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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SOONG HO UM AND SEUNG WON SHIN

Appeal 2017-003300
Application 14/513,970[1]
Technology Center 1600

Before DONALD E. ADAMS, DEBORAH KATZ, and
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of producing a DNA-lipid particle, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

STATEMENT OF THE CASE

"Liposomes are spherical vesicles in which a phospholipid bilayer surrounds an aqueous phase filling an inner space of the vesicle." (Spec. 1.) "[L]iposomes are receiving attention as a particle structure prepared through

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[1] Appellant, is the Applicant, RESEARCH & BUSINESS FOUNDATION SUNGKYUNKWAN UNIVERSITY, which Appellant identifies as the real party in interest. (*See* BIB DATA SHEET; Appeal Br. 3.)

assembly with polymers, drugs, and antigens." (*Id.* at 2.) The claimed invention is directed at making particles using water-soluble polymers, lipids, and an organic solvent.

Claims 12, 14–16, and 23–26 are on appeal.[2] Claim 12 is representative and reads as follows:

> 12. A method of producing a particle, comprising:
>
> a) mixing a water-soluble polymer, a lipid, and an organic solvent to form a mixed solution;
>
> b) preparing an emulsion by stirring the mixed solution or treating the mixed solution with ultrasonic waves; and
>
> c) removing the organic solvent from an upper layer of the emulsion by centrifugation of the emulsion,
>
> wherein the water-soluble polymer is a polydeoxyribonucleic acid crosslinked by covalent bond.

(Appeal Br. 17.)

The following grounds of rejection by the Examiner are before us on review:

Claims 12, 14–16, and 23–25 under 35 U.S.C. § 103 as unpatentable over Irvine,[3] Schneider[4] and Tiwari.[5]

Claim 26 under 35 U.S.C. § 103 over Irvine, Schneider, Tiwari, and Payne.[6]

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[2] Claims 17–22 stand withdrawn from consideration. (Appeal Br. 17.)
[3] Irvine et al., US 2010/0323018 A1, published Dec. 23, 2010.
[4] Schneider, US 4,224,179, issued Sep. 23, 1980.
[5] Tiwari et al., *Development and characterization of novel carrier gel core liposomes based transmission blocking malaria vaccine*, 140 J. Controlled Release, 157–65 (2009).
[6] Payne et al., US 4,744,989, issued May 17, 1988.

DISCUSSION

Obviousness of claims 12, 14–16, and 23–25

The Examiner finds that Irvine teaches making lipid-coated DNA-hydrogel nanoparticles. (Final Action 3.) The Examiner explains that the process Irvine teaches does not require the use of organic solvents and involves mixing dried phospholipid film with an aqueous solution of X-DNA and a crosslinking agent and then sonicating the mixture. (*Id.*) The Examiner explains that Irvine teaches that a solvent-less process allows for the resultant nanoparticles to be suitable for in vivo use. (*Id.*) The Examiner notes, that while a solvent is not required by Irvine, Irvine does not teach away from the use of a solvent in the process of making a lipid-coated DNA-hydrogel nanoparticle. (*Id.*; *see also* Ans. 5–6.)

The Examiner notes that Schneider teaches a method of preparing liposomes that uses an organic solvent. (Final Action 3) In the Schneider method, explains the Examiner, a solution of a phospholipid in an organic solvent is sonicated with a solution to be encapsulated and then the liposome precursor formed is centrifuged, which results in the precursor moving from the organic solvent phase to the aqueous phase crossing the organic-water interphase that includes a lipid barrier. (*Id.*) The liposome encapsulating the desired solution forms during passage through the lipid barrier. (*Id.*) The Examiner notes that Schneider "teaches that this method has improved yields and avoids the need for recovery and replenishment of the concentration in active ingredients of the initial aqueous liquid." (*Id.* at 4.) The Examiner relies on Tiwari for teaching that the method of preparing liposomes described in Schneider is suitable for preparing gel core liposomes. (*Id.*)

The Examiner contends that it would have been obvious to one of ordinary skill in the art to have used an organic solvent as taught in Schneider with the amphiphilic phospholipid and X-DNA of Irvine and then to have removed the solvent with centrifugation as taught by Schneider because such a process would have been expected to result in improved yields and to avoid the "need for recovery and replenishment of the concentration in active ingredients of the initial aqueous liquid." (*Id.*)

Appellant argues that the Examiner's rejection is in error for two reasons. First, Appellant argues that Irvine teaches away from using an organic solvent. (Appeal Br. 11–13; Reply Br. 2–3.) Second, Appellant argues that Schneider is a very different process from that described by claim 12 and thus "[a] person skilled in the art would not have been motivated to combine Irvine, Schneider, and Tiwari to arrive at claim 12." (Appeal Br. 14).[7]

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[7] In its Reply Brief, Appellant newly argues that the method taught by Schneider "is not applicable to Irvine and/or Tiwari" because "Schneider's methods are for preparing a second aqueous liquid containing liposomes that encapsulate a first aqueous liquid" whereas "Irvine or Tiwari does not involve encapsulating a first aqueous liquid into a second aqueous liquid." (Reply Br. 4) "[T]he reply brief [is not] an opportunity to make arguments that could have been made in the principal brief on appeal to rebut the Examiner's rejections, but were not." *Ex parte Borden*, 93 USPQ2d 1473, 1474 (BPAI 2010) (informative). As stated in *Ex parte Borden*, consideration by the Board of new arguments presented for the first time in the Reply Brief that could have been presented earlier would "vitiate the force of the requirement in Board Rule 37(c)(1)(vii) that '[a]ny arguments or authorities not included in the brief . . . will be refused consideration by the Board, unless good cause is shown.'" *Id.* Appellant has not demonstrated any specific Examiner findings presented for the first time in the Answer necessitating this new argument in rebuttal in the Reply Brief. Nor do we

We do not find Appellant's arguments persuasive.

We agree with the Examiner that Irvine does not teach away from using an organic solvent. It is true, as Appellant asserts, that a reference teaches away from a claimed invention if it "criticize[s], discredit[s], or otherwise discourage[s]" modifying the reference to arrive at the claimed invention. *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). That is not what Irvine does, however. Irvine merely explains that an organic solvent is not needed in some embodiments of its disclosure. (Irvine ¶ 26 ("In some embodiments, the method does not comprise the use of organic solvents."), ¶ 96 ("the particles *may be* synthesized in aqueous conditions without the use of organic solvents"), and ¶ 104 ("The method does not require the use of organic solvents.").) "A reference does not teach away, [] if it merely expresses a general preference for an alternative invention but does not criticize, discredit, or otherwise discourage investigation into the invention claimed." *Galderma Labs., L.P. v. Tolmar, Inc.,* 731 F.3d 731, 738 (Fed. Cir. 2013).

Under 35 U.S.C. § 103, a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. *In re Lamberti*, 545 F.2d 747 (CCPA 1976); *In re Simon*, 461 F.2d 1387 (CCPA 1972). That Irvine discloses that an organic solvent is not needed in some embodiments, fairly suggests that an organic solvent can be used. That is true even though Irvine teaches that when an organic solvent is not used, there are advantages to the particle so produced, i.e., they are suitable for in

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find any substantial differences in the Examiner's initial findings and the Examiner's findings stated in the Answer that would warrant the new arguments presented in the Reply Brief for the first time.

vivo use. (Reply Br. 4 (quoting Irvine ¶ 104).) As Irvine teaches, the particles are contemplated for in vitro use as well. (Irvine ¶ 175.)

Regardless of whether the particles are to be used in vivo, or in vitro, Schneider teaches that when lipid particles encapsulating another ingredient are made in the presence of an organic solvent, the solvent is separated from the particles by classical methods, such as centrifugation. (Schneider 5:37–43 3:32–60.) In light of the teachings of Irvine and Schneider, it would have been obvious to have used an organic solvent in the method of Irvine, as Irvine itself suggests, and it would have been obvious to have removed the organic solvent from the particles using centrifugation, a classical separation technique, as taught by Schneider. "It is well-established that the Board is free to affirm an examiner's rejection so long as 'appellants have had a fair opportunity to react to the thrust of the rejection.'" *In re Jung*, 637 F.3d 1356, 1365 (Fed. Cir. 2011) (*citing In re Kronig*, 539 F.2d 1300, 1302–03 (CCPA 1976)). While the Examiner gave a different reason for relying on Schneider, we note that the Examiner, nevertheless, pointed Appellant to disclosure in Schneider that teaches separation of lipid particles from organic solvent by centrifugation and indicated that such a procedure would have been obvious to one of ordinary skill in the art to separate the lipid particles in the aqueous medium from the separate organic solvent phase. (Final Action 3–4). Thus, we determine that Appellant has had an opportunity to respond to the thrust of the obviousness of claim 12 as we articulated it above. [8]

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[8] We further note that while the Examiner relies on Tawari to establish that the method of Schneider can be used to make gel core liposomes, which is the particle made in Irvine, we do not find it necessary to rely on the

Appellant's second argument appears to suggest that Schneider is non-analogous art because it is "significantly different" than the claimed invention. (Appeal Br. 13.) We disagree. "Two criteria have evolved for determining whether prior art is analogous: (1) whether the art is from the same field of endeavor, regardless of the problem addressed, and (2) if the reference is not within the field of the inventor's endeavor, whether the reference still is reasonably pertinent to the particular problem with which the inventor is involved." *In re Clay*, 966 F.2d 656, 658–59 (Fed. Cir. 1992). As Appellant acknowledges, Schneider teaches sonicating a mixture to create particles. (Appeal Br. 13.) We further note that the particles that are created are lipid based particles obtained from a mixture of water-soluble polymer, lipid, and an organic solvent. These are the compositional elements required of claim 12 to form the claimed particles. Thus, we find that Schneider is in the same field of endeavor as the claimed invention, even if there are differences between Schneider and claim 12.

For the reasons set forth above, we are not persuaded that the Examiner erred in rejecting claim 12 as being obvious over Irvine, Schneider, and Tawari.

Claims 14–16 and 23–25 have not been argued separately and therefore fall with claim 12. 37 C.F.R. § 41.37(c)(1)(iv).

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teachings of Tawari to affirm the Examiner's obviousness rejection. *See In re Bush*, 296 F.2d 491, 496 (CCPA 1961) (holding that the Board may rely on fewer references than relied upon by the Examiner without designating it as a new ground of rejection).

Obviousness of Claim 26

The Examiner relies on Payne for teaching that the use of ethyl acetate as the organic solvent for forming liposomes would have been obvious to one of ordinary skill in the art. (Final Action 5.) Appellant does not contest the Examiner's findings in this regard. Rather, Appellant argues only that "Payne does not cure the deficiency that the combination of Irvine, Schneider and Tiwari lacks to make claim 12 obvious to a person skilled in the art." (Appeal Br. 14.) For the reasons discussed previously, however, we do not find Appellant's arguments concerning the alleged infirmity of the Examiner's rejection of claim 12 over the combination of Irvine, Schneider, and Tawari persuasive. Thus, we are not persuaded that the Examiner erred in rejecting claim 26 as being obvious over Irvine, Schneider, Tawari, and Payne.

SUMMARY

We affirm the rejection of claims 12, 14–16, and 23–25 under 35 U.S.C. § 103(a) as unpatentable over Irvine, Schneider and Tiwari.

We affirm the rejection of claim 26 under 35 U.S.C. § 103(a) over Irvine, Schneider, Tiwari, and Payne.

TIME PERIOD FOR RESPONSE

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

AFFIRMED