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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KARL KOLTER, MAXIMILIAN ANGEL, MATTHIAS KARL, SILKE GEBERT, and MICHAEL KLEMENS MŰLLER

Appeal 2018-000219
Application 13/919,092
Technology Center 1600

Before ERIC B. GRIMES, TAWEN CHANG and JOHN E. SCHNEIDER, *Administrative Patent Judges.*

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, 2, 4–6, 17, and 18. 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 BASF SE (BASF), Ludwigshafen, Germany. Appeal Br. 3.

BACKGROUND

CLAIMED SUBJECT MATTER

The claims are directed to a solid dispersion. Claim 1 is illustrative:

> 1. A solid dispersion comprising a hydrophobic active ingredient and an antioxidant embedded in a polymer matrix that comprises a cationic copolymer of N,N-diethylaminoethyl methacrylate and methyl methacrylate in a weight ratio of the monomers of from 35:65 to 55:45, wherein the solid dispersion comprises 10 to 50% by weight of the hydrophobic active ingredient and the hydrophobic active ingredient is not an antioxidant and wherein the hydrophobic active ingredient is present in amorphous form, is embedded in the polymer matrix in microdisperse or molecular disperse form, and is a biologically active ingredient selected from the group consisting of pharmaceutical active ingredients for humans and animals for orally administrable formulations.

Appeal Br. A-1 (Claims App.).

REJECTION(S)

A. Claims 1, 2, 4–6, 17, and 18 are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over the Kollicoat® Presentation[2] and

[2] BASF, Kollicoat® Smartseal 30D: The First Aqueous Polymer Dispersion for Taste Masking & Moisture Protection (Oct. 2010) ("Kollicoat® Presentation").

Papageorgiou,[3] as evidenced by the definition of alkannin in Dictionary.com.[4] Ans. 2.

B. Claims 1, 2, 4–6, 17, and 18 are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Angel[5] and Löbmann.[6] Ans. 2.

DISCUSSION

A. Obviousness over the Kollicoat® Presentation and Papageorgiou, as evidenced by the definition of alkannin in Dictionary.com (Claims 1, 2, 4–6, 17, and 18)

1. Issue

The Examiner finds that the Kollicoat® Presentation teaches a composition comprising a caffeine core and a spray dried coating, wherein the coating comprises Kollicoat® Smartseal 30D, which reads on the copolymer of the invention. Final Act. 4–5.

With respect to the limitations relating to "[a] solid dispersion" wherein the active ingredient is "embedded in the polymer matrix in microdisperse or molecular disperse form," the Examiner finds that the Kollicoat® Presentation teaches that its composition is prepared as a liquid suspension comprising the polymer and other agents and finds that,

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[3] Vassilios P. Papageorgiou et al., *The Chemistry and Biology of Alkannin, Shikonin, and Related NAphthazarin Natural Products*, 38 ANGEWANDTE CHEMIE INT'L EDITION 270 (1999).
[4] "Alkannin." Dictionary.com, https://www.dictionary.com/browse/alkannin (last visited Oct. 23, 2019) (defining alkannin as "a dark red, amorphous, water-insoluble powder, $C_{16}H_{16}O_5$, obtained from the root of the alkanet: used chiefly for coloring fats, oils, and phamaceuticals").
[5] Angel et al., US 2011/0033532 A1, published Feb. 10, 2011.
[6] Korbinian Löbmann et al., *Coamorphous Drug Systems: Enhanced Physical Stability and Dissolution Rate of Indomethacin and Naproxen*, 8 MOLECULAR PHARMACEUTICS 1919 (2011).

> [b]ecause all the agents are combined and dispersed in a liquid solvent prior to drying, it can be assumed that the polymer and the other active agents are homogenously dispersed. Once sprayed, the composition is dried as a film, which is implied as being a solid composition, wherein the actives are homogenously mixed (i.e. embedded) into the polymer. . . . No alternative or special definition of "embedded" is provide[d], thus the Examiner is interpreting simply mixing the polymer matrix and the active agent will result in an embedded mixture wherein the active agent is microdisperse or molecularly dispersed. Moreover, it can be presumed that all phases of the composition are solid, once dried, as required in the definition of a solid dispersion in the instant specification. Finally, the composition of [the Kollicoat® Presentation] is a coating applied as a dried film as a sprayed suspension . . . . The instant specification defines "solid dispersion" and teaches preparing films prepared by spray-drying compositions as suitable embodiments.

Final Act. 5 (citations omitted).

The Examiner finds that the Kollicoat® Presentation does not teach a non-antioxidant hydrophobic active agent. Final Act. 6. However, the Examiner finds that the Kollicoat® Presentation teaches that its composition may comprise 0–50% pigments and 2–10% colorants. *Id.* at 5. The Examiner finds that Papageorgiou teaches that alkannin is a pigment for food colorings and cosmetics that is not toxic when administered orally and that has also been shown to have "significant anti-tumor, antibacterial, and anti-inflammatory activities." *Id.* at 6. The Examiner finds that dictionary.com defines alkannin as "an amorphous water-insoluble (aka hydrophobic) powder obtained from the root of alkanet." *Id.*

The Examiner concludes that

> [i]t would have been *prima facie* obvious to have made the coating composition of [the Kollicoat® Presentation] as a solid dispersion and adjusted . . . the amount of pigment in the range

> of 0–50%, which overlaps with the claimed range of 20–50% of active agent. . . . Since [the Kollicoat® Presentation] allows for any pigment to be used, the skilled artisan would have found it obvious to look to Papageorgiou, which teaches alkannin as a pigment useful in cosmetic compositions. The resulting composition would comprise alkannin in 0–50%, addressing instant claims 1–6 and 17–18.

Id.

Appellant contends that the Kollicoat® Presentation "fails to teach or suggest a solid dispersion of an *amorphous, hydrophobic active ingredient* embedded in a polymer matrix in microdisperse or micromolecular form," as required by independent claim 1. *Id.* at 14, 18.

In particular, Appellant contends that "[t]he core/coating disclosed in [the Kollicoat® Presentation] is substantially different from the presently claimed *solid dispersion* wherein the hydrophobic active ingredient is embedded in the polymer matrix in a microdisperse form or a molecular disperse form." Appeal Br. 13. Appellant contends that the coating composition of the Kollicoat® Presentation is a dried suspension rather than a solid dispersion. *Id.* at 16. Appellant also contends that caffeine, the active ingredient in the composition described in the Kollicoat® Presentation, is neither hydrophobic nor in amorphous form. *Id.* at 13. Appellant further contends that "[a] skilled person would not consider solubilizing a pharmaceutically active ingredient" based on the teachings of the Kollicoat® Presentation. *Id.* at 14.

With respect to the Examiner's assertion that alkannin, a pigment, is also a "pharmaceutical active ingredient," Appellant contends that dyes are not pharmaceutically active ingredients within the meaning of the claims. *Id.* at 15. Appellant contends that Papageorgiou discloses wound-healing and anti-inflammatory effects of alkannin solely for ointments and does not

suggest that alkannin has any antitumor, antimicrobial, or antithrombotic activities. *Id.* at 11, 16–17. Appellant contends that alkannin is not necessarily in an amorphous form. *Id.* at 17. Appellant contends that a skilled artisan would not consider a cosmetic pigment such as alkannin to be an orally administrable drug, particularly because alkannin has toxic effects. *Id.* at 18.

Appellant further contends that a skilled artisan has no reason to combine, or a reasonable expectation of success in combining, the Kollicoat® Presentation with Papageorgiou to arrive at the claimed invention. *Id.* at 18–19.

Finally, Appellant contends that the claimed subject matter exhibits unexpected results. *Id.* at 19–20.

The issue with respect to this rejection is whether a skilled artisan would have had reason to combine the teachings of the Kollicoat® Presentation and Papageorgiou to arrive at the claimed invention.

2. Analysis

On balance, we find Appellant to have the better case.

Kollicoat® Smartseal 30D is a "30% aqueous dispersion" of a 6:4 methyl methacrylate — diethylaminoethyl methacrylate copolymer, which meets the polymer matrix limitation of claim 1, the only independent claim. Kollicoat® Presentation 5–6. However, as the Examiner acknowledges, the Kollicoat® Presentation does not suggest embedding in the polymer matrix a non-antioxidant, hydrophobic, and orally administrable "pharmaceutical active ingredient[] for humans and animals," as recited in claim 1. Final Act. 6.

As discussed above, the Examiner argues that these limitations are nevertheless met because the Kollicoat® Presentation also recommends that

Kollicoat® Smartseal 30D be formulated with pigments such as talc, and Papageorgiou teaches that alkannin, a pigment which is used for food coloring, is also pharmaceutically active. Final Act. 5–6. The Examiner asserts that such use of alkannin would have been obvious since the Kollicoat® Presentation does not limit the pigments that may be used in the formulation of Kollicoat® Smartseal 30D and Papageorgiou teaches that alkannin is useful as a pigment.

We are not persuaded because the Examiner has not sufficiently articulated a reason for a skilled artisan to use alkannin as the pigment in Kollicoat® Smartseal 30D. In particular, the Examiner has not cited persuasive evidence that all pigments are functionally equivalent for the purposes of their usefulness in Kollicoat® Smartseal 30D. For instance, the Kollicoat® Presentation explains that pigments are particularly important for moisture barrier formulations and that talc shows the best results. Kollicoat® Presentation 12. The Examiner has not cited evidence that alkannin is functionally equivalent to talc as a moisture barrier.[7]

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of

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[7] In response to the Appeal Brief, the Examiner states that the Kollicoat® Presentation teaches that its coating composition "may further comprise coloring agents such as titanium dioxide, which is known as being a hydrophobic active agent." (Ans. 3.) We are not persuaded. As an initial matter, the Examiner does not cite, and we have not been able to locate, where the Kollicoat® Presentation teaches inclusion of titanium dioxide as a coloring agent. More importantly, the Examiner has not cited evidence that titanium dioxide is a "pharmaceutical active ingredient[] for humans and animals for orally administrable formulations," as required by claim 1.

obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (*quoting In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). Accordingly, we reverse the Examiner's rejection of claims 1, 2, 4–6, 17, and 18 as obvious over the combination of the Kollicoat® Presentation and Papageorgiou in view of the definition of alkannin set forth in Dictionary.com.

B. Obviousness over Angel and Löbmann (Claims 1, 2, 4–6, 17, and 18)

1. Issue

The Examiner finds that Angel teaches a composition formulated as a mixture of polymer dispersion and excipient in powder form. Final Act. 13. The Examiner finds that the polymer of Angel's composition comprises the claimed ingredients in a weight ratio that overlaps the claimed ranges. *Id.* The Examiner finds that Angel teaches that "[t]he polymeric dispersion has a solids content . . . of 10–50% by weight of the total composition" and can comprise at least one pharmaceutically acceptable active ingredient, including hydrophobic active agents that may be administered orally, as required by claim 1. *Id.* at 13–14.

With respect to the limitation that the composition be a solid dispersion wherein the hydrophobic active ingredient is "present in amorphous form" and "embedded in the polymer matrix in microdisperse or molecular disperse form," the Examiner finds that "simply mixing the polymer matrix and the active agent will result in an embedded mixture wherein the active agent is microdisperse or molecularly dispersed." *Id.* at 14. The Examiner further finds that

> it can be presumed that all phases of the composition are solid, once dried, as required in the definition of a solid dispersion in the instant specification. The instant specification . . . teaches

> preparing films prepared by spray-drying compositions as suitable embodiments. Angel teaches that the polymer dispersion of their invention can be "intimately mixed" for making a coating composition. The coating composition, which comprises the polymer dispersion, active agent, and excipient, can be dried into a film by use of heat. Thus, it can be at once envisaged that the intimate mixing of the dispersion with the active followed by heating to dry results in the active embedding in the polymer and the overall composition being a solid dispersion.

Id. (citations omitted).

The Examiner finds that Angel does not teach the active agent being amorphous. *Id.* at 15. However, the Examiner finds that Löbmann teaches converting a crystalline drug into an amorphous form in order to increase its solubility. *Id.*

The Examiner concludes that a skilled artisan would have found it obvious to combine the various elements in Angel discussed above because such combination is no more than "the predictable use of prior art elements according to their established functions." *Id.* at 16. The Examiner further concludes that a skilled artisan would have found it obvious to use an amorphous form of the active agent in the combination because Löbmann teaches that "converting a crystalline agent to an amorphous one increases dissolution and solubility of said agents." *Id.*

Appellant contends that, like the Kollicoat® Presentation, Angel "merely discloses a polymeric shell surrounding a drug core" and "does not teach or suggest embedding a hydrophobic active ingredient and an antioxidant in [the] polymer matrix, let alone in an amorphous form *and* in a microdisperse or molecular disperse form." Appeal Br. 23. Appellant contends that a skilled artisan would not have had reason to "select[] a claimed pharmaceutical active from the extensive list of . . . pharmaceutical

agents disclosed" in Angel and then to modify Angel to arrive at the claimed invention, with a reasonable expectation of success. *Id.* at 25.

Appellant contends that a skilled artisan would have had no reason to combine Angel with Löbmann, because Angel is "directed *solely* to the coating for a drug core." *Id.* at 26. Appellant contends that, in any event, Löbmann fails to cure the deficiencies of Angel because Löbmann teaches "a coamorphous formulation in which a polymer is *eliminated*" in order to "overcome the disadvantages of a polymer-stabilized amorphous drug form." *Id.* at 25. Appellant contends that, based on Löbmann, a skilled artisan "would have had no apparent reason to consider stabilizing an amorphous drug with a polymer," because "Löbmann discourages the use of a polymer as a stabilizer for amorphous drugs." *Id.*

Finally, Appellant contends that the Examiner's rejection is based on impermissible hindsight and that the subject matter of the invention exhibits unexpected results. *Id.* at 26.

The issue with respect to this rejection is whether a skilled artisan would have had reason to combine the teachings of Angel and Löbmann to arrive at the claimed invention.

2. Analysis

On balance, we find Appellant to have the better argument.

The Examiner asserts that Angel teaches a composition comprising a polymer dispersion that meets the copolymer limitation of claim 1, excipients such as antioxidants and pigments, and pharmaceutical active ingredient. Final Act. 13–14. The Examiner asserts that, "under the broadest reasonable interpretation of the prior art, the composition may be blended together as required in the instant claims." *Id.* at 17.

We are not persuaded. We agree that Angel teaches a composition comprising a hydrophobic active ingredient, a copolymer of N,N-diethylaminoethyl methacrylate and methyl methacrylate, and antioxidant, as recited in claim 1. *See, e.g.*, Angel ¶¶ 42–49 (teaching a polymer dispersion comprising N,N-diethylaminoethyl methacrylate and methyl methacrylate wherein the N,N-diethylaminoethyl methacrylate is preferably in an amount from 25–65% by weight and methyl methacrylate is preferably in an amount from 35–75% by weight), ¶¶ 98, 137, and 213 (possible to add conventional excipients and additives to the polymer dispersion, including, e.g., antioxidants), ¶¶ 185–188, 192 and claim 63 (describing pharmaceutical composition comprising a polymer composition obtainable by drying and/or forming a film of the polymer dispersion, a pharmaceutically acceptable active ingredient, and a pharmaceutically acceptable excipient, and listing examples of suitable active ingredients).

Nevertheless, the Examiner has not articulated a persuasive reason why a skilled artisan would have combined these components in the particular manner recited in claim 1, the only independent claim, i.e., where the hydrophobic active ingredient is embedded in the polymer matrix.

The Examiner asserts that a skilled artisan would have found it obvious to combine the various teachings of Angel in the manner of claim 1 because such combination is no more than "the predictable use of prior art elements according to their established functions." Final Act. 16. However, the Examiner has cited to no persuasive evidence that embedding a pharmaceutical active ingredients in a polymer matrix to form a solid dispersion is a predictable use of these prior art elements.

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning

with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (*quoting In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). Accordingly, we reverse the Examiner's rejection of claims 1, 2, 4–6, 17, and 18 as obvious over the combination of Angel and Löbmann.

CONCLUSION

In summary:

Claims Rejected	**35 U.S.C. §**	**Reference(s)/Basis**	**Affirmed**	**Reversed**
1, 2, 4–6, 17, 18	103(a)	Kollicoat® Presentation, Papageorgiou, definition of alkannin from Dictionary.com		1, 2, 4–6, 17, 18
1, 2, 4–6, 17, 18	103(a)	Angel, Löbmann		1, 2, 4–6, 17, 18
Overall Outcome				1, 2, 4–6, 17, 18

REVERSED