

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PASCAL CAVAILLON, NATHALIE LLORCA,
OLIVIER LOUIS, and PATRICK ROSIER

Appeal 2008-3510
Application 10/364,257
Technology Center 1600

Decided: July 18, 2008

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 44-57, 59-74, 85-87, 95, and 96. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF CASE

The claims are directed to aerosol formulations which comprise therapeutic drug particles, coated with an excipient and a surfactant, and

which are suspended in a propellant gas. Both composition and methods of making the aerosol formulation are pending.

Claims 44-57, 59-74, 85-87, 95, and 96, which are all the pending claims, stand rejected under 35 U.S.C. § 103(a) as obvious over Green (WO 96/19968, published Jul. 4, 1996), Sasatani (WO 96/41628, published Dec. 27, 1996¹), and Taylor (WO 92/08446, published May 29, 1992) (Ans. 3).

The only pending independent claims are claims 44 and 59 which are reproduced below:

44. A pharmaceutical aerosol formulation comprising:
therapeutic drug particles having a first spray-dry coating of at least one excipient selected from the group consisting of lactose and trehalose and a second spray-dry coating of at least one surfactant, said coated therapeutic drug particles being in suspension in a liquid propellant selected from the group consisting of 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane and mixtures thereof.

59. A process for preparing a pharmaceutical aerosol formulation, comprising the steps of:
providing a therapeutic agent, said therapeutic agent being in the form of particles;
providing a suspending medium, said therapeutic agent particles being insoluble in said suspending medium;

¹ WO96/41628 is cited in the statement of the grounds of rejection, but the text of U.S. Pat. 5,876,760, characterized as “equivalent” to the WO, is referenced in the Answer in setting forth the basis of the rejection (Ans. 3, 5). Because the WO is not in the English language, apparently both the Examiner and Appellants considered the “equivalent” U.S. patent to be its translation. As Appellants have not challenged this, we rely on U.S. Pat. 5,876,760 as the translation of the cited WO. Thus, all references to Sasatani are to the text of the U.S. Patent.

preparing a suspension by placing said therapeutic agent particles and at least one surfactant in said suspending medium, said suspension preparation step further including the step of dissolving at least one excipient in said suspending medium;

spray drying said suspension to obtain therapeutic agent particles coated with said excipient and said surfactant; and

suspending said coated therapeutic agent particles in a propellant gas.

ISSUE ON APPEAL

The Examiner contends that a person of ordinary skill in the art would have been prompted to modify Green's aerosolic drug particulate by coating it with lactose for the advantages described by Sasatani. Appellants contend that Sasatani is directed to tablets and capsules, and thus its teachings about lactose would not be considered helpful in improving drug stability in an aerosol, the type of formulation described in Green and to which the instant claims are directed. In view of these conflicting positions, we frame the issue in this rejection as follows: whether the Examiner erred in finding that Sasatani provides a reason to have coated Green's aerosolic drug particulate with lactose.

SCOPE AND CONTENT OF THE PRIOR ART

In making an obvious determination, the Examiner must first identify the scope and content of the prior art and then ascertain the differences between the prior art and the claimed invention. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). Thus, we first turn to the prior art. The following numbered findings of fact ("FF") summarize the prior art relied upon by the Examiner in setting forth the basis of the rejection (Ans. 3-5):

Green

1. Green relates to aerosol formulations for the administration of a therapeutic drug particulate (“medicament”) by inhalation (Green, at 1, ll. 3-5).
2. The drug particulate is combined with a sugar, such as lactose (Green, at 4, ll. 22-24; *see Ans.* 4).
3. The drug particulate and sugar are dispersed in a propellant, preferably 1,1,1,2-tetrafluoroethane or 1,1,1,2,3,3,3-heptafluoro-n-propane (Green, at 5, ll. 5-9; *see Ans.* 4).
4. Green teaches that the aerosol formations can also comprise surfactants (Green, at 5, ll. 30 to 6, l. 21; *see Ans.* 4).
5. The “surfactant may be incorporated into the aerosol formulation in the form of a surface coating on the” drug. (Green, at 6, ll. 23-25; *see Ans.* 4.)
6. The sugar can be dispersed with the drug in the selected propellant or it can “be pre-filled into canisters . . . before filling with the medicament in the selected propellant” (Green, at 7, ll. 20-25; *see Ans.* 4). The sugar can also be coated onto the interior surface of the empty canister by dissolving the sugar in a suitable liquid and adding it to the canister (Green, at 9, ll. 12-15).
7. Green also states that its formulations may comprise other excipients, but does not describe the drug particulate as being coated with them (Green, at 7, ll. 10-14).

Sasatani

8. Sasatani teaches “spray-dried granules of pranlukast having improved adhesiveness which are useful for preparing pranlukast-containing tablets or capsules” (Sasatani, at col. 1, ll. 8-11).
9. Sasatani states that

pranlukast is fine powder having very strong adhesiveness. When pranlukast merely mixed with additives is formed into such dose forms as tablets or capsules, the pranlukast powder adheres to a punch, a die, a rotary table and the like, making continuous product difficult.

(Sasatani, at col. 1, ll. 38-42.)

10.

[I]t has now been found that the surface of strongly adhesive pranlukast can be improved . . . by spray-drying to easily and efficiently provide granules having a high pranlukast content (concentration) which have a narrow particle size distribution and very good flow properties with little surface adhesiveness and that the resulting granules can be tableted or capsule-filled in a continuous production with no problem.”

(Sasatani, at col. 2, ll. 17-39.)

Taylor

11. Taylor teaches that a surface coating of surfactant on a medicament enhances its stability in fluorocarbon propellants when used as an aerosol formulation for drug delivery (Taylor, at 1-2; *see Ans.* 5).

DIFFERENCES BETWEEN THE PRIOR ART AND THE CLAIMED INVENTION

Once the scope and content of the prior art has been determined, the next step is to identify the differences between the prior art and the claimed invention. *Graham*, 383 U.S. 1 at 17. The following numbered findings of fact are pertinent to this issue.

The claimed invention

11. Claim 44 is directed to a pharmaceutical aerosol formulation comprising four components:

12. 1) therapeutic drug particles;
13. 2) lactose or trehalose which is spray-dry coated on to the drug particles;
14. 3) at least one surfactant which is spray-dry coated on to the drug particles; and
15. 4) a liquid propellant which comprises 1,1,1,2-tetrafluoroethane or 1,1,1,2,3,3,3-heptafluoropropane.
16. Claim 59 is drawn to a process of preparing a pharmaceutical aerosol formulation comprising spray drying a suspension of an excipient and a surfactant “to obtain therapeutic particles coated with said excipient and said surfactant” and “suspending” the “coated therapeutic agent particles in a propellant gas.”

Differences between the prior art and the claimed invention

17. Green teaches drug coated with surfactant (FF 4, 5) as required by claim 44.
18. As in claim 44, Green’s surfactant coated particles can be suspended in 1,1,1,2-tetrafluoroethane or 1,1,1,2,3,3,3-heptafluoro-n-propane (FF 3).
19. Green’s aerosol formulation contains lactose and other excipients (FF 2, 6, 7), but not coated on the drug as in claim 44.
20. In regard to claim 59, Green describes a drug coated with a surfactant, but not an excipient (FF 2, 6, 7) as required by the claim.
21. Green also does not teach that the surfactant is coated on the particle by spray drying as recited in claim 59.

REASON TO COMBINE THE PRIOR ART

Once the differences between the prior art and the claimed invention have been ascertained, the next step is to identify a reason why persons of

ordinary skill in the art would have been prompted to combine the prior art to have made the claimed invention. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

In this case, the Examiner contends that Sasatani “teaches the coating of lactose onto an anti-inflammatory agents can improve the flowability of the powders during the manufacturing process (See col. 2, lines 5-10)” (Ans. 5). Based on this teaching, the Examiner states:

One of ordinary skill in the art would have been motivated to coat the medicament particles with at least one coating excipient and at least one surfactant [as required by claims 44 and 59] because coating the drug particles with lactose and/or surfactants would improve the surface properties of the steroidial drug particles and thereby having the advantages during manufacturing process. Therefore one of ordinary skill in the art would have reasonably expected that coating the medicament particles with an excipient such as lactose, and surfactants would be effective as an aerosol formulation.

(*id.*)

ANALYSIS

During patent examination, the examiner bears the initial burden of establishing a *prima facie* case of obviousness. *In re Kumar*, 418 F.3d 1361, 1366 (Fed. Cir. 2005). In making an obviousness determination, a reason must be provided as to why persons of ordinary skill in the art would have combined the prior art to have arrived at the claimed invention. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

After reviewing the scope and content of the prior art and the reason for combining it, we conclude that *prima facie* obviousness of the subject matter of claims 44 and 59 has not been established. The difference between the prior art and the claimed invention is that the prior art does not describe

an excipient, such as lactose, coated on a drug particle as required by claims 44 and 59, respectively (FF 19, 20). The Examiner finds, however, that lactose – which is an excipient – is described by Sasatani as having the ability to “improve the flowability of the powders during the manufacturing process” when coated on a drug (Ans. 5). Appellants contend that the Examiner erred in this finding. They state:

[Sasatani] relates to spray-dried granules comprising pranlukast which are useful for preparing pranlukast-containing tablets or capsules. It teaches use of a saccharide to reduce the adhesiveness of pranlukast during mechanical processing into tablets and capsules, i.e., to a punch, die, rotary table, and the like (column 1, lines 8-12, lines 38-42). This patent does not relate to the field of Applicants’ endeavor, aerosol formulations . . . [Sasatani] offers absolutely no suggestion that the use of an excipient coating would be considered to help improve the stability of drug suspensions in propellant gas.

(App. Br. 7.) (Underlining removed.)

We are persuaded by Appellants’ argument that the Examiner erred in combining the references. According to Sasatani, pranlukast is a strongly adhesive fine powder that adheres to a punch, die, etc., when being formed into tablets and capsules (FF 9). To address this problem, Sasatani describes coating it with a saccharide, such as lactose, to enable “continuous production [of tablets and capsules] with no problem” (FF 10). Sasatani does not disclose or suggest that the coating would be useful for aerosols in which the particles are suspended in a propellant. Rather, Sasatani teaches that the lactose coating is useful for making tablets and capsules (FF 8-10). The Examiner has not provided any evidence that persons of ordinary skill in the art would have recognized that the benefits of lactose describes by Sasatani for tablets and capsules that are produced mechanically in dies

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would have been advantageous for drug particulates dispersed in a liquid aerosol. To the contrary, Green either disperses the lactose and drug in the aerosol propellant or coats the lactose to the canister surface (FF 6). Thus, on this record, we do not find any facts that would have prompted a person to have coated the drug with lactose, or any other excipient, when used in an aerosol formulation as recited in claims 44 and 59.

We reverse the rejection of claim 44-57, 59-74, 85-87, 95, and 96 under 35 U.S.C. § 103(a) as obvious over Green, Sasatani, and Taylor.

REVERSED

Ssc:

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