

By submitting this Information Disclosure Statement, the undersigned makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. § 102, or an admission by Applicant as prior art.

Notwithstanding any statements by the undersigned, the Examiner is urged to form his or her own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

The Director is hereby authorized to charge any deficiency or credit any overpayment in the fees occasioned by the filing of this Information Disclosure Statement to our Deposit Account No. 23/2825 under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Respectfully submitted,

By: /David F. Cauble/
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

Docket No.: U0157.70023US03
Date: July 2, 2021

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 08/11/2021

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
08/11/2021	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Office Action Summary	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.	
	Examiner NOBLE E JARRELL	**Art Unit** 1699	**AIA (FITF) Status** No

-- 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 27 May 2021.

☐ 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) 37-50 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 37-50 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 2 July 2021.

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

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Response to Amendment

The amendment filed 27 May 2021 overcomes the 35 U.S.C. 112 (b) rejection regarding "GRAS compounds". The other rejections of 5 February 2021 under 35 U.S.C. 112 and double patenting are maintained for the reasons stated below.

Information Disclosure Statement

The information disclosure statement filed 2 July 2021 is acknowledged and considered.

Claim Rejections - 35 USC § 112

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him.

Claim(s) 37-50 is/are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph due to lack of written description.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons. Each synthon is formed from a stoichiometric amount of at least one active pharmaceutical ingredient (API) and at least one co-crystal former. The synthons are associated together through non-covalent hydrogen bonding. The universe of pharmaceutical compositions comprising an API and co-crystal former includes any co-crystal comprising an API and co-crystal bound together by noncovalent H-bonding.

(1) Level of skill and knowledge in the art:

HSU (*Acta Crystallographica*, **1974**, *B30*, 843-846, cited in IDS) describes a 1:1 cocrystal of salicylamide and 5-ethylisoamylbarbituric acid (title and abstract). Hydrogen bonding is used to bind the compounds together (abstract; page 845, column 2 to page 846, column 1, paragraph 1).

MIROSHNYK (*Expert Opinion in Drug Delivery*, **2009**, *6(4)*, 333-341, cited previously) describes how cocrystals are bound together and examples of the same (table 1, page 336; table 2, page 339).

(2) Partial structure:

A partial structure encompasses a pharmaceutical composition comprising a cocrystal of an API and a co-crystal former bound together by non-covalent H-bonding.

(3) Physical and/or chemical properties and (4) Functional characteristics:

Examples 1-19 (page 16, paragraph [0056]) to page 33, paragraph [00177]) describe different properties of the compositions selected from crystal data, IR spectroscopy, DSC, TGA, and XRPD. The examples provide a wide range of solid phases having properties such as melting point, solubility, dissolution rate, chemical stability, thermodynamic stability, and/or bioavailability.

(5) Method of making the claimed invention:

Example 1 shows a representative method of making a pharmaceutical composition where 50 mg of acetaminophen and 52 mg of 4,4'-bipyridine were dissolved in hot water and allowed to stand. Slow evaporation lead to colorless needles of 1:1:1 acetaminophen:4,4'-bipyridine:water co-crystal (figure 4B).

The MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 37-50 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any a pharmaceutical composition comprising an API and a co-crystal former that are associated through non-covalent hydrogen binding. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus. While having written description of examples 1-18 and compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments

Applicants argue that the claims fulfill the requirements of written description. The table below shows the components, the ratio of components to one another, and the type of interaction between the components.

Example #	Active Pharmaceutical ingredient (API)	Co-crystal former #1 (CCF1)	Co-crystal former #2 (CCF2)	Stoichiometry of components (API: CCF1: CCF2)	Hydrogen bond type(s)
1	acetaminophen	4,4'-bipyridine	water	1:1:1	H (amide)---N (pyridine N or imine) and H (hydroxy)---O (water)
2	Phenytoin	Pyridine		1:1	N (pyridine N or imine) ---H (amide)
3	Aspirin	4,4'-bipyridine		2:1	N pyridine N or imine)---H (carboxylic acid)
4	Ibuprofen	4,4'-bipyridine		2:1	N pyridine N or imine)---H (carboxylic acid)

5	Flurbiprofen	4,4'-bipyridine	2:1	N pyridine N or imine---H (carboxylic acid)
6	Flurbiprofen	Trans-1,2-bis-(4-pyridyl)ethylene	2:1	N pyridine N or imine---H (carboxylic acid)
7	Carbazepine	*p*-phthaldehyde	1:1	O (amide)---H (aldehyde) and O (aldehyde)---H (amide)
8	Carbazepine	Nicotinamide	1:1	N (amide)---H (amide) and O (amide)---H (amide)
9	Carbazepine	Saccharin	1:1	O (amide)---H (amide) and O (sulfonyl)---H (amide)
10	Carbazepine	2,6-pyridinecarboxylic acid	2:3	O (amide)---H (carboxylic acid)
11	Carbazepine	5-nitroisophthalic acid	1:1	O (amide)---H (carboxylic acid)

12	Carbazepine	Acetic acid	1:1	O (amide)---H (carboxylic acid)
13	Carbazepine	1,3,5,7-adamantanecarboxylic acid	1:1	O (amide)---H (carboxylic acid)
14	Carbazepine	Benzoqunone	1:1	O (ketone)---H (amide)
15	Carbazepine	Butyric acid	1:1	O (amide)---H (carboxylic acid) and O (carboxylic acid)---H (amide)
16	Carbazepine	DMSO	1:1	O (sulfone)---H (amide)
17	Carbazepine	Formamide	1:1	O (amide)---H (amide) and O (amide)---H (amide)
18	Carbazepine	Formic acid	1:1	O (amide)---H (carboxylic acid) and O (carboxylic acid)---H (amide)
19	Carbazepine	Trimesic acid	1:1	O (amide)---H (carboxylic acid) and O

(carboxylic

acid)---H

(amide)

The rejection is maintained because the instant claims do not show possession of the complete scope of non-covalent interactions through hydrogen bonding. Applicants argue that examples 1-19 of the specification show a structure function relationship of groups that can participate in H-bonding. Although these examples show the relationship of different groups for H-bonding (as seen in the table above), they do not limit the scope of the claims. The broad and reasonable interpretation of claim 37 encompasses more than groups participating in H-bonding in examples 1-19. Additionally, the types of H-bonding described in the examples are not incorporated in the instant rejected claims. Therefore, under BRI, it would be improper to import only the types of H-bonding in the examples into the claims.

> 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 37-50 are 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 applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

Claims 37-50 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the required structural components of an API and a co-crystal former and the functional groups that are used for non-covalent hydrogen bonding. None of claims 37-50 fully define the required structural elements of the API or the cocrystal former. Rather, an API and cocrystal former are defined by their properties. Hsu (same reference as above) prepares a complex of salicylamide and 5-ethyl-5-isoamylbarbituric acid. Miroshnyk (same reference as above) describes three broad methods of non-covalent H-bonding interactions and various combinations of seven different API's with various cocrystal formers.

Response to Arguments

This rejection is maintained because the applicants have not fully defined the complexes formed. Claims 37-50 do not fully characterize or describe the active pharmaceutical ingredient (API) and the co-crystal former. Claim 37 only recites that the API is pharmaceutically active. What or how is the ingredient active? What are the required

structural features of the API? The co-crystal former is unclear because it only defined as having a complimentary chemical functionality to the API. Claim 38 recites four different generic co-crystal formers defined by property not by the required structural elements. One looking at the claim cannot determine the complex that the pharmaceutical composition contains. Applicants point to a laundry list of different functional groups that can participate in H-bonding. It is improper to limit the claims with the specification. Paragraph [0009] is open-ended ("non-limiting") with regard to a functional group that can be used.

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 conflicting claims 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 re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *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 nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) 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 www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 37-50 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37 and 45 of U.S. Patent No. 10633344 (hereinafter '344). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of '344. Claim 37 of '344 overlaps with instant claims 37 and 39. Claim 45 of '344 is embraced by instant claims 37 and 40.

Claims 37, 38 and 42 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37, 38, and 42 of copending Application No. 16/270981 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of 16/270981. Claims 37, 38, and 42 of '981 overlap with instant claims 37, 38, and 42. Example 1 (page 16, paragraph [0056] to page 17, paragraph [0059]) shows a co-crystal of acetaminophen, bipyridine, and water.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Arguments

The terminal disclaimers filed 9 October 2020 are not approved because the person who signed the terminal disclaimer is not the applicant, patentee, or an attorney or agent of record (see 37 CFR 1.321 (a) and (b) and FP 14.26.08). Additionally, applicant has requested the rejections be held in abeyance. Consequently the double patenting rejections are maintained

Conclusion

Claims 37-50 are not presently allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE E JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on 9:00 AM to 5:00 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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 https://ppair-my.uspto.gov/pair/PrivatePair. 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.

/NOBLE E JARRELL/
Primary Examiner, Art Unit 1699

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/639,223	Zaworotko et al.
	Examiner	Art Unit
	NOBLE E JARRELL	1699

CPC - Searched*		
Symbol	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystal cocrystals co near crystals).clm.	02/19/2019	NJ

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystalcocrystals co near crystals).clm.	02/19/2019	NJ
stn registry and hcaplus	02/19/2019	NJ
inventor search in PALM and EAST	02/19/2019	NJ
stn registry and hcaplus	10/30/2019	NJ

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
C07D	223/26	02/19/2019	NJ

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1625	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 363 of 415

FORM PTO-1449/A and B (modified PTO/SB/08)				APPLICATION NO.: 15/639,223	ATTY. DOCKET NO.: U0157.70023US03
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				FILING DATE: June 30, 2017	CONFIRMATION NO.: 8089
				FIRST NAMED INVENTOR: Michael J. Zaworotko	
Sheet	1	of	1	GROUP ART UNIT: 1699	EXAMINER: N. E. Jarrell

U.S. PATENT DOCUMENTS

Examiner's Initials #	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or Issue of Cited Document MM-DD-YYYY
		Number	Kind Code		

FOREIGN PATENT DOCUMENTS

Examiner's Initials #	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
		WO	2006/007448	A2	Transform Pharmaceuticals, Inc.	01-19-2006	

OTHER ART – NON PATENT LITERATURE DOCUMENTS

Examiner's Initials #	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
		KOBAYASHI et al., Supramolecular architecture consisting of an enantiopure amine and an achiral carboxylic acid: application to the enantioseparation of racemic alcohols. Org Lett. 2004 Aug 19;6(17):2941-4. doi: 10.1021/ol048948b.	
		KODAMA et al., Two-component supramolecular helical architectures: creation of tunable dissymmetric cavities for the inclusion and chiral recognition of the third components. Chemistry. 2007;13(7):2144-52. doi: 10.1002/chem.200601295.	

[NOTE – No copies of U.S. patents, published U.S. patent applications, or pending, unpublished patent applications stored in the USPTO's Image File Wrapper (IFW) system, are included. See 37 CFR § 1.98 and 1287OG163. Copies of all other patent(s), publication(s), unpublished, pending U.S. patent applications, or other information listed are provided as required by 37 CFR § 1.98 unless 1) such copies were provided in an IDS in an earlier application that complies with 37 CFR § 1.98, and 2) the earlier application is relied upon for an earlier filing date under 35 U.S.C. § 120.]

EXAMINER:	DATE CONSIDERED:
/NOBLE E JARRELL/	07/28/2021

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

9372490.1

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /N.J/

UNITED STATES PATENT AND TRADEMARK OFFICE
COMMISSIONER FOR PATENTS
P.O.BOX 1450
ALEXANDRIA VA 22313-1451

PRESORTED
FIRST-CLASS MAIL
U.S. POSTAGE PAID
POSTEDIGITAL
NNNNN

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

Courtesy Reminder for
Application Serial No: 15/639,223

Attorney Docket No: U0157.70023US03
Customer Number: 23628
Date of Electronic Notification: 08/11/2021

This is a courtesy reminder that new correspondence is available for this application. If you have not done so already, please review the correspondence. The official date of notification of the outgoing correspondence will be indicated on the form PTOL-90 accompanying the correspondence.

An email notification regarding the correspondence was sent to the following email address(es) associated with your customer number:
Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

To view your correspondence online or update your email addresses, please visit us anytime at **https://ppair-my.uspto.gov/pair/PrivatePair.**
If you have any questions, please email the Electronic Business Center (EBC) at EBC@uspto.gov or call 1-866-217-9197.

Doc Code: A.NE.AFCP
Document Description: After Final Consideration Pilot Program Request

PTO/SB/434 (12-20)

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0

Practitioner Docket No.:	Application No.:	Filing Date:
U0157.70023US03	15/639,223-Conf. #8089	June 30, 2017

First Named Inventor:	Title:
Michael J. Zaworotko	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.

1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (*e.g.*, a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c).

2. The above-identified application contains an outstanding final rejection.

3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect.

4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection.

5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response.

6. This certification and request is being filed electronically using the Office's electronic filing system (EFS-Web).

7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.]

8. By filing this certification and request, applicant acknowledges the following:

- Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0.
- The examiner will verify that the AFCP 2.0 submission is compliant, *i.e.*, that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions:
  - The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, by mailing an advisory action.
  - If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview.
    - The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate.
    - If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116.

Signature	Date	Practitioner Registration No.
/David F. Cauble/	November 12, 2021	73,490
Name (Print/Typed)	**Telephone Number**	
David F. Cauble, PhD, JD	617.646.8000	

***Note**: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.*

☐ * Total of 1 forms are submitted.

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 12, 2021 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 366 of 415

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1699

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 12, 2021 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

RESPONSE AFTER FINAL ACTION UNDER 37 C.F.R. § 1.116

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Final Office Action dated August 11, 2021, please enter the following in the above-identified U.S. patent application. Thursday, November 11, 2021 was a Federal Holiday. As such, this Response is timely filed on Friday, November 12, 2021.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 367 of 415

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior listings, and versions, of claims currently in the application.

1 – 36. (Canceled)

37. (Currently amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons, each supramolecular synthon formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and at least one co-crystal former and each supramolecular synthon comprising a heterosynthon formed via non-covalent hydrogen bonding,

wherein the API has a first chemical functionality that permits formation of API homosynthons through non-covalent hydrogen bonding when the API is in its pure form, and wherein the first chemical functionality is selected from carboxylic acid, amide, N-heterocycle, and alcohol;

wherein the co-crystal former has a second chemical functionality complimentary to the first chemical functionality via non-covalent hydrogen bonding,

wherein supramolecular synthons comprise non-covalent hydrogen bonding between the first chemical functionality of the API and the second chemical functionality of the co-crystal former, and

wherein the supramolecular synthons comprise an acid, an amide, an amine, or an alcohol.

38. (Previously presented) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is selected from the group consisting of a different active pharmaceutical ingredient, a food additive, a low toxicity organic, and a metal-organic complex.

39. (Previously presented) The pharmaceutical composition of claim 37, wherein the at least one co-crystal former is a solid at room temperature and atmospheric pressure when the co-former is in its pure form.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 368 of 415

40. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of at least one active pharmaceutical ingredient (API) and one co-crystal former.

41. (Previously presented) The pharmaceutical composition of claim 37, wherein each supramolecular synthon is formed from stoichiometric amounts of one active pharmaceutical ingredient (API) and one co-crystal former.

42. (Cancelled)

43. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an acid.

44. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amine.

45. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an amide.

46. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise an alcohol.

47. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon.

48. (Cancelled)

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 369 of 415

49. (Previously presented) The pharmaceutical composition of claim 37, wherein the supramolecular synthons comprise a homosynthon and a heterosynthon.

50. (Currently amended) The pharmaceutical composition of claim ~~48~~ 1, wherein the heterosynthon comprises an alcohol/amine interaction.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 370 of 415

REMARKS

Claims 37-50 were previously pending in this application. By way of amendment, claims 37 and 50 have been amended, and claims 42 and 48 have been cancelled. Claim 37 has been amended to recite the elements of claims 39 and 48, and to specify that the first chemical functionality is selected from carboxylic acid, amide, N-heterocycle, and alcohol. Support for this amendment can be found in paragraph [0048] of the Application as originally filed. Claim 37 has been further amended to specify that the supramolecular synthons comprise an acid, an amide, an amine, or an alcohol. Support for this amendment can be found, for example, in original claim 13. No new matter is added.

Claim Rejections – 35 USC § 112

Claims 37-50 are rejected under 35 U.S.C. 112 (pre-AIA), first paragraph on the ground that the claims allegedly lack written description. Applicant disagrees. However, solely to expedite prosecution, claim 37 has been amended to specify that each supramolecular synthon comprises a heterosynthon formed via non-covalent hydrogen bonding, and that the first chemical functionality is selected from carboxylic acid, amide, N-heterocycle, and alcohol.

Page 7 of the Office Action, the Office maintains that Applicant has not shown possession of the complete scope of non-covalent interactions through hydrogen bonding. The Office concedes that examples 1-19 show the relationship of different groups for H-bonding, but argues that "claim 37 encompasses more than the groups…of examples 1-19," noting that "the types of H-bonding described in the examples are not incorporated in the instant rejected claims." Solely to expedite prosecution, claim 37 has been amended to specify that the first chemical functionality is selected from the functional groups exemplified in examples 1-19.

For example, the API of Example 1 (acetaminophen), comprises both an alcohol and an amide. The API of Example 2 (phenytoin) comprises an N-heterocycle. The API of Example 3 (acetylsalicylic acid) comprises a carboxylic acid. The API of Example 4 (ibuprofen) comprises a carboxylic acid. The API of Examples 5 and 6 (flurbiprofen) comprises a carboxylic acid. The API of Examples 7-19 (carbamazepine) comprises an H-heterocycle in combination with 13 different co-

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 371 of 415

formers. These examples correspond to Figures 3, 5B, 6C, 7C-D, 8C-D, 9A-B, 10B, 11, 12, and 14A-B through 23A-B.

As amended, claim 37 recites the chemical functional groups of the API that form hydrogen bonds with the co-former. The recited groups are exemplified in the Examples and Figures discussed above. Amended claim 37 also recites specific functional groups that are present in the supramolecular synthons. These functional groups are also exemplified in the Examples and Figures discussed above. As such, claim 37 is adequately supported by the description of the Application as filed, and Applicant requests withdrawal of this rejection.

Claims 37-50 are rejected under 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 Applicant regards as the invention. Applicant notes that the Office has not elaborated on the grounds for this rejection in the present office action. In contrast, in the non-final rejection dated February 5, 2021, the Office made the same rejection, explaining that it considered the term "GRAS compound" to be unclear. In its response of May 27, 2021, Applicant deleted the term "GRAS compound." As such, Applicant believes that the rejection under 35 U.S.C. 112 (pre-AIA) is overcome.

Claims 37-50 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being incomplete for omitting essential elements, such as omission amounting to a gap between the elements. Specifically, the Office alleges that the claims omit "the required structural components of an API and co-crystal former and the functional groups that are used for non-covalent hydrogen bonding. Applicant respectfully disagrees. However, solely to expedite prosecution, claim 37 has been amended to specify that the supramolecular synthon comprises a heterosynthon, that the first chemical functionality of the API is selected from carboxylic acid, amide, N-heterocycle, and alcohol, and that the supramolecular synthons comprise an acid, an amide, an amine, or an alcohol.

Claims 37-50 do not omit essential elements and Applicant requests withdrawal of this rejection.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 372 of 415

Double Patenting

Claims 37-50 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37 and 45 of U.S. Patent No. 10,633,344. The Office states that claim 37 of '344 overlaps with instant claims 37 and 39, and that claim 45 of '344 is embraced by instant claims 37 and 40.

As a preliminary matter, Applicant notes that U.S. Patent No. 10,633,344 only has 21 claims, and as such does not have a claim 37 or 45. For the purpose of this Response, however, Applicant assumes that "claim 37 of '344" corresponds to claim 1 as issued in U.S. Patent No. 10,633,344 and that "claim 45 of '344" corresponds to claim 15 as issued in U.S. Patent No. 10,633,344. As described above, instant claim 37 has been amended to specify that the supramolecular synthon comprises a heterosynthon, that the first chemical functionality of the API is selected from carboxylic acid, amide, N-heterocycle, and alcohol, and that the supramolecular synthons comprise an acid, an amide, an amine, or an alcohol. The claims of 10,633,344, alone or in combination, do not recite all of the elements of amended claim 37. As such, amended claim 37 is not anticipated by any claim of 10,633,344, and the Office has not provided a rationale for the obviousness of amended claim 37 over any claim of 10,633,344. As such, Applicant requests withdrawal of this rejection.

Claims 37, 38, and 42 are previously rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37, 38, and 42 of copending Application No. 16/270,981. Claim 37 has been amended to recite the elements of claim 48. Claim 48 is not rejected. Accordingly, Applicant requests withdrawal of this rejection.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 373 of 415

CONCLUSION

In view of the foregoing, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this response, the application is not in condition for allowance, the Examiner is requested to call the undersigned at the telephone number indicated below to discuss any outstanding issues.

Applicant believes no fee is due with this Amendment. However, if a fee is due with this Amendment, please charge our Deposit Account No. 23/2825, under Docket No. U0157.70023US03 from which the undersigned is authorized to draw.

Dated: November 12, 2021

Respectfully submitted,

By /David F. Cauble/
David F. Cauble, PhD, JD
Registration No.: 73,490
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
617.646.8000

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 374 of 415

Electronic Acknowledgement Receipt

EFS ID:	44270801
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Cathy Nicholson
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	12-NOV-2021
Filing Date:	30-JUN-2017
Time Stamp:	15:01:07
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	U015770023US03-TRN-DFC.pdf	26561 4a406530e3e6b3a76de7475aea6550dc2bd e0f82	no	1

Warnings:

Information:					
2	After Final Consideration Program Request	U015770023US03-RAFPP-DFC.pdf	31175 b3bf5a3a61a051d5c5a71e13c9289308ce39ca00	no	1
Warnings:					
Information:					
3		U015770023US03-116AMN-DFC.pdf	48515 d6c909e281a92cd59dac0a5df4bc6eb0535b7150	yes	8

Multipart Description/PDF files in .zip description

Document Description	Start	End
Response After Final Action	1	1
Claims	2	4
Applicant Arguments/Remarks Made in an Amendment	5	8

Warnings:	
Information:	
Total Files Size (in bytes):	106251

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Art Unit	1699
Examiner Name	N. E. Jarrell
Total Number of Pages in This Submission	
Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

- [ ] Fee Transmittal Form
  - [ ] Fee Attached
- [x] Amendment/Reply
  - [x] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) (please Identify below):

Certification and Request for Consideration Under The After Final Consideration Pilot Program

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	November 12, 2021	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 12, 2021 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

9780513.1

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 11/30/2021

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
11/30/2021	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 378 of 415

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.	
	Examiner NOBLE E JARRELL	**Art Unit** 1699	**AIA (FITF) Status** No

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

THE REPLY FILED 12 November 2021 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

NO NOTICE OF APPEAL FILED

1. ☑ The reply was filed after a final rejection. No Notice of Appeal has been filed. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114 if this is a utility or plant application. Note that RCEs are not permitted in design applications. The reply must be filed within one of the following time periods:
   a) ☑ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action; or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection.The current period for reply expires ____ months from the mailing date of *the prior Advisory Action* or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.
   Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANTS FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) or (c) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37CFR 41.37(a).

AMENDMENTS

3. ☑ The proposed amendments filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   a) ☑ They raise new issues that would require further consideration and/or search (see NOTE below);
   b) ☐ They raise the issue of new matter (see NOTE below);
   c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: See Continuation Sheet (See 37CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicants reply has overcome the following rejection(s): _____
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☑ For purposes of appeal, the proposed amendment(s):(a) ☑ will not be entered, or (b) ☐ will be entered, and an explanation of how the new or amended claims would be rejected is provided below or appended.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____
9. ☐ The affidavit or other evidence filed after final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
10. ☐ The affidavit or other evidence filed after the date of filing the Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
11. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

12. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
13. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
14. ☐ Other: _____.

STATUS OF CLAIMS

15. The status of the claim(s) is (or will be) as follows:
    Claim(s) allowed:_____.
    Claim(s) objected to:_____.
    Claim(s) rejected:37-50.
    Claim(s) withdrawn from consideration:_____.

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1699	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 379 of 415

Continuation of 3. NOTE: A new search is required based on the amendments to parent claim 37. The claim set of the final rejection did not require the limitations added on 12 November 2021. After looking at the double patenting rejection, it would be maintained because an alcohol can be present in the supramolecular synthon. Additionally, the written description would be maintained because the prepared complexes do not completely support the amended claims. Example 2 provided support for pyridine in the active pharmaceutical ingredient.

Docket No.: U0157.70023US03
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Named Inventor:	Michael J. Zaworotko
Application No.:	15/639,223
Confirmation No.:	8089
Filed:	June 30, 2017
For:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
Examiner:	N. E. Jarrell
Art Unit:	1699

Certificate of Electronic Filing under 37 C.F.R. § 1.8
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: November 12, 2021 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

RESPONSE AFTER FINAL ACTION UNDER 37 C.F.R. § 1.116

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INTRODUCTORY COMMENTS

In response to the Final Office Action dated August 11, 2021, please enter the following in the above-identified U.S. patent application. Thursday, November 11, 2021 was a Federal Holiday. As such, this Response is timely filed on Friday, November 12, 2021.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks begin on page 5 of this paper.

DO NOT ENTER: /N.J/

11/24/2021

9752659.1

Request for Continued Examination (RCE) Transmittal		
Address to: Mail Stop RCE Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Application Number	15/639,223-Conf. #8089
	Filing Date	June 30, 2017
	First Named Inventor	Michael J. Zaworotko
	Art Unit	1699
	Examiner Name	N. E. Jarrell
	Attorney Docket Number	U0157.70023US03

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.

Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, to any international application that does not comply with the requirements of 35 U.S.C 371, or to any design application. See Instruction Sheet for RCEs (not to be submitted to the USPTO on page 2.)

1. Submission required under 37 CFR 1.114 Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).
   - a. [X] Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.
     - i. [ ] Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
     - ii. [ ] Other _____
   - b. [ ] Enclosed
     - i. [ ] Amendment/Reply
     - ii. [ ] Affidavit(s)/ Declaration(s)
     - iii. [ ] Information Disclosure Statement (IDS)
     - iv. [ ] Other _____
2. Miscellaneous
   - a. [ ] Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)
   - b. [ ] Other _____
3. Fees The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.
   - a. [ ] The Director is hereby authorized to charge the following fees, any underpayment of fees, or credit any overpayments, to Deposit Account No. 23/2825 .
     - i. [X] RCE fee required under 37 CFR 1.17(e)
     - ii. [X] Extension of time fee (37 CFR 1.136 and 1.17)
     - iii. [ ] Other _____
   - b. [ ] Check in the amount of $ _____ enclosed
   - c. [X] Payment by credit card (~~Form PTO-2038 enclosed~~)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED			
Signature	/David F. Cauble/	Date	January 7, 2022
Name (Print/Type)	David F. Cauble, PhD, JD	Registration No.	73,490

CERTIFICATE OF MAILING OR TRANSMISSION			
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450 or facsimile transmitted to the U.S. Patent and Trademark Office on the date shown below.			
Signature			
Name (Print/Type)		Date	

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: January 7, 2022 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

9937520.1

Electronic Patent Application Fee Transmittal

Application Number:	15639223
Filing Date:	30-Jun-2017
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Filer:	David F. Cauble/Cathy Nicholson
Attorney Docket Number:	U0157.70023US03

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 2 months with $0 paid	2252	1	320	320
Miscellaneous:				
RCE- 1ST REQUEST	2801	1	680	680
		Total in USD ($)		**1000**

Electronic Acknowledgement Receipt

EFS ID:	44693648
Application Number:	15639223
International Application Number:	
Confirmation Number:	8089
Title of Invention:	MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT
First Named Inventor/Applicant Name:	Michael J. Zaworotko
Customer Number:	23628
Filer:	David F. Cauble/Cathy Nicholson
Filer Authorized By:	David F. Cauble
Attorney Docket Number:	U0157.70023US03
Receipt Date:	07-JAN-2022
Filing Date:	30-JUN-2017
Time Stamp:	13:12:02
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$1000
RAM confirmation Number	E202217D12232766
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	U015770023US03-TRN-DFC.pdf	26293 9a79f6d4859566bc69324337f6218c6ee029ec6d	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	U015770023US03-FEE-DFC.pdf	37607 fefdf2c9e819eda0270a371f84a3d1e535dff21f	no	1
Warnings:					
Information:					
3	Extension of Time	U015770023US03-EXT-DFC.pdf	25185 b924777a38b57bf8487bed1be9d7d9c15ba42846	no	1
Warnings:					
Information:					
4	Request for Continued Examination (RCE)	U015770023US03-RCE-DFC.pdf	29129 1a37847620ec52b0e7c839d80158d3e84ad3f56c	no	1
Warnings:					
This is not a USPTO supplied RCE SB30 form.					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	40680 9de7781000f8af7e44b4a2fdd012f79d5e496739	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	158894		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc Code: TRAN.LET
Document Description: Transmittal Letter

USED IN LIEU OF PTO/SB/21 (07-09)

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission	

Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Art Unit	1699
Examiner Name	N. E. Jarrell
Attorney Docket Number	U0157.70023US03

ENCLOSURES (*Check all that apply*)

- [x] Fee Transmittal Form
- [ ] Fee Attached
- [ ] Amendment/Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [x] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
- [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) (please Identify below):

Request for Continued Examination (RCE)

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	WOLF, GREENFIELD & SACKS, P.C.		
Signature	/David F. Cauble/		
Printed name	David F. Cauble, PhD, JD		
Date	January 7, 2022	Reg. No.	73,490

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: January 7, 2022 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

9937517.1

FEE TRANSMITTAL

Complete if known	
Application Number	15/639,223-Conf. #8089
Filing Date	June 30, 2017
First Named Inventor	Michael J. Zaworotko
Examiner Name	N. E. Jarrell
Art Unit	1699
Practitioner Docket No.	U0157.70023US03

[X] Applicant asserts small entity status. See 37 CFR 1.27.

[ ] Applicant certifies micro entity status. See 37 CFR 1.29. Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

TOTAL AMOUNT OF PAYMENT ($)1,000.00

METHOD OF PAYMENT (check all that apply)

[ ] Check [X] Credit Card [ ] Money Order [ ] None [ ] Other (please identify): _____

[X] Deposit Account Deposit Account Number: 23/2825 Deposit Account Name: Wolf, Greenfield & Sacks, P.C.

For the above-identified deposit account, the Director is hereby authorized to (check all that apply):

[ ] Charge fee(s) indicated below

[ ] Charge fee(s) indicated below, **except for the filing fee**

[X] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17, **except for any excess claims fees or multiple dependent claim fee**

[ ] Charge any additional fee(s) or underpayment of fee(s) under 37 CFR 1.16 and 1.17

[X] Credit any overpayment of fee(s)

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES (U = undiscounted fee; S = small entity fee; M = micro entity fee)

	FILING FEES			SEARCH FEES			EXAMINATION FEES			
Application Type	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**U ($)**	**S ($)**	**M ($)**	**Fees Paid ($)**
Utility	320	160*	80	700	350	175	800	400	200	
Design	220	110	55	160	80	40	640	320	160	
Plant	220	110	55	440	220	110	660	330	165	
Reissue	320	160	80	700	350	175	2,320	1,160	580	
Provisional	300	150	75	0	0	0	0	0	0	

* The $160 small entity status filing fee for a utility application is further reduced to $80 for a small entity status applicant who files the application via EFS-Web.

2. EXCESS CLAIM FEES

Fee Description	**Undiscounted Fee ($)**	**Small Entity Fee ($)**	**Micro Entity Fee ($)**
Each claim over 20 (including Reissues)	100	50	25
Each independent claim over 3 (including Reissues)	480	240	120
Multiple dependent claims	860	430	215

Total Claims	**Extra Claims**	**Fee ($)**	**Fee Paid ($)**
_____ - 20 or HP =	_____ x	_____ =	_____

HP = highest number of total claims paid for, if greater than 20.

Indep. Claims	**Extra Claims**	**Fee ($)**	**Fee Paid ($)**
_____ - 4 or HP =	_____ x	_____ =	_____

HP = highest number of independent claims paid for, if greater than 3.

Multiple Dependent Claims	**Fee ($)**	**Fee Paid ($)**
	_____	_____

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper (excluding electronically filed sequence or computer listings under 37 CFR 1.52(e)), the application size fee due is $420 ($210 for small entity) ($105 for micro entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	**Extra Sheets**	**Number of each additional 50 or fraction thereof**	**Fee ($)**	**Fee Paid ($)**
_____ - 100 =	_____ /50 =	_____ (round **up** to a whole number) x	_____ =	_____

4. OTHER FEE(S)

	Fees Paid ($)
Non-English specification, $130 fee (no small or micro entity discount)	
Non-electronic filing fee under 37 CFR 1.16(t) for a utility application, $400 fee ($200 small or micro entity)	
Other (e.g., late filing surcharge): 2252 Extension for response within second month	320.00
2801 Request for continued examination (RCE) - 1st ...	680.00

SUBMITTED BY

Signature	/David F. Cauble/	Registration No. (Attorney/Agent)	73,490	Telephone	617.646.8000
Name (Print/Type)	David F. Cauble, PhD, JD			Date	January 7, 2022

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: January 7, 2022 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

9937515.1

PTO/AIA/22 (10-20)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)	Docket Number (Optional) U0157.70023US03
Application Number 15/639,223-Conf. #8089	Filed June 30, 2017
For MULTIPLE-COMPONENT SOLID PHASES CONTAINING AT LEAST ONE ACTIVE PHARMACEUTICAL INGREDIENT	
Art Unit 1699	Examiner N. E. Jarrell

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
☐ One month (37 CFR 1.17(a)(1))	$220	$110	$55	$
☒ Two months (37 CFR 1.17(a)(2))	$640	$320	$160	$ 320.00
☐ Three months (37 CFR 1.17(a)(3))	$1,480	$740	$370	$
☐ Four months (37 CFR 1.17(a)(4))	$2,320	$1,160	$580	$
☐ Five months (37 CFR 1.17(a)(5))	$3,160	$1,580	$790	$

☒ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

☐ A check in the amount of the fee is enclosed.

☒ Payment by credit card. ~~Form PTO-2038 is attached~~.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 23/2825 .

☒ Payment made via EFS-Web.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

I am the

☐ applicant.

☐ attorney or agent of record. Registration number _____ .

☒ attorney or agent acting under 37 CFR 1.34. Registration number 73,490 .

/David F. Cauble/	January 7, 2022
Signature	Date
David F. Cauble, PhD, JD	617.646.8000
Typed or printed name	Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

☐ * Total of 1 forms are submitted.

Certificate of Electronic Filing under 37 C.F.R. § 1.8

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office's electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4).

Dated: January 7, 2022 Signature: /Cathy Nicholson/ (Cathy T. Nicholson)

9937521.1

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 03/22/2022

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
03/22/2022	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Office Action Summary	Application No. 15/639,223	Applicant(s) Zaworotko et al.	
	Examiner NOBLE E JARRELL	Art Unit 1699	AIA (FITF) Status No

-- 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 07 January 2022.

☐ 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) 37-41,43-47 and 49-50 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 37-41,43-47 and 49-50 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 _____.

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

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7 January 2022 has been entered. Newly amended claims 37-41, 43-47, 49, and 50 are pending and are examined.

Claim Objections

Claims 40 and 41 are duplicate objected to because of the following informalities: each claim has the same language. Consequently, the claims are duplicative. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him.

Claim(s) 37-41, 43-47, 49, and 50 is/are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph due to lack of written description.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a co-crystal comprising supramolecular synthons. Each synthon is formed from a stoichiometric amount of at least one active pharmaceutical ingredient (API) and at least one co-crystal former. The synthons are associated together through non-covalent hydrogen bonding. The universe of pharmaceutical compositions comprising an API and co-crystal former includes any co-crystal comprising an API and co-crystal bound together by noncovalent H-bonding.

(1) Level of skill and knowledge in the art:

HSU (*Acta Crystallographica*, **1974**, *B30*, 843-846, cited in IDS) describes a 1:1 cocrystal of salicylamide and 5-ethylisoamylbarbituric acid (title and abstract). Hydrogen bonding is used to bind the compounds together (abstract; page 845, column 2 to page 846, column 1, paragraph 1).

MIROSHNYK (*Expert Opinion in Drug Delivery*, **2009**, *6(4)*, 333-341, cited previously) describes how cocrystals are bound together and examples of the same (table 1, page 336; table 2, page 339).

(2) Partial structure:

A partial structure encompasses a pharmaceutical composition comprising a cocrystal of an API and a co-crystal former bound together by non-covalent H-bonding. The API has a functional group selected from a carboxylic acid, carboxylic amide, an N-heterocycle, and an alcohol.

(3) Physical and/or chemical properties and (4) Functional characteristics:

Examples 1-19 (page 16, paragraph [0056]) to page 33, paragraph [00177]) describe different properties of the compositions selected from crystal data, IR spectroscopy, DSC, TGA, and XRPD. The examples provide a wide range of solid phases having properties such as melting point, solubility, dissolution rate, chemical stability, thermodynamic stability, and/or bioavailability.

(5) Method of making the claimed invention:

Example 1 shows a representative method of making a pharmaceutical composition where 50 mg of acetaminophen and 52 mg of 4,4'-bipyridine were dissolved in hot water and allowed to stand. Slow evaporation lead to colorless needles of 1:1:1 acetaminophen: 4,4'-bipyridine: water co-crystal (figure 4B).

The MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 37-41, 43-47, 49, and 50 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any a pharmaceutical composition comprising an API and a co-crystal former that are associated through non-covalent hydrogen binding. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of examples 1-18 and

compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments

Applicants argue that the claims fulfill the requirements of written description. The table below shows the components, the ratio of components to one another, and the type of interaction between the components.

Example #	Active Pharmaceutical ingredient (API)	Co-crystal former #1 (CCF1)	Co-crystal former #2 (CCF2)	Stoichiometry of components (API: CCF1: CCF2)	Hydrogen bond type(s)
1	acetaminophen	4,4'-bipyridine	water	1:1:1	H (amide)---N (pyridine N or imine) and H (hydroxy)---O (water)
2	Phenytoin	Pyridine		1:1	N (pyridine N or imine) ---H (amide)
3	Aspirin	4,4'-bipyridine		2:1	N pyridine N or imine)---H (carboxylic acid)
4	Ibuprofen	4,4'-bipyridine		2:1	N pyridine N or imine)---H

				(carboxylic acid)
5	Flurbiprofen	4,4'-bipyridine	2:1	N pyridine N or imine)---H (carboxylic acid)
6	Flurbiprofen	Trans-1,2-bis-(4-pyridyl)ethylene	2:1	N pyridine N or imine)---H (carboxylic acid)
7	Carbazepine	*p*-phthaldehyde	1:1	O (amide)---H (aldehyde) and O (aldehyde)---H (amide)
8	Carbazepine	Nicotinamide	1:1	N (amide)---H (amide) and O (amide)---H (amide)
9	Carbazepine	Saccharin	1:1	O (amide)---H (amide) and O (sulfonyl)---H (amide)
10	Carbazepine	2,6-pyridinecarboxylic acid	2:3	O (amide)---H (carboxylic acid)

11	Carbazepine	5-nitroisophthalic acid	1:1	O (amide)---H (carboxylic acid)
12	Carbazepine	Acetic acid	1:1	O (amide)---H (carboxylic acid)
13	Carbazepine	1,3,5,7-adamantanecarboxylic acid	1:1	O (amide)---H (carboxylic acid)
14	Carbazepine	Benzoquinone	1:1	H (amide)---O (ketone)
15	Carbazepine	Butyric acid	1:1	O (amide)---H (carboxylic acid) and O (carboxylic acid)---H (amide)
16	Carbazepine	DMSO	1:1	H (amide)---O (sulfone)
17	Carbazepine	Formamide	1:1	O (amide)---H (amide) and O (amide)---H (amide)
18	Carbazepine	Formic acid	1:1	O (amide)---H (carboxylic acid) and O (carboxylic acid)---H (amide)

19	Carbazepine	Trimesic acid	1:1	O (amide)---H (carboxylic acid) and O (carboxylic acid)---H (amide)

Response to Arguments

The rejection is maintained because the instant claims do not show possession of the complete scope of non-covalent interactions through hydrogen bonding. Applicants argue that examples 1-19 of the specification show a structure function relationship of groups that can participate in H-bonding. Although these examples show the relationship of different groups for H-bonding (as seen in the table above), they do not limit the scope of the claims. The broad reasonable interpretation (BRI) of claim 37 encompasses more than the functional groups participating in H-bonding in examples 1-19. The whole structure of each component of the co-crystal has to be taken into consideration. The functional groups only represent a one part of the API and one or more co-crystal former(s).

> 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.

Claims 37-41, 43-47, 49, and 50 are 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 applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention. Claim 50 is unclear because it depends on claim 1, which has been cancelled.

Claims 37-41, 43-47, 49, and 50 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the required structural components of an API and a co-crystal former. None of claims 37-41, 43-47, 49, and 50 fully define the required structural elements of the API or the cocrystal former. In the examined claims, the API and cocrystal former are defined by the present functional groups that participate in hydrogen bonding and ratio between the API and co-crystal former.

The term "low toxicity organic" in claim 38 is a relative term which renders the claim indefinite. The term "low toxicity organic" is not defined by the claim, the specification does not provide a standard for ascertaining the

requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Without guidance, the metes and bounds of the toxicity type and what is considered low renders the claim unclear. OSHA describes different types of hazards and ways to measure them (OSHA Hazard Communication guidance, **2016**, pages 1-424).

Claim 47 recites the limitation that the supramolecular synthons comprise a homosynthon. There is insufficient antecedent basis for this limitation in the claim because parent claim 37 states that the supramolecular synthon comprises a heterosynthon. For proper antecedent basis, the claim could say "wherein the supramolecular synthons further comprise a homosynthon".

Response to Arguments

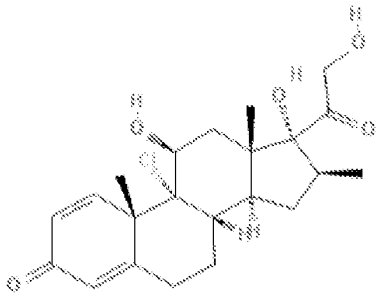
This rejection is maintained because the applicants have not fully defined the complexes formed. Claims 37-41, 43-47, 49, and 50 do not fully characterize or describe the active pharmaceutical ingredient (API) and the co-crystal former. Claim 37 only recites that the API is pharmaceutically active. In what way is the API active? What are the required structural features of the API? The co-crystal former is unclear because it only defined as having a complimentary chemical functionality to the API. Claim 38 recites four different generic co-crystal formers defined by a class with no recited required structural elements. One looking at the claims cannot immediately envisage a supramolecular synthon comprising an API and co-crystal carrier. It is improper to limit the claims with the specification.

Claim Rejections - 35 USC § 102

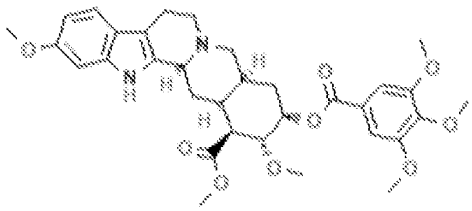
The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

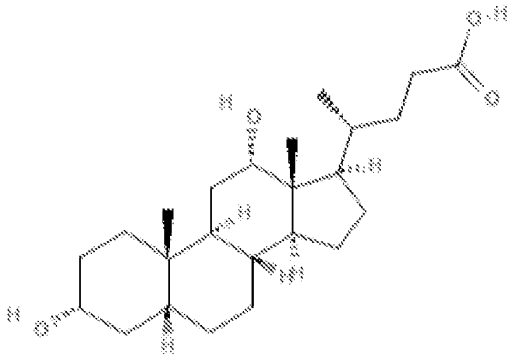
Claim(s) 37, 40, 41, 46, and 49 is/are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by LEI (*Journal of Chinese Pharmaceutical Sciences*, **1999**, *8(3)*, 142-147). Lei describes two solvates of beclomethasone dipropionate (BDP), ethyl acetate (BDP-EtOAc) and trichlorofluoromethane (BDP-P11) (abstract; page 142, column 1, paragraph 5 to page 143, column 2, paragraph 1). These compounds are used in inhalers (page 143, column 2, paragraph 4). The ratio of BDP to EtOAc or P11 is 1:1 in both solvates. Oleic acid Is the carrier in the inhaler. In BDP a hydroxyl H interacts with an ester O or a halogen.



Claim(s) 37, 40, 41, 43, 44, and 50 is/are rejected under pre-AIA 35 U.S.C. 102(b) as being anticipated by MALONE (*Journal of Pharmaceutical Sciences*, **1966**, *55(9)*, 972-974). Malone describes stoichiometric solvates of reserpine with desoxycholic acid (page 973, table 1). These compounds are used in oral compositions (page 972, column 2, paragraph 4; page 973, table II). Reserpine comprises an *N*-heterocycle and desoxycholic acid has an acid and an alcohol.



reserpine



Claim Rejections - 35 USC § 103

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

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

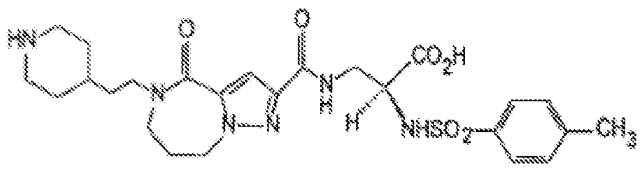
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 37, 40, 41, 43-45, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over BRAY (*Pharmaceutical Development and Technology*, **1999**, *4:1*, 81-87).

Determining the scope and contents of the prior art

Bray describes a pentahydrate of L-738167 (page 82, column 1; page 84, table 2). Since form B is the most stable at 90% relative humidty, it is suitable for development into an oral dosage form (page 87, column 1, paragraphs 2-4). L-738167 has an *N*-heterocycle, an amide, and an acid. One of these groups interacts with a hydroxy OH of water.



1

Structure 1. L-738,167.

Ascertaining the differences between the prior art and the claims at issue

In the claims at issue, a pharmaceutical composition with a supramolecular complex in which one of the synthons has a carboxylic acid, amide, N-heterocycle, and alcohol. In the prior art, Bray implies an oral dosage form can be prepared with a pentahydrate of L-738167.

Resolving the level of ordinary skill in the pertinent art

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position (MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of compounds of the elected group).

Considering objective evidence present in the application indicating obviousness or nonobviousness

A reasonable expectation of success to make an oral dosage form with the pentahydrate of L-738167 because it absorbs the least amount of water at 90% relative humidity (page 86, column 1, paragraph 3).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success

in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S. Ct. 1727, 82 USPQ2d 1385, 1395-97 (2007) identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in *Graham*. The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit.

Exemplary rationales that may support a conclusion of obviousness include:

(A) Combining prior art elements according to known methods to yield predictable results;
(B) Simple substitution of one known element for another to obtain predictable results;
(C) Use of known technique to improve similar devices (methods, or products) in the same way;
(D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
(E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
(F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;
(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

Note that the list of rationales provided is not intended to be an all-inclusive list. Other rationales to support a conclusion of obviousness may be relied upon by Office personnel.

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 conflicting claims 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 re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *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 nonstatutory double patenting provided the reference application or

patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) 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 www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 37, 40, 41, 45, 46, 47, and 49 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 10-13 of U.S. Patent No. 10633344 (hereinafter '344). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of '344. Claim 37 of '344 overlaps with instant claims 37 and 39. Claims 10-13 of '344 are embraced by instant claims 37 and 40. Example 1 is an example of both a homosynthon and heterosynthon because the hydroxyl group acetaminophen can interact with a H of water and the amide H interacts with an N of 4,4-bipyridine (column 11, line 60 to column 12, line 23).

Claims 37, 38 and 46 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 37 and 42 of copending Application No. 16/270981 (reference application). Although the claims at issue are not identical, they are not patentably distinct from each other because the instant claims are embraced by the specified claims of 16/270981. Claims 37, 38, and 42 of '981 overlap with instant claims 37, 38, and 42. Example 1 (page 16, paragraph [0056] to page 17, paragraph [0059]) shows a co-crystal of acetaminophen, bipyridine, and water. Acetaminophen has both amide and hydroxyl groups.

This is a provisional nonstatutory double patenting rejection because the patentably indistinct claims have not in fact been patented.

Response to Amendment

Newly amended claims 37-41, 43-47, 49, and 50 have been examined with respect to double patenting.

Conclusion

Claims 37-41, 43-47, 49, and 50 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE E JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached 9:00 AM to 5:00 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NOBLE E JARRELL/
Primary Examiner, Art Unit 1699

Notice of References Cited	Application/Control No. 15/639,223	Applicant(s)/Patent Under Reexamination Zaworotko et al.	
	Examiner NOBLE E JARRELL	Art Unit 1699	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
	A					
	B					
	C					
	D					
	E					
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	OSHA Hazard Communication guidance, 2016, pages 1-424 (Year: 2016)
	V	LEI. Journal of Chinese Pharmaceutical Sciences, 1999, 8(3), 142-147 (Year: 1999)
	W	MALONE. Journal of Pharmaceutical Sciences, 1966, 55(9), 972-974 (Year: 1966)
	X	BRAY. Pharmaceutical Development and Technology, 1999, 4:1, 81-87 (Year: 1999)

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/639,223	Zaworotko et al.
	Examiner	Art Unit
	NOBLE E JARRELL	1699

CPC - Searched*		
Symbol	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystal cocrystals co near crystals).clm.	02/19/2019	NJ

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
c07d223/26.cpc. and (cocrystal co NEAR crystalcocrystals co near crystals).clm.	02/19/2019	NJ
stn registry and hcaplus	02/19/2019	NJ
inventor search in PALM and EAST	02/19/2019	NJ
stn registry and hcaplus	10/30/2019	NJ
stn registry and hcaplus	03/11/2022	NJ

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
C07D	223/26	02/19/2019	NJ

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1625	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 406 of 415

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	15/639,223	Zaworotko et al.
	Examiner	Art Unit
	NOBLE E JARRELL	1699

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1625	

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 407 of 415

d his full

```
      FILE 'HCAPLUS' ENTERED AT 09:08:05 ON 11 MAR 2022
L1                4 SEA SPE=ON    ABB=ON    PLU=ON    US20170362182/PN
                    SEL RN

      FILE 'REGISTRY' ENTERED AT 09:08:59 ON 11 MAR 2022
L2              121 SEA SPE=ON    ABB=ON    PLU=ON    (110588-57-3/BI OR 111-96-6/BI OR
                    169590-42-5/BI OR 171228-49-2/BI OR 639010-33-6/BI OR 639010-34
                    -7/BI OR 639010-35-8/BI OR 639010-40-5/BI OR 84625-61-6/BI OR
                    848585-75-1/BI OR 848585-76-2/BI OR 848701-00-8/BI OR 872-50-4/
                    BI OR 919287-67-5/BI OR 919287-68-6/BI OR 919287-69-7/BI OR
                    922499-54-5/BI OR 107-06-2/BI OR 107-21-1/BI OR 108-10-1/BI OR
                    108-20-3/BI OR 108-88-3/BI OR 109-99-9/BI OR 110-54-3/BI OR
                    110-71-4/BI OR 110-82-7/BI OR 123-91-1/BI OR 1244029-16-0/BI
                    OR 1244029-24-0/BI OR 127-19-5/BI OR 129530-31-0/BI OR
                    132539-06-1/BI OR 1330-20-7/BI OR 1374345-89-7/BI OR 141-52-6/B
                    I OR 1419516-19-0/BI OR 142-82-5/BI OR 1441915-02-1/BI OR
                    17455-13-9/BI OR 181695-72-7/BI OR 22204-53-1/BI OR 26159-34-2/
                    BI OR 284035-30-9/BI OR 33100-27-5/BI OR 500225-89-8/BI OR
                    57-55-6/BI OR 572916-55-3/BI OR 572916-56-4/BI OR 572916-60-0/B
                    I OR 594-19-4/BI OR 595564-72-0/BI OR 595564-73-1/BI OR
                    595564-74-2/BI OR 595564-75-3/BI OR 595564-76-4/BI OR 595564-77
                    -5/BI OR 595564-78-6/BI OR 595564-79-7/BI OR 595564-80-0/BI OR
                    632338-18-2/BI OR 632338-20-6/BI OR 632338-24-0/BI OR 632338-26
                    -2/BI OR 632338-30-8/BI OR 632338-32-0/BI OR 632338-34-2/BI OR
                    632338-40-0/BI OR 632338-42-2/BI OR 632338-44-4/BI OR 632338-47
                    -7/BI OR 639010-36-9/BI OR 639010-42-7/BI OR 64-17-5/BI OR
                    67-56-1/BI OR 67-63-0/BI OR 68-12-2/BI OR 691397-13-4/BI OR
                    71-23-8/BI OR 71-36-3/BI OR 724433-98-1/BI OR 724433-99-2/BI
                    OR 724434-00-8/BI OR 724706-10-9/BI OR 724706-11-0/BI OR
                    724706-12-1/BI OR 7439-93-2/BI OR 7439-95-4/BI OR 7440-09-7/BI
                    OR 7440-23-5/BI OR 7440-70-2/BI OR 75-65-0/BI OR 756835-47-9/BI
                     OR 756835-49-1/BI OR 756835-51-5/BI OR 756835-56-0/BI OR
                    756835-59-3/BI OR 756835-62-8/BI OR 756835-63-9/BI OR 756835-66
                    -2/BI OR 756835-79-7/BI OR 756835-98-0/BI OR 756836-16-5/BI OR
                    7647-14-5/BI OR 78-92-2/BI OR 78-93-3/BI

      FILE 'HCAPLUS' ENTERED AT 09:09:25 ON 11 MAR 2022
L3                  QUE SPE=ON    ABB=ON    PLU=ON    "CRYSTAL STRUCTURE"+OLD,NT/CT
                    E SOLVATES/CT
                    E E3+ALL
L4                  QUE SPE=ON    ABB=ON    PLU=ON    SOLVATES+NT/CT
                    E E65+ALL
L5            18644 SEA SPE=ON    ABB=ON    PLU=ON    L3 AND L4
                    E DRUG/CT
                    E E3+ALL
                    E E2
                    E CARBOXYLIC ACID/CT
                    E E3+ALL
                    E E2+OLD,NT1
L6                  QUE SPE=ON    ABB=ON    PLU=ON    "CARBOXYLIC ACIDS"+OLD,NT1/CT
                    E CARBOXYLIC AMIDES/CT
                    E AMIDE/CT
                    E E3+ALL
                    E CARBOXYLIC AMIDE/CT
                    E ALCOHOL/CT
                    E E3+ALL
                    E E2+OLD,NT1
```


NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 408 of 415

```
L7                QUE SPE=ON   ABB=ON   PLU=ON   ALCOHOLS+OLD,NT1/CT
                  E HETEROCYCLIC COMPOUNDS/CT
                  E E1+ALL
                  E E2+OLD,NT1
                  E E74+OLD,NT1
L8          32871 SEA SPE=ON   ABB=ON   PLU=ON   HETEROCYCLIC/CW (L) NITROGEN
L9             26 SEA SPE=ON   ABB=ON   PLU=ON   L5 AND L8
L10          1572 SEA SPE=ON   ABB=ON   PLU=ON   L6 AND L5
L11          3255 SEA SPE=ON   ABB=ON   PLU=ON   L7 AND L5
                  E COCRYSTALLIZATION/CT
                  E E3+ALL
L12               QUE SPE=ON   ABB=ON   PLU=ON   AY<=2002 OR PY<=2002 OR PRY<=2002
L13           163 SEA SPE=ON   ABB=ON   PLU=ON   (L10 OR L11) AND L12
L14             3 SEA SPE=ON   ABB=ON   PLU=ON   L9 AND COMPOSIT?
L15             1 SEA SPE=ON   ABB=ON   PLU=ON   L9 AND L12
                  D SCA
L16            22 SEA SPE=ON   ABB=ON   PLU=ON   L13 AND COMPOSIT?
L17             0 SEA SPE=ON   ABB=ON   PLU=ON   L1 AND L5
L18             4 SEA SPE=ON   ABB=ON   PLU=ON   L1 AND L2
L19             4 SEA SPE=ON   ABB=ON   PLU=ON   L18 AND L12
```

FILE HOME

FILE HCAPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 11 Mar 2022 VOL 178 ISS 1
FILE LAST UPDATED: 10 Mar 2022 (20220310/ED)

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 MAR 2022 HIGHEST RN 2761993-64-8
DICTIONARY FILE UPDATES: 10 MAR 2022 HIGHEST RN 2761993-64-8

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy

TSCA Inventory information is current through August 2021.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/training/stn/database-specific

=>

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 410 of 415

d his full

```
     FILE 'HCAPLUS' ENTERED AT 12:29:40 ON 11 MAR 2022
                  E SOLVATES/CT
                  E E3+ALL
L1                QUE SPE=ON   ABB=ON   PLU=ON   SOLVATES+NT/CT
                  E CRYSTALS/CT
                  E E3+ALL
L2                QUE SPE=ON   ABB=ON   PLU=ON   CRYSTALS+NT/CT
                  E E86+ALL
                  E CRYSTALLINITY/CT
                  E E3+ALL
L3                QUE SPE=ON   ABB=ON   PLU=ON   CRYSTALLINITY+OLD/CT
                  E E15+ALL
L4                QUE SPE=ON   ABB=ON   PLU=ON   CRYSTALLIZATION+NT/CT
                  E HYDRATES/CT
                  E E3+ALL
                  E E10+ALL
L5          21637 SEA SPE=ON   ABB=ON   PLU=ON   L1 AND (L2 OR L3 OR L4)
                  E DRUG DELIVERY SYSTEMS/CT
                  E E3+ALL
L6                QUE SPE=ON   ABB=ON   PLU=ON   "DRUG DELIVERY SYSTEMS"+OLD,NT/CT
L7              890 SEA SPE=ON   ABB=ON   PLU=ON   L5 AND L6
L8             1042 SEA SPE=ON   ABB=ON   PLU=ON   L6 (L) (SOLVATE? OR HYDRATE?)
L9              257 SEA SPE=ON   ABB=ON   PLU=ON   L8 AND (L2 OR L3 OR L4)
L10             172 SEA SPE=ON   ABB=ON   PLU=ON   L8 AND L6 (L) ?CRYSTAL?
L11               QUE SPE=ON   ABB=ON   PLU=ON   PRD<=20030303 OR AD<=20030303 OR
                  PD<=20030303
L12              16 SEA SPE=ON   ABB=ON   PLU=ON   L11 AND L9
L13              19 SEA SPE=ON   ABB=ON   PLU=ON   L10 AND L11
L14              27 SEA SPE=ON   ABB=ON   PLU=ON   (L12 OR L13)

     FILE HOME

     FILE HCAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.

     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.    Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
     strictly prohibited.

     FILE COVERS 1907 - 11 Mar 2022 VOL 178 ISS 1
     FILE LAST UPDATED: 10 Mar 2022 (20220310/ED)

     CAS Information Use Policies apply and are available at:

     http://www.cas.org/legal/infopolicy

     This file contains CAS Registry Numbers for easy and accurate
     substance identification.

=>
```


NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 411 of 415

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 05/02/2022

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
05/02/2022	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Applicant-Initiated Interview Summary	**Application No.** 15/639,223	**Applicant(s)** Zaworotko et al.		
	Examiner NOBLE E JARRELL	**Art Unit** 1699	**AIA (First Inventor to File) Status** No	**Page** 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	**Title**	**Type**
NOBLE E JARRELL	Primary Examiner	Telephonic
David Cauble	Attorney of Record	

Date of Interview: 27 April 2022

Issues Discussed:

Other

Mr. Cauble asked for a copy of the reference in the firs t 102 rejection. It was inadvertently not attached. It is attached to this communication.

/NOBLE E JARRELL/ Primary Examiner, Art Unit 1699	

Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04
Please further see:
MPEP 713.04
Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b)
37 CFR § 1.2 Business to be transacted in writing

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/639,223	06/30/2017	Michael J. Zaworotko	U0157.70023US03	8089

23628 7590 12/06/2022

WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1699	

NOTIFICATION DATE	DELIVERY MODE
12/06/2022	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_eOfficeAction@WolfGreenfield.com
WGS_eOfficeAction@WolfGreenfield.com

Notice of Abandonment	Application No.	Applicant(s)
	15/639,223	Zaworotko et al.

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

This application is abandoned in view of:

1. ☑ Applicant's failure to timely file a proper reply to the Office letter mailed on 22 March 2022.
   (a) ☐ A reply was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply (including a total extension of time of _____ month(s)) which expired on _____.
   (b) ☐ A proposed reply was received on _____, but it does not constitute a proper reply under 37 CFR 1.113 to the final rejection. (A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) if this is utility or plant application, a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. Note that RCEs are not permitted in design applications.)
   (c) ☐ A reply was received on _____ but it does not constitute a proper reply, or a *bona fide* attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 8 below).
   (d) ☑ No reply has been received.

2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
   (a) ☐ The issue fee and publication fee, if applicable, was received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
   (b) ☐ The submitted fee of $ _____ is insufficient. A balance of $ _____ is due.
   The issue fee required by 37 CFR 1.18 is $ _____. The publication fee, if required by 37 CFR 1.18(d), is $ _____.
   (c) ☐ The issue fee and publication fee, if applicable, has not been received.

3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
   (a) ☐ Proposed corrected drawings were received on _____ (with a Certificate of Mailing or Transmission dated _____), which is after the expiration of the period for reply.
   (b) ☐ No corrected drawings have been received.

4. ☐ The letter of express abandonment which is signed by the attorney or agent of record or other party authorized under 37 CFR 1.33(b). See 37 CFR 1.138(b).

5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34) upon the filing of a continuing application.

6. ☐ The decision by the Patent Trial and Appeal Board rendered on _____ and because the period for seeking court review of the decision has expired and there are no allowed claims.

7. ☐ The dismissal of the appeal in an application having no allowed claims. (When an appeal is dismissed in an application having no allowed claims the application stands abandoned. See MPEP 1215.04 subsections I-V for an explanation of the reasons why an appeal is dismissed.)

8. ☐ The reason(s) below:

_____

/KIMBERLY D JONES/

Petitions to revive under 37 CFR 1.137, or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.

NOVARTIS EXHIBIT 1022
Novartis v. Regents, IPR2023-01346
Page 415 of 415