

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte MARSHALL D. CREW,
DWAYNE T. FRIESEN,
BRUNO C. HANCOCK, CHRIS MACRI
JAMES A.S. NIGHTINGALE, and
RAVI M. SHANKER

Appeal No. 2006-3379
Application No. 10/393,549

ON BRIEF

Before MILLS, GREEN, and LEBOVITZ, Administrative Patent Judges.

LEBOVITZ, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to process for forming a pharmaceutical composition containing amorphous dispersion particles. The Examiner has rejected the claims as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 134. We affirm-in-part.

Background

“Type 2 diabetes is often treated by drugs designed to suppress hepatic glucose production.” Specification, page 1, lines 5-6. A particularly effective drug is

5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxy-pyrrolidin-1-yl)-3-oxopropyl] amide referred to as “Drug A.” Id., page 1, lines 13-24.

Drug A is a “sparingly soluble” drug which has low bioavailability when administered orally. Id., page 1, line 28-page 2, line 2. The instant application provides pharmaceutical compositions in which Drug A is combined with a concentration-enhancing polymer that increases the concentration of Drug A in blood. Id., page 2, lines 5-31. The pharmaceutical composition can be in the form of an amorphous dispersion. Id., page 2, lines 5-31; page 3, lines 29-34.

Claim status

Claims 74-78, 80, and 84-88 are pending. There are two grounds of rejection: 1) Claims 74-77 and 84-88 stand rejected under 35 U.S.C. § 102(b); and 2) Claims 78 and 80 stand rejected under 35 U.S.C. § 103(a). Answer, pages 3-4. The claims within each grouping stand or fall together because Appellants have not provided separate reasons for patentability for any individual claims. 37 C.F.R. § 41.37(c)(1)(vii). We select claims 74 and 78 as representative of each group of claims on appeal.

74. A process for forming a pharmaceutical composition, comprising the steps of:
- (a) forming solid amorphous dispersion particles each comprising a sparingly soluble drug and a concentration enhancing polymer, wherein at least a major portion of said drug is amorphous;
 - (b) blending said solid amorphous dispersion particles and matrix material to form a blend;
 - (c) feeding said blend to a melt-congeal process to form a molten mixture comprising said solid amorphous dispersion particles and said matrix material; and
 - (d) cooling said molten mixture and forming solid particles each comprising said solid amorphous dispersion particles trapped within said matrix material.

78. A process for forming a pharmaceutical composition, comprising the steps of:
- (a) forming a solution comprising a sparingly soluble drug, a concentration-enhancing polymer, and a solvent;
 - (b) spray drying said solution under conditions whereby said solution is atomized to form droplets ranging in size from 1 to 500 μm , said droplets solidifying to form solid amorphous dispersion particles comprising said drug and said concentration-enhancing polymer; and
 - (c) further drying said solid amorphous dispersion particles in a separate drying apparatus, thereby removing residual solvent to less than 1 wt% of said composition.

Anticipation

Claims 74-77 and 84-88 stand rejected under 35 U.S.C. § 102(b) as anticipated by Kigoshi.¹

Claim construction

Claim 74 is a process of forming a pharmaceutical composition which has four steps. In the first step (a), a solid amorphous dispersion is formed of a sparingly soluble drug and a concentration enhancing polymer. The amorphous dispersion is blended with a matrix material in the second step (b). The blend in step (c) is fed “to a melt congeal process to form a molten mixture.” Finally, in step (d), the molten mixture is cooled, “forming solid particles each comprising said solid amorphous dispersion particles trapped within said matrix material.”

The term “amorphous” is defined in the specification to mean “a non-crystalline state.” Specification, page 4, lines 35-36; page 21, lines 9-15. The “concentration-enhancing polymer” can be “cellulosic and non-cellulosic” polymers. *Id.*, page 10, lines 35-36. “The amorphous solid dispersion of drug may be prepared by any of the known ways . . . including, for example, by melt fusion, by melt congealing, by

¹ Kigoshi et al. (Kigoshi), EP 0 784 974 A1, published July 23, 1997

lyophilization, by extended mechanical processing . . . , or in a twin-screw extruder or in a ball mill, or by solvent processing.” Id., page 20, lines 30-36.

The solid amorphous dispersion particles are blended with a matrix material in step (b) which is fed to melt-congeal process in step (c) to form a molten mixture. Examples of matrix materials include citric acid, sugar, lipid, or wax. Id., page 35, line 35-page 36, line 2; page 36, lines 30-page 37, line 1. According to the specification, the melt-congeal process can be performed according to prior art methods. Id., page 36, lines 9-19. When the molten mixture resulting from the melt-congeal process is cooled, it forms (d) “solid amorphous dispersion particles trapped within said matrix material.”

Kigoshi

Kigoshi teaches a solid dispersion of a “slightly soluble” xanthine derivative. Kigoshi, page 2, lines 21-22. The xanthine derivative is blended with a polymer. The “solid dispersion . . . can be prepared by a co-grinding method, a solvent method, a melting method, a heat-melt-kneading method, or the like.” Id., page 4, lines 16-17. Examples of polymers include rubber compounds, gelatin, polysaccharides, cellulose derivatives, polyvinyl derivatives, and methacrylate copolymers. Id., page 3, line 55-page 4, line 9. Dosage forms of the solid dispersion can further comprise additives, “such as a coloring agent, a corrigent, an excipient, a disintegrator, a lubricant, and a surfactant.” Id., page 5, lines 37-38.

The Examiner argues that Kigoshi discloses a solid dispersion comprising “polymer and additives such as surfactant, coloring agent, starch, dextrin, triethyl citrate, polyethylene glycol, triacetin, sucrose-fatty acid esters, lactose, amino acids,

disintegrants and lubricants (page 4, line 39 to page 5 line 44) The additives meet the limitations of the matrix material.” Answer, page 7, lines 7-11. For step (c) of claim 74 which requires feeding a blend of solid amorphous dispersion particles “to a melt-congeal process to form a molten mixture,” the Examiner relies on Kigoshi’s disclosure of melting and heat-melt-kneading methods (page 4, lines 16-17) for forming the solid dispersion. Answer, page 7, line 16-page 8, line 10.

Appellants challenge the rejection on several grounds. First, they contend that Kigoshi is concerned with the production of solid dispersions, and does not describe the claimed “process for making a product in which dispersion particles are trapped within a matrix material.” Brief, page 5. They assert that the product which is produced by their claimed process is “a two-phase system . . . analogous to raisin bread, in which the raisins correspond to trapped [dispersion] particles and the bread corresponds to the matrix in which the raisins are trapped.” Id., page 4. Appellants state that Kigoshi’s process does not result in a composition having this two-phase system. They also argue that Kigoshi does not describe step (c) of claim 74 in which “a blend of solid amorphous dispersions and a matrix material” are fed to a melt-congeal process. Id., page 6.

“[C]laim limitations can not be ignored. See Perkin-Elmer Corp. v. Westinghouse Elec. Corp., 822 F.2d 1528, 1532, 3 USPQ2d 1321, 1324 (Fed. Cir. 1987) (the court can not ignore a plethora of meaningful limitations). Patentability is determined for the invention as claimed, with all its limitations. It is improper to delete explicit limitations from the claim.” In re Schreiber, 128 F.3d 1473, 1480, 44 USPQ2d 1429, 1435 (Fed. Cir. 1997) (Newman, dissenting opinion). In this case, the Examiner does not accord

proper weight to the limitation in claim 74 of “solid particles each comprising said solid amorphous dispersion particles trapped within said matrix material.” Although it is expressly recited in the claim, we do not find that the Examiner addressed it in her Answer. Appellants’ reference to “raisin bread” is shorthand for this limitation. See above. Thus, the Examiner was incorrect to conclude that “the ‘raisin bread’ analogy is not set forth in the claims.” Answer, page 7.

To anticipate, every element and limitation of the claimed invention must be found in a single prior art reference, arranged as in the claim. Karsten Mfg. Corp. v. Cleveland Golf Co., 242 F.3d 1376, 1383, 58 USPQ2d 1286, 1291 (Fed. Cir. 2001). It is the Examiner’s burden to come forward with evidence to establish that the prior art reference meets this requirement. On the record before us, we find no evidence put forward by the Examiner that Kigoshi’s process of forming a solid dispersion with a drug, polymer, and excipient by melting or heat-melt-kneading methods (Kigoshi, page 4, lines 16-17) would result in solid amorphous particles “trapped” in a matrix material as required by claim 74.

Furthermore, claim 74 requires that the amorphous dispersion particles are blended with a matrix material and then fed to a melt-congeal process to form a molten mixture. The Examiner asserts that Kigoshi’s process in which an amorphous dispersion is formed by heat melting meets this requirement. Answer, pages 7-8. We agree that if Kigoshi’s heat melting process could form dispersion particles of the drug and polymer, while at the same time forming a molten mixture that would cool to form “solid amorphous dispersion particles trapped” in the matrix material, it would be anticipatory to the claimed method. However, the Examiner has provided no evidence

or a reasonable basis for presuming this structure is present in Kigoshi. To the contrary, Kigoshi characterizes it as a “solid dispersion” in an apparently amorphous form. Kigoshi, page 7, lines 30, 42-43 and 50-51. Thus, Kigoshi’s own words conflict with the Examiner’s conclusion.

As Appellants have recognized, the Examiner’s rejection appears to be grounded in inherency. Reply Brief, pages 8-9. The prior art may anticipate the claimed subject matter when the claimed limitations are not expressly found in the reference, but are inherent to it. Inherency asks whether a subject matter is “necessarily” present in the prior art reference. “Inherent anticipation requires that the missing descriptive material is ‘necessarily present,’ not merely probably or possibly present, in the prior art.” Trintec Indus. v. Top-U.S.A., 295 F.3d 1292, 1295, 63 USPQ2d 1597, 1599 (Fed. Cir. 2002). We find no evidence of record that Kigoshi’s process would necessarily form a solid amorphous particles surrounded by a matrix material upon cooling as required by claim 74.

For the foregoing reasons, we conclude that the Examiner has not provided adequate evidence to establish a prima facie case that each and every element of claim 74 is described in the prior art. This rejection is also reversed for dependent claims 75-77 and 84-88.

Obviousness

Claims 78 and 80 stand rejected under 35 U.S.C. § 103(a) as being obvious over Kigoshi.

Claim construction

Claim 78 is drawn to a method of forming a pharmaceutical composition. It comprises three steps: (a) forming a solution of a sparingly soluble drug, a polymer, and a solvent; (b) spray drying the solution to form droplets which solidify into amorphous dispersion particles; and (c) “further drying said solid amorphous dispersion particles in a separate drying apparatus, thereby removing residual solvent to less than 1 wt% of said composition.” The additional drying is required to occur in a “separate drying apparatus,” but it does not otherwise specify the characteristics of the drying apparatus or the nature of the drying process. Consequently, we construe this limitation to include any apparatus in which spray-dried particles are subjected to additional drying, including the apparatus in which the spray drying was accomplished.

Kigoshi

Kigoshi has been described above for teaching a solid dispersion comprising a slightly soluble drug. It describes a solvent method of producing a solid dispersion “using, for example, a fluidized-bed granulator, an agitating granulator, a spray-dry granulator, or a vacuum-dry granulator.” Kigoshi, page 4, lines 37-38. For performing spray-drying, “a granulator may be used which is further equipped with a vacuum-drying unit or microwave drying unit.” Id., page 4, lines 58-59.

The Examiner states that Kigoshi describes the claimed process, but does not specifically disclose the claimed droplet size. Answer, page 5. However, she argues that Kigoshi’s spray drying process would result in particles having the

claimed droplet size, citing an admission in the instant application to support this position. Id. The Examiner asserts that the vacuum-drying or microwave drying unit disclosed by Kigoshi in the spray-drying step meets the claim limitation “(c) further drying said solid amorphous dispersion in a separate drying apparatus.” Id.

Appellants state that “[t]here is no disclosure or any suggestion in Kigoshi relating to such a further drying step in which solvent is removed to less than [sic] 1 wt%. That is, there is nothing in Kigoshi relating to Appellants’ claim 78 step (c).” Brief, page 10. They also argue:

At Kigoshi, page 4, lines 58-59 which was cited by the Examiner, one skilled in the art would realize that Kigoshi is not spray-drying with a granulator because granulators cannot be used for spray drying, The skilled person would realize that Kigoshi is describing granulating the coated absorbent carrier disclosed in the paragraph immediately preceding, and that the vacuum drying unit or the microwave unit are being used for drying in the first instance since granulators do not themselves effect drying.

Reply Brief, page 10.

We do not find Appellants’ argument persuasive. The claim requires “further drying said solid amorphous particles in a separate drying apparatus.” Kigoshi’s process describes “a vacuum-drying unit or microwave drying unit.” We agree with the Examiner that this unit constitutes “a separate drying apparatus” as required by the claim. Appellants read the claim to require that the “further drying” step must occur in drying unit which is different from the unit in which the spray drying is accomplished. However, we do not find this limitation in step (c) of claim 78. Step (c) entails “further drying” the already formed solid

amorphous particles in “a separate drying apparatus.” We have construed the latter to any apparatus in which spray-dried particles are subjected to additional drying, including the apparatus in which the spray-drying was accomplished. Thus, the fact that “the vacuum drying unit or the microwave unit are being used for drying in the first instance” (Reply Brief, page 10) does not foreclose them from being used for “further drying” once the particle are formed. For this reason, we also do not agree with Appellants that Kigoshi teaches away from additional drying because it states that solid dispersion can be used “as they are’.” Reply Brief, page 10.

Kigoshi also states in its description of the solvent method (which uses spray-drying to remove solvent) that, “[a]s to removal of the organic solvent, operating conditions such as the treatment temperature and time period are ordinarily at room temperature to 150°C and for several minutes to more than ten hours, though they are altered depending on the compound, the polymer, the solvent, or the like to be used.” Kigoshi, page 4, lines 34-36. It would be reasonable for one of ordinary skill in the art to presume that longer operating conditions, which are explicitly suggested by Kigoshi, “would be expected to produce dried solid particles” (Answer, page 9) with “residual solvent to less than 1 wt% of said composition” as claimed. Appellants have not rebutted this or explained why Kigoshi’s process would not have enabled a process resulting in the claimed amount of residual solvent content. Accordingly, this rejection is affirmed. Since separate reasons for patentability were not provided, claim 80 falls with claim 78.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

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