UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte FREDERIC BATTEUX, and BERNARD WEILL

Appeal 2007-0622
Application 10/475,555
Technology Center 1600

HEARD: March 8, 2007

Before SCHEINER, GRIMES, and LINCK, *Administrative Patent Judges*.

LINCK, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellants appeal the Examiner's §§ 102(b) and 103(a) rejections of claims 1-5 and 8-18, all pending claims in the above-identified application, filed October 22, 2003.[1] We have jurisdiction to decide this appeal under 35 U.S.C. § 6(b).

We affirm.

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[1] The assignee is Universite Rene Descartes (Paris V).

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STATEMENT OF THE CASE

The claimed invention is "[a] method for treating hepatocellular deficiency, comprising administering mangafodipir to a patient in need thereof." Claim 1. Some of the dependent claims limit the hepatocellular deficiency to one "of toxic origin" (claim 2), or induced by acetaminophen (claim 3) or alcohol (claim 4); or to a deficiency that "manifests itself in the form of fulminant hepatitis" (claim 5). Others specify dosage ranges (claims 8 and 9), or the method of administration (claims 10-14), or both dosage range and method of administration (claims 15-18).

There are three grounds of rejection in this case. The first to be reviewed on appeal is of claims 1, 2, 9, 11, 14, and 18 under 35 U.S.C. § 102 (b) based on Yicheng et al., "Experimental Liver Cancers: Mn-DPDP-enhanced Rims in MR-Microangiographic-Histologic Correlation Study," Radiology 1993; 188: 45-51 ("Yicheng"). The second ground to be reviewed is of claims 1 and 8-18 under § 102(b) based on Karlsson et al. WO 97/49409, published December 31, 1997. The last ground to be reviewed is of claims 2-5 under 35 U.S.C. § 103(a) based on Karlsson and Cecil, Textbook of Medicine, vol. 1, 815 & 817 (21st ed. 2000) (W.B. Saunders Co., editor) ("Cecil").

The Examiner also relies on portions of "Drugs of the Future" (1997) and Stedman's Medical Dictionary (27th ed. (on-line) ("Stedman's")) to establish the molecular weight of mangafodipir ("MnDPDP") and the meaning of certain terms, respectively. Appellants do not challenge the Examiner's use of these references.

ISSUES ON APPEAL

Claim 1

The Examiner contends that Yicheng's administration of MnDPDP to mice and rabbits suffering from hepatocellular carcinoma ("HCC"), induced with a chemical carcinogen, anticipates claim 1. Answer 5-6, 11-17. The Examiner further contends that Karlsson's treatment of a patient with MnDPDP either prior to, during or subsequent to a liver transplant anticipates claim 1. Answer 6-8, 17-21. To support his position and respond to Appellants' arguments, the Examiner relies on, inter alia, *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365, 52 USPQ2d 1303, 1305-06 (Fed. Cir. 1999). Answer 4 ("it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art").

Appellants contend they have discovered a new use for an old compound and thus are entitled to a patent (Br. 4), given that neither reference administered MnDPDP "with the specific intent" to treat hepatocellular deficiency (Br. 7, 14). Appellants further contend the Examiner has not established that "the prior art regimen would necessarily result . . . in practicing the claimed methods" (Br. 8 (discussing Yicheng)). *See also* Br. 14 (making the same argument with respect to Karlsson). To support their contentions, Appellants rely heavily on *Jansen v. Rexall Sundown Inc.*, 342 F.3d 1329, 68 USPQ2d 1154 (Fed. Cir. 2003) and *Rapoport v. Dement*, 254 F.3d 1053, 59 USPQ2d 1215 (Fed. Cir. 2001).

We frame the issues to be decided as follows:

Do Yicheng and/or Karlsson inherently anticipate claim 1, even though neither reference discloses any intent to treat patients for hepatocellular deficiency? Would the disclosed prior art methods necessarily result in "treating hepatocellular deficiency"?

FINDINGS OF FACT

Interpretation of Claim 1

Claim 1 does not specify a dosage or any treatment regimen, or require that "an effective amount" of MnDPDP be administered to a patient. Thus, claim 1 does not require "treating" to be effective against hepatocellular deficiency.

The term "hepatocellular deficiency" is interpreted broadly in view of the definition in the specification and includes hepatocellular carcinoma, or HCC, and the total absence of the liver. See Spec. at 3 ("A set of pathological manifestations resulting from the destruction of hepatocytes are included under the term 'hepatocellular deficiency'" (quoted by the Examiner (Answer 15))). *See also* Answer 5-6.

The term "patient in need thereof" includes animals such as mice and rabbits. *See* Answer 6.

Claim 1 does not require administration of MnDPDP for any particular length of time or any number of treatments.

The Prior Art Teachings

Yicheng discloses "both animal and clinical studies" with MnDPDP, a contrasting agent "designed to be taken up by hepatocytes." Yicheng at 1.

Yicheng describes administering MnDPDP to mice and rabbits to image liver tumors, induced with chemical carcinogens. *Id.*

The term "toxin" includes chemical carcinogens. *See* Answer 5.

Yicheng uses a dosage calculated to be within that disclosed by Appellants (19 mg/kg). *See* Answer 6 (citing Yicheng at 46, col. 1, middle of 2nd full paragraph).

Karlsson discloses treating patients with MnDPDP to prevent or treat ischemia-related diseases and discloses using it to treat a patient in connection with a liver transplant: "A further use of the compounds . . . is in relation to organ transplantation, e.g. with . . . liver . . . transplants. In this regard, the compounds may be administered to the organ donor or recipient either prior to, during or subsequent to transplant surgery." Karlsson at 7.

Karlsson teaches a dosage range calculated to overlap with that disclosed by Appellants (0.007-76 mg/kg). *See* Answer 7-8 (citing Karlsson at 14, 2nd full paragraph).

Other Findings

Substantially all liver transplants are due, at least in part, to "hepatocellular deficiency," as broadly defined. *See* Cecil at 817, Table 155-1 (identifying the "10 most common indications for liver transplantation"). The "Surgeon General Reports," submitted by Appellants, also supports this finding. Br. 13 (reference "describes that liver transplantation is a therapy for a variety of indications *causing damage to the liver*") (emphasis added).

A patient suffering from "hepatocellular deficiency" would necessarily be treated for that deficiency if administered MnDPDP, as required by claim 1 and as taught by Yicheng or Karlsson.

PRINCIPLES OF LAW

Regarding claim interpretation during patent prosecution,

> the Board is required to use a different standard for construing claims than that used by district courts. . . . [I]t is error for the Board to "appl[y] the mode of claim interpretation that is used by courts in litigation, when interpreting the claims of issued patents in connection with determinations of infringement and validity." *In re Zletz,* 893 F.2d 319, 321 (Fed.Cir.1989); *accord In re Morris,* 127 F.3d 1048, 1054 (Fed.Cir.1997) ("It would be inconsistent with the role assigned to the PTO in issuing a patent to require it to interpret claims in the same manner as judges who, post-issuance, operate under the assumption the patent is valid."). Instead . . . , the PTO is obligated to give claims their broadest reasonable interpretation during examination.

In re American Academy of Science Tech Center, 367 F.3d 1359, 1369, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004).

Following a long line of cases, the Federal Circuit clarified the law on inherency, i.e., whether those skilled in the art must be aware of the inherent characteristic, particularly with respect to method claims:

> A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation. *Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565 [24 USPQ2d 1321] (Fed. Cir. 1992). Thus, a prior art reference without express reference to a claim limitation may nonetheless anticipate by inherency. *See In re Cruciferous*

> *Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claim's limitations, it anticipates." *Id.* (quoting *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999). Moreover, "[I]nherency is not necessarily coterminous with knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art." *Id.*; *see also Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition in the prior art) (citing *In re Cruciferous Sprout Litig.*, 301 F.3d at 1351; *MEHL/Biophile*, 192 F.3d at 1366).

Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1375-76, 77 USPQ2d 1321, 1325-26 (Fed. Cir. 2005).[2] "Thus, when considering a prior art method, the anticipation doctrine examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure." *Id.* at 1378, 77 USPQ2d at 1327.

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. [Citations omitted.] If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

Hansgirg v. Kemmer, 102 F.2d 212, 214, 40 USPQ 665, 667 (CCPA 1939), *quoted in Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1269,

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[2] We note this case was decided only a few days before Appellants' Appeal Brief was filed.

20 USPQ2d 1746, 1749 (Fed. Cir. 1991). In other words, "a limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." *Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1379, 67 USPQ2d 1664, 1669 (Fed. Cir. 2003), *quoted in Perricone*, 432 F.3d at 1377, 77 USPQ2d at 1327.

With respect to a number of the dependent claims, the "existence of overlapping or encompassing ranges shifts the burden to the applicant to show that his invention would not have been obvious." *In re Peterson*, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1383 (Fed. Cir. 2003). *See also In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990).

DISCUSSION

This case turns on two questions: (1) Do Yicheng and/or Karlsson inherently anticipate claim 1, even though neither reference discloses any intent to treat patients for hepatocellular deficiency? (2) Would the disclosed prior art methods necessarily result in "treating hepatocellular deficiency"? Based on the record before us and our above findings, we conclude the answer to both these questions is yes.

Appellants argue *Jansen* and *Rapoport* require a different result. *See* Br. *passim*. The Examiner distinguishes these cases. Answer *passim*. We agree with the Examiner that these cases can be distinguished, both on their facts and on their procedural postures.

Jansen was an infringement case, requiring the court to construe the subject claim "so as to sustain [its] validity, if possible." *Whittaker Corp. v. UNR Indus.*, 911 F.2d 709, 712, 15 USPQ2d 1742, 1743 (Fed. Cir. 1990)

(citing *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 932 (Fed.Cir.1984). In contrast, during prosecution, a claim must be given its broadest reasonable interpretation. Unlike the case here, in *Jansen*, the *patentee* was arguing a broad construction to establish infringement. 342 F.3d at 1331, 68 USPQ2d at 1156. However, the court "strictly construed" the claim against the inventor, in view of statements made during prosecution. *Id.* at 1334, 68 USPQ2d at 1158.

In *Rapoport* (an interference proceeding), the Board found no inherent anticipation. In affirming the Board, the Federal Circuit stated: "Most importantly . . . , the issue of anticipation—whether by inherency or otherwise—is a question of fact, and we uphold decisions of the Board on factual matters if there is substantial evidence in the record to support the Board's findings." 254 F.3d at 1063, 59 USPQ2d at 1222.

Further, at least two panels of the Board have previously distinguished *Jansen* and/or *Rapoport* in similar circumstances. *See Ex parte Hempstead,* App. No. 2006-0611 (decided April 5, 2006). *See also Ex Parte Renshaw*, App. No. 2006-1066 (2006 WL 2558174).

In any case, to the extent they cannot be distinguished, we believe the better line of cases is that culminating in *Perricone*. Unless the claim language distinguishes the claimed method, the subject matter cannot be patented, as it is already in the public domain.

In spite of lack of intent to treat hepatocellular deficiency, we find both Yicheng and Karlsson anticipate claim 1, either expressly or under the doctrine of inherency. Yicheng administers MnDPDP to mice and rabbits ("patients") in which HCC (a "hepatocelluar deficiency") has been induced.

Given the broad language of claim 1, "treating hepatocellular deficiency, comprising administering mangafodipir to a patient in need thereof" is the "natural result flowing from" Yicheng's disclosure. Yicheng's lack of intent to treat hepatocellular deficiency does not impact our analysis. *See, e.g., Perricone*, 432 F.3d at 1378, 77 USPQ2d at 1327 (quoted above).

Likewise, Karlsson expressly teaches administering MnDPDP to a patient undergoing a liver transplant, either before or during surgery. During those time periods, such a patient would be suffering from a hepatocellular deficiency, regardless of the underlying cause. Thus, administration of MnDPDP during those time periods, "treating hepatocellular deficiency, comprising administering mangafodipir to a patient in need thereof" would be the "natural result flowing from" such administration. Again, Karlsson's lack of intent to treat hepatocellular deficiency does not influence our analysis.

Turning to the second question, Appellants argue that application of Karlsson "would not necessarily result in practicing the claimed methods." Br. 14. This argument appears to be based on the fact that Karlsson "doesn't care which organ is to be transplanted" and "does not identify a patient to whom the compound is to be administered, the time [of] administration, whether it be the donor, the recipient, or both." *Id.* We disagree with Appellants' position. We acknowledge Karlsson describes treating patients in circumstances not involving a liver transplant and administering the drug at times other than before or during such a transplant. However, inclusion of situations not involving treating hepatocellular deficiency does not negate Karlsson's other, more relevant, teachings. When administered to a patient

before or during a liver transplant, Karlsson's treatment would "necessarily result" in practicing the method of claim 1.

Appellants further argue: "While the patient population to be treated in Karlsson **may** overlap those with hepatocellular deficiency, there are other patients that perhaps wouldn't need a liver transplant but would still benefit significantly from the treatment described and claimed by the Applicants." Br. 15 (emphasis Appellants'). While this may be true, Appellants must claim their invention such that the claim does not overlap the prior art. They have failed to do so here.

Thus, we find both Yicheng and Karlsson anticipate claim 1.

Rejection of Dependent Claims 2, 9, 11, 14, and 18 in view of Yicheng

In addition to claim 1, the Examiner rejected claims 2, 9, 11,14, and 18 under § 102(b) based on Yicheng.

Claim 2 further limits claim 1 by requiring the hepatocellular deficiency be "of toxic origin." Yicheng induces HCC with a chemical carcinogen and thus satisfies this additional limitation.

Claim 9 further limits claim 1 by including a dosage range for the mangafodipir, "between 5 and 50 mg/kg/day." Yicheng teaches using 25 μmol/kg (Yicheng 46, col. 1), calculated to be 19mg/kg. Answer 6. Since this dose was "administered during the day" of Yicheng's experiment, it "represents 19mg/kg/day which is encompassed by . . . a dosage [range] of between 5 and 50 mg/kg/day." Answer 6.[3]

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[3] Appellants do not dispute either of the Examiner's calculations.

Claim 11 further limits claim 1 by requiring administration "via injection." Karlsson discloses such administration. Karlsson, at 12.

Claim 14 further requires the mangafodipir be administered by "intravenous injection." Yicheng injects mangfodipir into "the ear vein of the rabbit or the tail vein of the rat." Yicheng at 45, col. 3. *See also* Answer 5.

Claim 18 depends upon claim 9, limiting the dosage to between 5 and 50 mg/kg/day and requiring administration "via injection." These additional limitations are disclosed in Yicheng. See the discussion above with respect to claims 9 and 14.

Thus, we agree with the Examiner that claims 2, 9, 11, 14, and 18 are anticipated by Yicheng.

Rejection of Dependent Claims 8-18 in view of Karlsson

In addition to claim 1, the Examiner has rejected claims 8-18 under § 102(b) as anticipated by Karlsson.

Claims 8 and 9 require mangafodipir to be administered in ranges comprising "between 0.1 and 10 mg/kg/day" and "between 5 and 50 mg/kg/day," respectively. Karlsson discloses a dosage range between "10^{-2} and 100 µmol/kg of body weight." Karlsson at 14. The Examiner has calculated this range to be 0.007 to 76 mg/kg. Answer 8. According to the Examiner, a "per day" rate would be immediately envisaged by one of ordinary skill in the art. *Id.* We agree with the Examiner's finding.

Claims 10-14 each recite a mode of administration, i.e., "orally" (claim 10), or "via injection" (claim 11) (which is further limited to

"subcutaneous" (claim 12), "intramuscular" (claim 13), or "intravenous" (claim 14)). Karlsson expressly discloses administering MnDPDP orally, and via injection, intravenous injection, and parenteral injection (defined by Stedman's to be "intravenous, subcutaneous, intramuscular, or intramedullary injection"). Karlsson at 12-13. *See also* Answer 7-8.

Claims 15-18 further require that mangafodipir be administered orally or via injection in the dosage ranges of claims 8 and 9. Karlsson discloses these additional limitations, as explained above.

Thus, we find claims 8-18 are anticipated by Karlsson.

Rejection of Claims 2-5 Under 35 U.S.C. § 103(a)

The Examiner rejected claims 2-5 over Karlsson and Cecil, as Karlsson does not expressly disclose the specific causes of hepatocellular deficiency requiring a liver transplant. Claims 2-5 are limited to hepatocellular deficiency "of toxic origin" (claim 2), "induced by acetaminophen" (claim 3), "induced by alcohol" (claim 4) or "manifests itself in the form of fulminant hepatitis" (claim 5).

Cecil identifies each of these causes of liver failure. Answer 9 (citing Cecil at 815, col. 2; 817, col. 2; and Table 155-1). Based on Cecil's teachings, the Examiner concludes "because the liver transplant recipient of Karlsson et al. could have been reasonably expected to be as such because of liver damage caused by alcohol, acetaminophen or liver failure, the claimed subject matter would have been obvious to one of ordinary skill in the art." *Id.* We agree with the Examiner that the subject matter of claims 2-5 would have been obvious in view of the teachings of Karlsson and Cecil.

CONCLUSIONS

We affirm the Examiner's rejection of claims 1, 2, 9, 11, 14, and 18 under § 102(b) based on Yicheng and that of claims 1 and 8-18 under § 102(b) based on Karlsson. These references anticipate the subject matter of the rejected claims, either expressly or inherently. We also affirm the Examiner's § 103(a) rejection of claims 2-5 based on Karlsson and Cecil.

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

Toni R. Scheiner)
Administrative Patent Judge)
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Eric Grimes) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
)
) INTERFERENCES
)
Nancy J. Linck)
Administrative Patent Judge)

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA VA 22314