UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SONKE SVENSON,
CHRISTOPHER J. TUCKER, and JAMES E. HITT

Appeal 2009-008798
Application 10/213,907
Technology Center 1600

Decided: January 8, 2010

Before DONALD E. ADAMS, LORA M. GREEN and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a dry powder comprising particles. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

Statement of the Case

Background

"It is known that the rate of dissolution of a particulate drug can increase with increasing surface area, such as by decreasing particle size. Furthermore, crystalline drug particles are desirable because of the greater stability as opposed to amorphous particles" (Spec. 1, ll. 15-17).

The Claims

Claims 1, 3-9, and 11-19 are on appeal. Claims 1 and 7 are representative and read as follows:

> 1. A dry powder comprising particles, the particles comprising:
>
> a plurality of crystalline domains having an average size of less than about 400 Angstroms, wherein each crystalline domain is oriented differently than any of the adjacent domains; and
>
> a plurality of interfacial regions surrounding the crystalline domains;
>
> wherein the crystalline domains comprise a drug substance, and wherein the interfacial regions comprise at least one stabilizer.
>
> 7. A dry powder comprising drug particles, the drug particles prepared according to a process comprising the steps of:
>
> (a) dissolving a drug substance in a solvent; and
>
> (b) adding the product of step (a) to water to form precipitated drug particles; wherein the drug particles comprise:
>
> a plurality of crystalline domains having an average size of less than about 400 Angstroms, each domain being oriented differently than any of the adjacent domains, wherein the domains comprise a drug substance; and a plurality of interfacial regions surrounding the crystalline

domains, the interfacial regions comprising at least one stabilizer.

The prior art

The Examiner relies on the following prior art references to show unpatentability:

Kipp	US 6,607,784 B2	Aug. 19, 2003

The issues

A. The Examiner rejected claims 1, 3-9, and 11-19 under 35 U.S.C. § 102(e) as anticipated by Kipp (Ans. 3-4).

B. The Examiner rejected claims 1, 3-9, and 11-19 under 35 U.S.C. § 103(a) as obvious over Kipp (Ans. 4-5).

A. 35 U.S.C. § 102(e) over Kipp

The Examiner finds that Kipp teaches "a method for preparing submicron crystalline particles having an average effective particle size of about 400 nm to 2 microns (see col. 3, lines 36-37). The particles disclosed by Kipp et al are prepared by dissolving a drug in a solvent and adding water" (Ans. 3). The Examiner finds that "[s]ince the process of preparing particles advanced by Kipp et al is equivalent to the process of particle preparation in the instant claims, the product is expected to be equivalent" (Ans. 4).

Appellants argue that "Kipp does not teach or suggest particles having crystalline domains, and more specifically, Kipp does not teach or suggest particles having crystalline domains of less than about 400 Angstroms" (App. Br. 3).

In view of these conflicting positions, we frame the anticipation issue before us as follows:

Have Appellants demonstrated that the Examiner erred in finding that Kipp inherently teaches particles comprising "a plurality of crystalline domains having an average size of less than about 400 Angstroms"?

Findings of Fact (FF)

1. Figure 1 of the Specification is reproduced below:

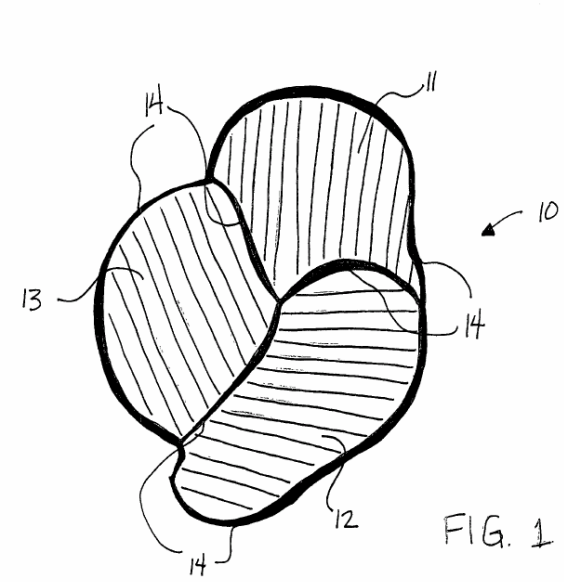


FIG. 1

The Specification teaches that as "shown in Figure 1, the interfacial regions 14 are in between each of the crystalline domains 11, 12, and 13, and the interfacial regions 14 are also on the outside surface of the particle 10" (Spec. 4, ll. 22-25).

2. The Specification teaches that the "crystalline domains are preferably less than 500 Angstroms in size. More preferably, the crystalline

domains are less than about 450 Angstroms, and even more preferably less than about 400 Angstroms" (Spec. 4, ll. 19-21).

3. The Specification teaches that the "size of particle 10 as determined by light scattering techniques is not critical. In a preferred embodiment, however, the particles of the present invention are relatively small" (Spec. 5, ll. 27-28).

4. The Specification teaches that "preferably, the particles of the present invention have a mean particle size of less than about 20 microns, even more preferably less than about 10 microns, and yet even more preferably less than about 5 microns" (Spec. 5, ll. 29-31).

5. The Specification teaches that "[s]uitable drug substances can be selected from a variety of known classes of drugs" (Spec. 4, ll. 2-3).

6. The Specification teaches specific drugs including:

> analgesics, anti-inflammatory agents, anthelmintics, anti-arrhythmic agents, antibiotics (including penicillins), anticoagulants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytic sedatives (hypnotics and neuroleptics), astringents, beta-adrenoceptor blocking agents, blood products and substitutes, cardiacinotropic agents, contrast media, corticosterioids, cough suppressants (expectorants and mucolytics), diagnostic agents, diagnostic imaging agents, diuretics, dopaminergics (antiparkinsonian agents), haemostatics, immuriological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin and biphosphonates, prostaglandins, radio-pharmaceuticals, sex hormones (including steroids), anti-allergic agents, stimulants and anoretics,

> sympathomimetics, thyroid agents, vasidilators and xanthines

(Spec. 4, ll. 3-15).

7. The Specification teaches that:

> Suitable surfactants include gelatin, casein, lecithin, phosphatides, gum acacia, cholesterol, tragacanth, fatty acids and fatty acid salts, benzalkonium chloride, glycerol mono and di fatty acid esters and ethers, cetostearyl alcohol, cetomacrogol 1000, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, e.g., the commercially available Tweens, polyethylene glycols, poly(ethylene oxide/propylene oxide) copolymers, e.g., the commercially available Poloxomers or Pluronics, polyoxyethylene fatty acid ethers, e.g., the commercially available Brijs, polyoxyethylene fatty acid esters, sorbitan fatty acid esters, e.g., the commercially available Spans, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol (PVA), sodium lauryl sulfate, polyvinylpyrrolidone (PVP), poly(acrylic acid), and other anionic, cationic, zwitterionc and nonionic surfactants.

(Spec. 5, ll. 6-19).

8. The Specification teaches that:

> Suitable organic solvents include but are not limited to methanol, ethanol, isopropanol, 1-butanol, t-butanol, trifluoroethanol, polyhydric alcohols such as propylene glycol, PEG 400, and 1,3-propanediol, amides such as n-methyl pyrrolidone, N,N-dimethylformamide, tetrahydrofuran, propionaldehyde, acetone, n- propylamine, isopropylamine, ethylene diamine, acetonitrile, methyl ethyl

> ketone, acetic acid, formic acid, dimethylsulfoxide, 1,3-dioxolane, hexafluoroisopropanol, and combinations thereof

(Spec. 7, ll. 17-23).

9. The Specification teaches that "the particles are prepared by way of a controlled precipitation process" (Spec. 7, l. 6).

10. The Specification defines a "controlled precipitation process" as "a process comprising the following steps: (a) dissolving a drug substance in a solvent; and (b) adding the product of step (a) to water to form precipitated drug particles" (Spec. 7, ll. 7-9).

11. The Specification teaches that in "a preferred embodiment, a stabilizer, such as those described above, is present in the solvent, in the water or in both the solvent and the water" (Spec. 7, ll. 9-11).

12. Kipp teaches that "[a]fter the energy-addition step the organic compound is in a crystalline form having an average effective particle size essentially the same as that of the presuspension (i.e., from about 400 nm to about 2μm)" (Kipp, col. 5, ll. 8-11).

13. Kipp teaches that:

> In Method A (see FIG. **1**), the organic compound ("drug") is first dissolved in the first solvent to define a first solution. The organic compound can be added from about 0.1% (w/v) to about 50% (w/v) depending on the solubility of the organic compound in the first solvent. Heating of the concentrate from about 30° C. to about 100° C. may be necessary to ensure total dissolution of the compound in the first solvent. A second aqueous solution is provided with one or more optional surface modifiers such as an anionic surfactant,

a cationic surfactant or a nonionic surfactant added thereto.

(Kipp, col. 6, ll. 33-43.)

14. Kipp teaches that the:

organic compound might be a pharmaceutically active compound from various groups such as, but not limited to: antihyperlipidemics; antimicrobials, e.g., antibacterials such as sulfadiazine, antifungals such as itraconazole; non-steroidal anti-inflammatory drugs, e.g., indomethacin; antihypercholesteremic agents, e.g., probucol; and steroidal compounds, e.g., dexamethasone; immunosuppresants, e.g., cyclosporin A, tacrolimus, and mycophenolate mofetil.

(Kipp, col. 5, l. 62 to col. 6, l. 3.)

15. Kipp teaches that:

Suitable anionic surfactants include but are not limited to potassium laurate, sodium lauryl sulfate, sodium dodecylsulfate, . . . sodium carboxymethylcellulose . . . Suitable cationic surfactants include but are not limited to quaternary ammonium compounds, such as benzalkonium chloride, cetyltrimethylammonium bromide . . . Suitable nonionic surfactants include: polyoxyethylene fatty alcohol ethers (Macrogol and Brij), polyoxyethylene sorbitan fatty acid esters (Polysorbates), polyoxyethylene fatty acid esters (Myrj), sorbitan esters (Span), glycerol monostearate, polyethylene glycols, polypropylene glycols, cetyl alcohol, cetostearyl alcohol, stearyl alcohol, aryl alkyl polyether alcohols, polyoxyethylene-polyoxypropylene copolymers (poloxomers), polaxamines, methylcellulose, hydroxycellulose, hydroxy propylcellulose, hydroxy propylmethylcellulose, noncrystalline cellulose, polyvinyl alcohol, and polyvinylpyrrolidone. In a preferred form of the invention the nonionic surfactant is a polyoxyethylene and polyoxypropylene copolymer and preferably a block

> copolymer of propylene glycol and ethylene glycol. Such polymers are sold under the tradename POLOXAMER

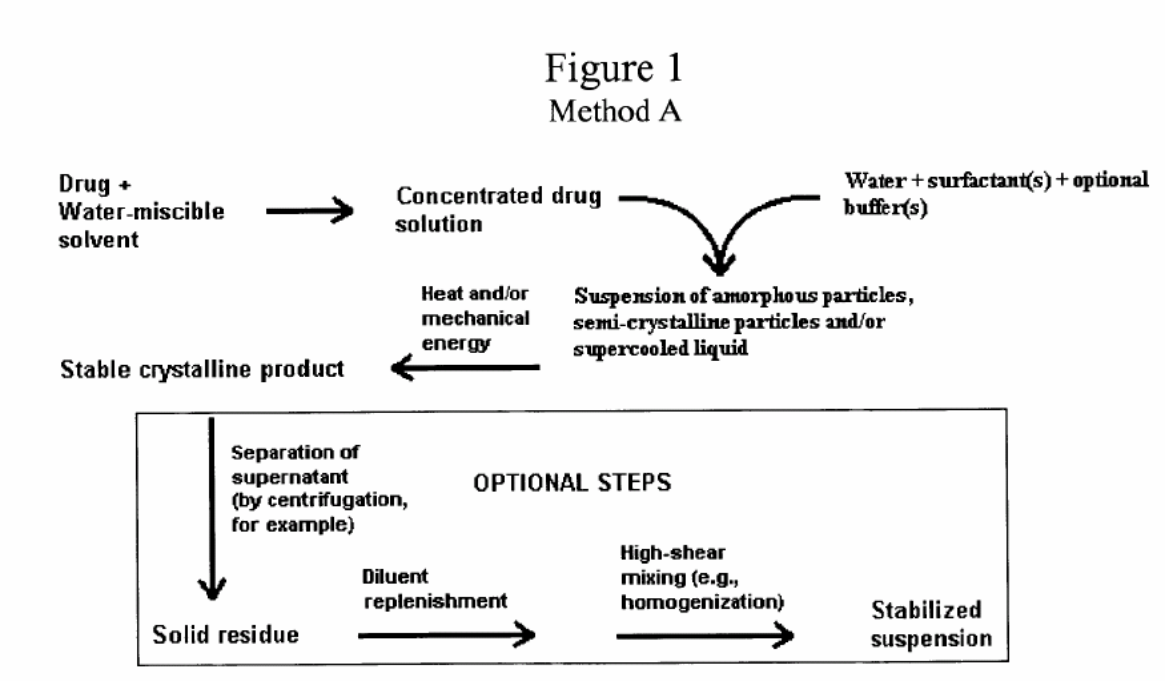
(Kipp, col. 6, l. 43 to col. 7, l. 12).

16. Kipp teaches that solvents:

> include, but are not limited to: polyvinylpyrrolidone, N-methyl-2-pyrrolidinone (also called N-methyl-2-pyrrolidone), 2-pyrrolidone, dimethyl sulfoxide, dimethylacetamide, lactic acid, methanol, ethanol, isopropanol, 3-pentanol, n-propanol, glycerol, butylene glycol (butanediol), ethylene glycol, propylene glycol, mono- and diacylated monoglycerides (such as glyceryl caprylate), dimethyl isosorbide, acetone, dimethylformamide, 1,4-dioxane, polyethylene glycol . . . polyethylene glycol sorbitans (such as PEG-20 sorbitan isostearate), polyethylene glycol monoalkyl ethers (examples such as PEG-3 dimethyl ether, PEG-4 dimethyl ether), polypropylene glycol (PPG), polypropylene alginate, PPG-10 butanediol, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-15 stearyl ether, propylene glycol dicaprylate/dicaprate, propylene glycol laurate.

(Kipp, col. 6, ll. 11-31.)

17. Figure 1 of Kipp is reproduced below:



"FIG. **1** shows a diagrammatic representation of one method of the present invention" (Kipp, col. 4, ll. 12-13).

Principles of Law

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987).

"It is well settled that a prior art reference may anticipate when the claim limitations not expressly found in that reference are nonetheless inherent in it." *In re Cruciferous Sprout Litigation*, 301 F.3d 1343, 1349 (Fed. Cir. 2002). *See*, e.g., *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed.Cir.1999) ("Under the principles of inherency, if the

prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates.")

Once a prima facie case of anticipation has been established, the burden shifts to the Appellant to prove that the prior art product does not necessarily or inherently possess the characteristics of the claimed product. *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) ("Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product."). *See also In re Spada*, 911 F.2d 705, 708-09 (Fed. Cir. 1990).

Analysis

Kipp teaches particles formed by a process where "the organic compound ("drug") is first dissolved in the first solvent to define a first solution . . . A second aqueous solution is provided with one or more optional surface modifiers such as an anionic surfactant, a cationic surfactant or a nonionic surfactant added thereto" (Kipp, col. 6, ll. 33-43; FF 13, 17). The Kipp process is identical to the "controlled precipitation process" disclosed in the Specification (FF 9-11).

Kipp further teaches the use of an overlapping genus of drug substances relative to those found in the Specification (FF 6, 14). Kipp also teaches an overlapping genus of solvents (FF 8, 16) and an overlapping genus of stabilizers (FF 7, 15).

We agree with the Examiner that "[s]ince the process of preparing particles advanced by Kipp et al is equivalent to the process of particle preparation in the instant claims, the product is expected to be equivalent" (Ans. 4).

Appellants' sole argument is that "Kipp does not teach or suggest particles having crystalline domains, and more specifically, Kipp does not teach or suggest particles having crystalline domains of less than about 400 Angstroms" (App. Br. 3). This argument misplaces the burden. The Examiner has provided significant evidence which supports the conclusion that the particles of Kipp are identical to those claimed. Consequently, under *Best*, the burden of proving that the particles of Kipp do not inherently satisfy the claims is placed on Appellants. *See In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) ("Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.").

Appellants have proffered no evidence that the particles of Kipp differ from those claimed.

Conclusion of Law

Appellants have not demonstrated that the Examiner erred in finding that Kipp inherently teaches particles comprising "a plurality of crystalline domains having an average size of less than about 400 Angstroms".

B. 35 U.S.C. § 103(a) over Kipp

We have already found that Kipp anticipates the products of claims 1 and 7. Anticipation is the epitome of obviousness. *In re McDaniel*, 293 F.3d 1379, 1385-1386 (Fed. Cir. 2002). Therefore, we affirm the § 103 rejection of claims 1 and 7. Claims 3-6, 9, and 11-19 fall with claims 1 and 7.

SUMMARY

In summary, we affirm the rejection of claims 1 and 7 under 35 U.S.C. § 102(e) over Kipp. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 3-6, 9, and 11-19 as these claims were not argued separately.

We affirm the rejection of claims 1 and 7 under 35 U.S.C. § 103(a) over Kipp. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 3-6, 9, and 11-19 as these claims were not argued separately.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

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