2021 Pat. App. LEXIS 5753

Patent Trial and Appeal Board

September 27, 2021, Decided

Appeal 2021-000948 ; Application 13/511,768 ; Technology Center 1600

USPTO Bd of Patent Appeals & Interferences; Patent Trial & Appeal Bd Decs.

Reporter
2021 Pat. App. LEXIS 5753 *

Ex parte HANLAN LIU, CHRIS WILLIS, RENU BHARDWAJ, DIANE P. COPELAND, ABIZER HARIANAWALA, JEFFREY SKELL, JOHN MARSHALL, JIANMEI KOCHLING, GERARD PALACE, JUDITH PETERSCHMITT, CRAIG SIEGEL, and SENG CHENG

Notice:

[*1] ROUTINE OPINION. Pursuant to the Patent Trial and Appeal Board Standard Operating Procedure 2, the opinion below has been designated a routine opinion.

Core Terms

salt, compound, crystalline, eliglustat, teach, hemitartrate, crystallize, tartrate, artisan, skill, prior art, anticipate, chemical, acetate, heptane, synthase, solvent, formula, acid, pharmaceutical, recite, solid, screen, heat, polymorphism, disclosure, homologue, molecule, glucosylceramide, synthesis

Panel: Before JEFFREY N. FREDMAN, TAWEN CHANG, and JOHN E. SCHNEIDER, Administrative Patent Judges.

Opinion By: TAWEN CHANG

Opinion

CHANG, *Administrative Patent Judge*.

DECISION ON APPEAL

Pursuant to *35 U.S.C. § 134(a)*, Appellant [1] appeals from the Examiner's decision to reject claims 1, 7, 13, 14, 16, 50, and 101-103. We have jurisdiction under *35 U.S.C. § 6(b)*.

We REVERSE.

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[1] We use the word "Appellant" to refer to "applicant" as defined in *37 C.F.R. § 1.42*. Appellant identifies the real party in interest as Genzyme Corporation. Appeal Br. 4.

STATEMENT OF THE CASE

The accumulation of glycosphingolipids (GSLs) has been linked to disease such as Tay-Sachs, Gaucher, and Fabry diseases, as well as certain cancers. Spec. 1:15-17. GSLs are derived from glucosylceramide (GlcCer), which in turn is produced from ceramide and UDP-glucose by the enzyme GlcCer synthase. Spec. 1:11-13.

The Specification states that "[c]ompounds which inhibit GlcCer synthase can lower GSL concentrations and have been reported to be useful for treating a subject with one of the aforementioned diseases." Spec. 2:1-3. The compound of Formula (I), reproduced below, is "also known as 'eliglustat'" and is "a GlcCer synthase inhibitor currently in clinical trials for the treatment of Gaucher disease":

Id. at 2:5-8; Ans. 5. According to the Specification, "[t]here is a need for salt forms **[*2]** of this drug candidate that are crystalline and otherwise have physical properties that are amenable to large scale manufacture." Spec. 2:9-11.

The Specification states "[i]t has been found that the hemitartrate salt of the compound of Formula (I) (hereinafter 'Formula (I) Hemitartrate') can be crystallized under well-defined conditions to provide certain nonhygroscopic crystalline forms" and has several advantageous properties, when compared to the free base and other salts of Formula (I), that makes it "amenable to large scale manufacture as a drug candidate." Spec. 2:15-3:2.

CLAIMED SUBJECT MATTER

The claims are directed to a recited hemitartrate salt and pharmaceutical compositions comprising the salt. Claim 1 is illustrative:

> Claim 1: A hemitartrate salt of a compound represented by the following structural formula:
>
> wherein the salt is in a crystalline form, the crystalline form characterized by at least two major X-ray powder diffraction peaks at 2θ angles selected from the group consisting of 5.1°, 6.6°, 10.7°, 11.0°, 15.9°, and 21.7°, wherein the specified 2θ angle means the specified value ±0.2°, and the X-ray powder diffraction diagram is obtained by using **[*3]** Cu Kα radiation.

Appeal Br. 26 (Claims App.).

REJECTIONS

A. Claims 1, 7, 13, 14, 16, 50, and 101-103 are rejected under *35 U.S.C. § 102(b)* as anticipated by McEachern. [2]

B. Claims 1, 7, 13, 14, 16, 50, and 101-103 are rejected under *35 U.S.C. § 103(a)* as obvious over McEachern, Hirth, [3] Brittain, [4] and Morissette. [5]

C. Claims 1, 7, 13, 14, 16, 50, and 101 are rejected under *35 U.S.C. § 102(b)* as anticipated by Cheng. [6]

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[2] Kerry Anne McEachern et al., *A Specific and Potent Inhibitor of Glucosylceramide Synthase for Substrate Inhibition Therapy of Gaucher Disease*, 91 MOLECULAR GENETICS & METABOLISM 259 (2007).

[3] Hirth et al., US 6,855,830 B2, issued Feb. 15, 2005.

[4] Sherry L. Morissette et al., *High-Throughput Crystallization: Polymorphs, Salts, Co-Crystals and Solvates of Pharmaceutical Solids*, 56 ADVANCED DRUG DELIVERY REVIEWS 275 (2004).

[5] 95 DRUGS & PHARMACEUTICAL SCI.: POLYMORPHISM IN PHARMACEUTICAL SOLIDS (Harry G. Brittain ed. 1999).

D. Claims 1, 7, 13, 14, 16, 50, and 101 are rejected under 35 U.S.C. § 103(a) as obvious over Cheng, Brittain, and Morissette.

OPINION

A. Anticipation by McEachern (claims 1, 7, 13, 14, 16, 50, 101-103) 1. Issue

The Examiner finds that McEachern teaches "a single pharmaceutical code-named 'Genz-112638,'" described as "a synthetic small molecule designed to inhibit . . . glucosylceramide synthase" and "a structural homologue of D-threo-ethylendioxyphenyl-2-palmitoylamino-3-pyrrilidino-propanol." Ans. 6. The Examiner finds **[*4]** McEachern teaches that "[t]he chemical structure of Genz-112638 . . . [is] described [in Hirth]." *Id.*

The Examiner points to Figure 4 of Hirth, which depicts D-threo-ethylendioxyphenyl-2-palmitoylamino-3-pyrrilidino-propanol (compound 5) and further depicts three of its homologs (compounds 6-8). Ans. 6-7; Hirth Fig. 4. The Examiner notes that the Specification, among other things, confirms that Compound 6 in Figure 4 of Hirth is Genz-112638. *Id.* at 7. The Examiner finds that, although only one of the compounds in Hirth's Figure 4 is McEachern's Genz-112638, "McEachern through referencing Hirth does teach the chemical structure of Genz-112638 in a manner that one of skill in the art would at once envisage based on the limited class of three alkyl homologues." *Id.*

The Examiner finds that "McEachern also teaches Genz-112638 is 'a tartrate salt' whose preparation was described generally by Hirth." Ans. 8. The Examiner concludes that a skilled artisan would understand "tartrate salt" to mean hemitartrate salt as hemitartrate is defined in the Specification. *Id.* at 3-6 (Anticipation - Claim Interpretation). The Examiner finds that Hirth teaches methods of preparing tartrate salt and Compound 6 that provides "a basis in fact and technical reasoning establishing that the prior art product and the claimed product are substantially identical (*same* chemical formula, salt form, and process for preparing (including the use of heptane and ethyl acetate . . .))," thus shifting the burden to Appellant to show that the products are not the same. *Id.* The Examiner further finds that Appellant has not provided evidence sufficient to satisfy this burden. *Id.* at 9-10.

Appellant contends that McEachern "is not sufficient to provide a skilled artisan with the information needed to determine the exact chemical structure of Genz-112638" and, thus, "does not disclose the hemitartrate salt of the compound recited in the instant claims." Appeal Br. 6. Appellant further argues that "McEachern does not provide any description regarding the physical form of Genz-112638, such as whether Genz-112638 is an amorphous solid, **[*5]** a crystalline solid, or an oil" and that, thus, "a skilled artisan viewing McEachern would have no reason to conclude that Genz-112638 is eliglustat hemitartrate salt, much less the specific crystalline form of eliglustat hemitartrate salt recited in the instant claims." *Id.* at 6-7; *see also id.* at 7 (contending that "the phrase 'formulated as a tartrate salt' does not necessarily indicate that a solid form with a particular stoichiometry was isolated" and that "[a] skilled artisan viewing McEachern would not know whether a salt of the structural homologue [described in the reference] was actually made and isolated, or whether tartaric acid was simply a component present in the formulation used in the animal studies described in the reference").

Appellant contends that Hirth's teachings does not render McEachern anticipatory, because "[m]any of the compounds disclosed in Hirth could be considered by a skilled artisan as structural homologues of D-threo-ethylendioxyphenyl-2-palmitoylamino-3-pyrrilidino-propanol," and "a person of ordinary skill viewing McEachern or Hirth would not have known which of the compounds disclosed in Hirth purportedly corresponds to Genz-112638." Appeal Br. 7. Appellant contends that the Examiner improperly relied on disclosures after the priority date of the application to establish that the prior art and the claimed products are substantially identical. *Id.* at 9-10.

Appellant contends that, "even if a skilled artisan were to look to Compound 6 of Hirth, as alleged by the Examiner, . . . Hirth does not specifically disclose any salt of Compound 6, much less the hemitartrate salt thereof," and "does not specifically disclose a procedure **[*6]** for making eliglustat hemitartrate salt." Appeal Br. 8, 10.

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[6] Cheng et al. WO 2006/053043 A2, published May 18, 2006.

Appellant contends that, furthermore, "the instant claims are directed specifically to the hemitartrate salt of eliglustat having a specific crystalline form, which is not disclosed in Hirth." *Id.* at 7.

Finally, citing to the Siegel Declaration, [7] Appellant contends that McEachern does not inherently disclose the claimed invention, because following the method of preparation described in Hirth "does not necessarily and inevitably produce eliglustat hemitartrate salt, as evidenced by the DSC thermograms and XRPD spectra." *Id.*

The issue with respect to this rejection is whether a preponderance of evidence supports the Examiner's finding that McEachern teaches the claimed crystalline form of eliglustat hemitartrate salt.

2. Findings of Fact

1. McEachern teaches that "Genz-112638 is a synthetic small molecule designed to inhibit the enzymatic activity of glucosylceramide synthase" and that "[i]t is a structural homologue of D-threo-ethylendioxyphenyl-2-palmitoylamino-3-pyrrilidino-propanol formulated as a tartrate salt." McEachern 260, right column.

2. McEachern teaches that "[t]he chemical structure of . . . and the procedure for [the] synthesis [of Genz-112638] **[*7]** are described" in Hirth. *Id.*

3. Hirth teaches that "[c]ompounds which inhibit GlcCer synthase . . . have been reported to be useful for treating [certain] disease." Hirth 1:45-47.

4. Hirth teaches that a number of "amino ceramide-like compounds" are known to be "potent inhibitors" of GlcCer synthase, but that known methods for preparing these compounds "are poorly suited for manufacturing on an industrial scale." *Id.* at 1:48-50, 1:56-58.

5. In particular, Hirth teaches that, because of the two chiral centers present in amino ceramide-like compounds, most known methods of syntheses of the compounds "generate four diastereoisomers, resulting in the need to separate diastereomers by chromatography and to isolate the desired enantiomer by crystallization after derivitization with optically active reagents," while a prior art method of enantioselective synthesis of the compounds using diastereoselective reductions "require over ten steps" and expensive reagents. *Id.* at 1:58-2:6.

6. Hirth discloses "a novel enantiomeric synthesis" of ceramidelike inhibitors of GlcCer synthase as well as "novel intermediates formed during the synthesis." *Id.* at Abstract; *see also id.* at 2:11-14.

7. The Examiner **[*8]** asserts, and Appellant has not disputed, that D-threo-ethylendioxyphenyl-2-palmitoylamino-3-pyrrilidino-propanol is Hirth's compound 5, the chemical structure of which is depicted in Hirth's Figure 4.

8. Hirth's Figure 4 is reproduced below:

Id. at Fig. 4. Figure 4 "shows the structures of [amino ceramide-like] Compounds (5)-(8)." *Id.* at 5:36.

9. The Examiner asserts, and Appellant has not disputed, that Genz-112638 is a code name that refers to Compound 6. Ans. 7.

10. Example 4 of Hirth describes the preparation of Compounds 6-8. Hirth 23:61-64.

11. Hirth teaches that "[c]ompounds of [its] invention which possess a sufficiently acidic, a sufficiently basic, or both functional groups, and accordingly can react with any of a number of inorganic bases, and inorganic and organic acids, to form a salt." *Id.* at 11:62-65.

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[7] Declaration of Craig Siegel under *37 C.F.R. § 1.132* (Feb. 24, 2017).

12. Hirth teaches that "[e]xamples of such salts include . . . tartrate . . . and the like." *Id.* at 12:8-22.

13. Brittain teaches that

> organic molecules can be obtained in more than one distinct crystal from, a property . . . known as polymorphism. . . . [A]n extremely large number of molecules were capable of exhibiting the phenomenon. In addition, **[*9]** numerous compounds were shown to form other nonequivalent crystalline structures through the inclusion of solvent molecules in the lattice.

Brittain iii.

14. Brittain teaches that "[t]he amorphous condition can be considered one polymorphic state available to all compounds." *Id.* at v.

3. Analysis

We find the Examiner has not established a prima facie case that McEachern anticipates the claims on appeal, because the Examiner has not established a prima facie case that McEachern expressly or inherently discloses the specific crystalline form of eliglustat tartrate claimed.

We do not disagree with the Examiner that McEachern discloses Genz-112638 as a structural homologue of D-threo-ethylendioxyphenyl-2-palmitoylamino-3-pyrrilidino-propanol formulated as a tartrate salt, and further refers to Hirth for the compound's chemical structure and method of synthesis. FF1, FF2. Likewise, we do not disagree that Hirth discloses D-threo-ethylendioxyphenyl-2-palmitoylamino-3-pyrrilidino-propanol and three of its homologues in Figure 4, including Compound 6, which has the chemical structure recited in claim 1. FF7, FF8. Finally, we acknowledge that Hirth describes a method of synthesizing free **[*10]** base Compound 6 and also generally teaches that a tartrate salt of a compound may be formed by reacting the compound with an organic acid (i.e., tartaric acid). FF10-FF12. Nevertheless, McEachern and Hirth do not expressly disclose a crystalline form of the tartrate salt of Genz-112638 or Compound 6.

Neither has the Examiner established a prima facie case that McEachern in light of Hirth inherently discloses the claimed crystalline form. The Examiner asserts that, because Hirth describes preparing Compound 6 by dissolving or suspending the solids in "5% ethyl acetate in heptane . . . heated to reflux and allowed to cool to room temperature over 4 hours," and also teaches that compounds of its invention can react with organic acids such as tartrate to form a salt, a skilled artisan "would synthesize Compound 6 as described by Hirth including reacting with the organic acid tartrate to form a salt, and then isolating the product by heating in '5% ethyl acetate in heptane . . . heated to reflux and allowed to cool to room temperature over 4 hours.'" Ans. 8 (quoting Hirth 11:62-65, 12:5-20, 24:61-66, 25:60-26:25). The Examiner asserts that, thus, there is a "basis in fact and technical **[*11]** reasoning establishing that the prior art product and the claimed product are substantially identical (*same* chemical formula, salt form, and process for preparing (including the use of heptane and ethyl acetate - see instant specification, p. 28-31, Tables 1 and 6))," which shifts the burden to Appellant to show that "the prior art products do not necessarily possess the characteristics of the claimed product." *Id.*

We are not persuaded. Brittain, cited by the Examiner in the obviousness rejection discussed below, teaches that "organic molecules can be obtained in more than one distinct crystal form, a property . . . known as polymorphism," and further teaches that "an extremely large number of molecules were capable of exhibiting the phenomenon." FF13. Likewise, Brittain teaches that "[t]he amorphous condition can be considered one polymorphic state available to all compounds." FF14. Thus, we do not agree that disclosure of the chemical formula and salt form of a compound necessarily (i.e., inherently) discloses a particular crystalline form.

The Examiner asserts that "all evidence of record shows that when the tartrate salt is formed, it possesses the inherent characteristic Appellant is **[*12]** claiming." Ans. 10. In particular, the Examiner asserts that,

> [g]iven that all of the demonstrations of preparing the crystalline form in the instant specification, including screening across a number of different solvents such as in Table 1 (page 28), show that all attempts result in the claimed product with a DSC of ~166 C, this supports the conclusion that the prior art product also would be in the same form.

Id.

We are not persuaded. Although it is the case that all of the eliglustat hemitartrate crystals obtained in the Specification for polymorphism screening had melting points between 162 and 167 °C, the Examiner has not provided persuasive evidence or scientific reasoning that eliglustat hemitartrate crystals having a melting point within this range necessarily have the same crystalline form. Neither has the Examiner explained why eliglustat hemitartrate necessarily exist in crystalline rather than amorphous form. *Scaltech Inc. v. Retec/Tetra L.L.C., 178 F.3d 1378, 1384 (Fed. Cir. 1999)* (citations omitted) (explaining that "[i]nherency may not be established by probabilities or possibilities" and that "[t]he mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency").

Neither **[*13]** are we persuaded by the Examiner's assertion that the prior art product and claimed product are substantially identical because McEachern, in light of Hirth, teaches the same preparation process used in the Specification to prepare the claimed eliglustat hemitartrate. Ans. 8.

First, Hirth at most discloses a general method of synthesizing tartrate salt (i.e., by reaction with tartaric acid). While Hirth teaches isolating Compound 6 (i.e., the free base) by dissolving or suspending the solids in 5% ethyl acetate in heptane, heating to reflux, then allowing to cool to room temperature over 4 hours, FF10, there is no disclosure that the synthesis of the *tartrate salt* of Compound 6 should include such a step. The Examiner's rationale for the anticipation rejection thus requires a skilled artisan to supplement Hirth's disclosures with his or her own knowledge or creativity, or to combine various disclosures in Hirth not directly related in Hirth itself. To anticipate, however, "it is not enough that the prior art reference discloses part of the claimed invention, which an ordinary artisan might supplement to make the whole, or that it includes multiple, distinct teachings that the artisan might **[*14]** somehow combine to achieve the claimed invention." *Net MoneyIN, Inc. v. VeriSign, Inc., 545 F.3d 1359, 1371 (Fed. Cir. 2008)*.

Moreover, although the Examiner cites to pages 28-31 (Example 2) and Tables 1 and 6 of the Specification (and points to the use of heptane and ethyl acetate) as showing that Hirth discloses an identical method for preparing eliglustat hemitartrate, the cited pages of the Specification do not disclose preparing a crystalline form of eliglustat hemitartrate by dissolving or suspending the solids in 5% ethyl acetate in heptane, heating to reflux, then cooling to room temperature over 4 hours. Ans. 8; Spec. 28-31. Instead, the only mention of heptane in Example 2 discloses that eliglustat hemitartrate is not soluble in heptane at room temperature and the use of dicholoromethane/heptane as an organic solvent in an anti-solvent method of preparing eliglustat hemitartrate crystals. Similarly, Example 2 discloses the use of ethyl acetate with acetone and dicholoromethane as solvents, but does not disclose a solvent of 5% ethyl acetate in heptane. Neither did the Examiner provide any articulated reasoning as to why a skilled artisan would consider 5% ethyl acetate in heptane to be substantially identical to ethyl acetate/acetone and **[*15]** dichloromethane/ethyl acetate in the context of a crystallization process.

Accordingly, we reverse the Examiner's rejection of the claims as anticipated over McEachern.

B. Obviousness over McEachern, Hirth, Brittain, and Morissette (claims 1, 7, 13, 14, 16, 50, 101-103)

1. Issue

As an alternative to the anticipation rejection over McEachern, the Examiner concludes that the claims on appeal are obvious over McEachern, Hirth, Brittain, and Morissette. Ans. 10-11. The Examiner asserts that the difference between the claimed invention and McEachern and Hirth, "if any, is the inherent properties of the product or the particular preparation steps." *Id.* at 11. The Examiner asserts that a skilled artisan would have been motivated to

crystallize eliglustat hemitartrate to improve its solid-state properties. *Id.* at 11-12. The Examiner further asserts that a skilled artisan would have had reasonable expectation of success at arriving at a preparation process identical to the process disclosed in the Specification, which would inherently result in the claimed crystalline form of eliglustat hemitartrate, because Brittain and Morissette teach common crystallization methods, crystallization optimization, and automated screening techniques. *Id.* at 11-12.

Appellant reiterates the arguments above with respect to the anticipation rejection, asserting that "McEachern in view of Hirth does not specifically disclose eliglustat hemitartrate salt, much less the particular crystalline form of eliglustat hemitartrate salt recited in the instant claims." Appeal Br. 15-16. Appellant further asserts that "Brittain and Morissette are directed to crystallinity generally and methods of crystallization," but "do not cure the deficiencies of McEachern and Hirth" because they do not "disclose eliglustat, much less the crystalline form of eliglustat hemitartrate salt recited in the instant claims." *Id.* at 16. Finally, Appellant contends that "the cited references do not provide a skilled artisan with the necessary direction to arrive at the instant claimed crystalline form of eliglustat hemitartrate salt with a reasonable expectation of success." *Id.* at 19.

The **[*16]** issue with respect to this rejection is whether a preponderance of evidence supports the Examiner's conclusion that, based on the cited prior art combination, a skilled artisan would have had reason to combine the teachings in the prior art to arrive at the claimed crystalline form of eliglustat hemitartrate, with a reasonable expectation of success.

2. Findings of Fact

15. Brittain teaches that

> the structure adopted by a given compound upon crystallization would exert a profound effect on the solid-state properties of that system. For a given material, the heat capacity, conductivity, volume, density, viscosity, surface tension, diffusivity, crystal hardness, crystal shape and color, refractive index, electrolytic conductivity, melting or sublimation properties, latent heat of fusion, heat of solution, solubility, dissolution rate, enthalpy of transitions, phase diagrams, stability, hygroscopicity, and rates of reactions are all determined primarily by the nature of the crystal structure.

Brittain iii.

16. Brittain teaches various methods employed to obtain unique polymorphic forms, including sublimation, crystallization from a single solvent through slow solvent evaporation, evaporation **[*17]** from a binary mixture of solvents, vapor diffusion, thermal treatment, crystallization from the melt, rapidly changing solution pH to precipitate acidic or basic substances, rapidly changing solution pH to precipitate acidic or basic substances, thermal desolvation of crystalline solvates, growth in the presence of additives, and grinding. *Id.* at 184-202; *see also id.* at 219 ("The pharmaceutical development scientist who is assigned the task of demonstrating that a substance exhibits only one crystalline form, or that of discovering whether additional forms exist, can utilize the techniques outlined in this chapter as a starting point.").

17. Brittain discloses solvents typically used for crystallization, including, e.g., "water, methanol, ethanol, propanol, isopropanol, acetone, acetonitrile, ethyl acetate, and hexane." *Id.* at 193; *see also id.* at 189.

18. Morissette teaches that "[high-throughput (HT)] crystallization methodologies are capable of screening hundreds or thousands of crystallization conditions in parallel using small amounts of compound for the identification and characterization of diverse forms of active pharmaceutical ingredients." Morissette 296, left column.

3. *Analysis*

We agree with Appellant that the Examiner did not establish a prima facie case that the claims are obvious over McEachern, Hirth, Brittain, and Morissette.

The Examiner acknowledges that "[t]he combined teaching of McEachern and Hirth do not specifically describe the XRPD peaks listed in the instant claims" but asserts **[*18]** that "such properties are inherent to the solid form produced by the well-known preparation processes which were specifically suggested by McEachern and Hirth" and further detailed in Brittain. Ans. 11. The Examiner asserts that a skilled artisan would have been highly motivated to use various well-known crystallization solvents to form the product in order to improve the solubility, stability, or hygroscopicity of eliglustat, because Brittain teaches that the crystalline structure of a compound exerts "a profound effect" on its solid-state properties. *Id.* The Examiner further asserts that a skilled artisan would have had a reasonable expectation of success in arriving at any one of the preparation processes disclosed in the instant specification, which would inherently result in the claimed crystalline form of eliglustat hemitartrate, because "crystallization optimization was so commonplace that automated screening techniques," such as the high-throughput ("HT") crystallization methodologies described in Morissette, were utilized in the art to screen "hundreds or thousands of crystallization conditions in parallel."

We are not persuaded. We agree that McEachern and Hirth suggest **[*19]** a tartrate salt of eliglustat. FF 1, 2, 8, 9, 11, 12. For the reasons already discussed, however, the Examiner has not established that McEachern and Hirth inherently disclose the specific crystalline form of eliglustat hemitartrate claimed. Similarly, while Brittain and Morissette generally teach the importance of crystalline forms on the properties of a compound, common crystallization conditions, and high throughput crystallization methodologies, these references do not refer to eliglustat hemitartrate in particular. FF16-FF18.

The Examiner has not explained why a skilled artisan would have considered the existence of a crystalline form of eliglustat hemitartrate obvious in light of the prior art, much less pointed to any specific teachings that would have led a skilled artisan to the specific crystalline form recited in the claims. Instead, the crux of the obviousness rejection appears to be that it would have been obvious to try to crystallize eliglustat hemitartrate and that, given the knowledge in the prior art regarding parameters affecting crystallization and the capability of high throughput crystallization methodologies to screen large numbers of crystallization conditions **[*20]** to identify optimal crystalline forms for, e.g., pharmaceutical ingredients, FF16-FF18, a skilled artisan would have had a reasonable expectation of hitting upon the conditions for formation of the claimed crystalline form of eliglustat tartrate.

The above rationale would appear to render obvious any crystalline form of a useful compound. As our reviewing court has explained, however, it would be error to equate "obvious to try" with "obviousness under § 103," where

> what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

In re Kubin, 561 F.3d 1351, 1359 (Fed. Cir. 2009) (quoting *In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988))*.

Accordingly, we reverse the obviousness rejection over McEachern, Hirth, Brittain, and Morissette.

C. Anticipation by Cheng (claims 1, 7, 13, 14, 16, 50, 101-103)

1. Issue

The Examiner finds that Cheng teaches glucosylceramide synthase inhibitors including a compound of formula (I):

Ans. 12. The Examiner finds that Cheng specifically claims the tartrate salt of the compound in claim 21, and "also teaches the formulation of a **[*21]** pharmaceutical composition with excipients routinely used in the art." *Id.*

The Examiner asserts that Cheng claims a compound "identical to that of the instant claims" and that "the X-ray powder diffraction limitations are inherent to the compound and would be present in the prior art product." Ans. 13.

Appellant contends that Cheng does not "specifically disclose the hemitartrate salt of eliglustat, much less the specific crystalline form of eliglustat hemitartrate salt recited in the instant claims," and also does not disclose "a method of preparing the specific crystalline form of eliglustat hemitartrate salt recited in the instant claims." Appeal Br. 20. Appellant further contends that, "[i]n the absence of a specific disclosure or teaching in Cheng to describe the specific chemical nature of eliglustat as a tartrate salt and a method of preparing the same, the specific crystalline form of eliglustat hemitartrate salt of the instant claims is not inherently described" in Cheng. *Id.* at 21.

The issue with respect to this rejection is whether a preponderance of evidence supports the Examiner's finding that Cheng teaches the claimed crystalline form of eliglustat hemitartrate salt.

[*22] *2. Findings of Fact*

19. Cheng teaches treating diabetes by administering a therapeutically effective amount of at least one compound, such as a ceramide analog, which inhibits glucosylceramide synthase. Cheng P 12.

20. Cheng teaches that the glucosylceramide synthase inhibitor may be 1(R)-(3',4'-ethylenedioxy)phenyl-2(R)-octanoylamino-3-pyrrolidino-1-propanol, which has the same chemical structure set out in claim 1. *Id.* P 63.

21. Cheng claims "[a] method of treating a subject having type 2 diabetes, the method comprising administering to the subject a therapeutically effective amount of a composition comprising" the tartrate salt of eliglustat. *Id.* at 31 (claim 21).

3. Analysis

For reasons similar to those discussed above with respect to the rejection over McEachern, we agree with Appellant the Examiner has not established a prima facie case that Cheng anticipates the claims.

In particular, we agree with the Examiner, and Appellant has not disputed, that Cheng discloses the "tartrate salt" of eliglustat. Ans. 12. Nevertheless, for the reasons already discussed, we do not agree that disclosure of the chemical formula and salt form of a compound necessarily (i.e., inherently) discloses its crystalline form. Likewise, we do **[*23]** not agree that the Examiner has established a prima facie case of inherency because "all of the demonstrations of preparing the crystalline form in the instant specification, including screening across a number of different solvents such as in Table 1 (page 28), show that all attempts result in the claimed product with a DSC of ~166 C." *Id.* at 13. As discussed above, the Examiner has not provided persuasive evidence or scientific reasoning that eliglustat hemitartrate crystals having a melting point within this range necessarily have the same crystalline form. *Scaltech, 178 F.3d at 1384*.

D. Obviousness over Cheng, Brittain, and Morissette (Claims 1, 7, 13, 14, 16, 50, 101)

As an alternative to the anticipation rejection over Cheng, the Examiner finds that the claims on appeal are obvious over Cheng, Brittain, and Morissette. Ans. 13. The Examiner asserts that "Cheng teaches . . . the identical product as in the instant claims," as discussed above, but concedes that "Cheng does not specifically teach a crystallization process." Ans. 13. The Examiner asserts, however, that the claims are obvious over Cheng, Brittain, and Morissette, for the same reasons discussed above with respect to the obviousness rejection over McEachern, Hirth, Brittain and Morissette. We are not persuaded for the reasons already discussed and reverse the obviousness rejection over Cheng, Brittain, and Morissette.

CONCLUSION

In summary:

Claim(s)	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
Rejected				
1, 7, 13,	102(b)	McEachern		1, 7, 13, 14, **[*24]**

Claim(s)	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
Rejected				
14, 16, 50, 101-103				16, 50, 101-103
1, 7, 13, 14, 16, 50, 101-103	103(a)	McEachern, Hirth, Brittain, Morissette		1, 7, 13, 14, 16, 50, 101-103
1, 7, 13, 14, 16, 50, 101	102(b)	Cheng		1, 7, 13, 14, 16, 50, 101
1, 7, 13, 14, 16, 50, 101	103(a)	Cheng, Brittain, Morissette		1, 7, 13, 14, 16, 50, 101
Overall Outcome				1, 7, 13, 14, 16, 50, 101-103

REVERSED

USPTO Bd of Patent Appeals & Interferences; Patent Trial & Appeal Bd Decs.

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