United States Court of Appeals for the Federal Circuit

IN RE HUAI-HUNG KAO, ANAND R. BAICHWAL, TROY MCCALL, AND DAVID LEE

2010-1307

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences in application Serial No. 11/680,432.

IN RE HUAI-HUNG KAO, ANAND R. BAICHWAL, TROY MCCALL, AND DAVID LEE

2010-1308

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences in application Serial No. 12/167,859.

IN RE HARRY AHDIEH

2010-1309

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences in application Serial No. 11/766,740.

Decided: May 13, 2011

JEFFREY I. D. LEWIS, Patterson, Belknap Webb & Tyler, LLP, of New York, New York, argued for appellants. With him on the briefs were MELISSA MANDRGOC, and CATHERINE A. WILLIAMS; and GUY DONATIELLO, Endo Pharmaceuticals, Inc., of Chadds Ford, Pennsylvania; and JOSEPH MAHONEY, Mayer Brown LLP, of Chicago, Illinois.

FRANCES M. LYNCH, Associate Solicitor, Office of the Solicitors, United States Patent and Trademark Office, of Alexandria, Virginia, argued for appellee in both 2010-1307 and 2010-1308. BENJAMIN D.M. WOOD, Associate Solicitor, argued for appellee in 2010-1309. With them on the briefs was RAYMOND T. CHEN, Solicitor.

Before RADER, *Chief Judge*, LINN and MOORE, *Circuit Judges*.

LINN, *Circuit Judge*.

Endo Pharmaceuticals, Inc. ("Endo") is the assignee of three patent applications related to controlled-release tablets containing the opioid narcotic oxymorphone. The Board of Patent Appeals and Interferences ("the Board"), in separate appeals, affirmed the rejection of the claims of each application as obvious, and Endo has separately appealed each decision to this court.

The Board affirmed the rejection of all pending claims of United States Patent Application No. 11/680,432 ("the '432 Application"), United States Patent Application No.

12/167,859 ("the '859 Application"), and United States Patent Application No. 11/766,740 ("the '740 Application") principally over a prior art international patent application that is involved in each appeal. Endo timely appealed each decision of the Board, and this court has jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

Because the Board based its conclusion of obviousness regarding the '432 Application on factual findings lacking in substantial evidence, this court vacates and remands. Because the Board's conclusions regarding the obviousness of the '859 and '740 Applications were supported by substantial evidence, this court affirms the Board's decisions regarding those two applications.

BACKGROUND

I. The '432 Application

The claimed invention of the '432 Application relates to drug formulations containing opioids, a type of narcotic frequently used to manage chronic pain. To provide consistent pain relief, a minimum level of the opioid must be maintained in the blood. Opioids, however, are typically available in immediate release formulations that quickly release the entire dose of the opioid into the body. Moreover, some opioids are rapidly metabolized by the liver (a phenomenon known as the "first-pass effect") resulting in the drug having a low "bioavailability." When a drug has low bioavailability this means that only a small amount of the drug is systemically available throughout the body. Because of these drawbacks, immediate release opioid formulations must be administered frequently (e.g., every 4-6 hours) to maintain continuous pain relief. But frequent administration of opioids can result in a variety of side effects, ranging from disturbed sleep to altered mental states.

To overcome the difficulties associated with immediate release formulations, the '432 Application discloses controlled release formulations containing the opioid oxymorphone, and capable of relieving pain for between twelve and twenty-four hours.

Independent claims 1 and 20, as well as dependent claims 2-3 and 5-19, are pending in the '432 Application. Because the '432 Application was filed under the Accelerated Examination Program of the United States Patent and Trademark Office ("the Office"), Endo was limited to arguing the patentability of independent claims 1 and 20. Claim 1 reads as follows (relevant terms emphasized):

> 1. An analgesically effective controlled release pharmaceutical composition with a twelve hour dosing interval in the form of a tablet, comprising oxymorphone or a pharmaceutically acceptable salt thereof as the sole active ingredient in the tablet and a controlled release delivery system comprising at least one pharmaceutical excipient, *wherein upon placement of the composition in an in vitro dissolution test comprising USP Paddle Method at 50 rpm in 500 ml media having a pH of 1.2 to 6.8 at 37° C, about 15% to about 50%, by weight, of the oxymorphone or salt thereof is released from the tablet at about 1 hour in the test.*

Claim 20 is similar to claim 1 but recites that "about 45% to about 80%, by weight, of the oxymorphone or salt thereof is released from the composition at about four hours in the test, and at least about 80%, by weight, of the oxymorphone or salt thereof is released from the composition at about 10 hours in the test."

The examiner rejected claims 1 and 20 as obvious in view of Patent Cooperation Treaty Publication No. WO 01/08661 to Maloney ("Maloney"), both alone and in

combination with United States Patent No. 5,047,248 to Calanchi et al. As is relevant here, the examiner found that, with the exception of the claimed dissolution rate, Maloney disclosed controlled release opioid formulations that taught the recited limitations. The examiner stated that the burden fell on Endo to show why Maloney failed to satisfy the claimed dissolution rate because, in her view, the controlled release system described by Maloney satisfied the other limitations of the claims.

In response, Endo submitted declarations explaining that because Maloney only disclosed a dissolution profile for a controlled release formulation containing oxycodone, an opioid with markedly different bioavailability than oxymorphone, it provided little guidance on the appropriate design of a controlled release oxymorphone formulation. The declarations further explained that controlled release oxymorphone formulations exhibit an unexpected result: Over time the formulations cause multiple peaks in oxymorphone blood concentration, which help prevent patients from building a tolerance to the opioid. Endo also included evidence that Opana® ER, a commercial embodiment of the invention, had experienced significant commercial success. The examiner concluded that the declarations were insufficient to show that Maloney did not suggest the claimed range of dissolution profiles. The examiner also found that the evidence of unexpected results and commercial success offered by Endo was not commensurate with the scope of the claims, because that evidence largely related to Opana® ER and the claims encompassed a large number of other formulations, for which no secondary considerations were shown.

On appeal, the Board affirmed the examiner's rejection, relying exclusively on Maloney and in particular on the controlled release formulation denominated "Formula 6." The Board recognized that Maloney disclosed that Formula 6 contains oxycodone instead of oxymorphone as

recited in the claims. The Board also recognized that Maloney disclosed dissolution data for Formula 6 measured by the USP Basket Method, not the claimed USP Paddle Method. Nevertheless, the Board concluded that Formula 6 rendered the claims obvious. The Board determined that it would have been obvious to one of skill in the art to replace the oxycodone in Formula 6 with oxymorphone because Maloney generally identifies oxymorphone as a preferred opioid for use in his invention. Regarding the claimed dissolution rate, the Board found that a declaration submitted by Endo in response to the first office action suggested that the dissolution rate as measured by the Basket Method was 1.3 times faster than the rate as measured by the Paddle Method. Applying this correlation to the dissolution data for the Formula 6 oxycodone disclosed in Maloney, the Board found that Formula 6 satisfied the claimed dissolution profile. The Board then appeared to reason that if one were to substitute oxymorphone for oxycodone in Maloney's Formula 6, the result would be an oxymorphone controlled release pill with a dissolution profile within the range of pending claim 1.

The Board then turned to the evidence of secondary considerations. It assumed that the evidence of commercial success and unexpected results presented by Endo was sufficient to overcome a prima facie case of obviousness with respect to the commercial embodiment but, like the examiner, concluded that the evidence was not commensurate with the scope of the claims and, therefore, failed to overcome the rejections.

II. The '859 Application

The '859 Application discloses a method of relieving pain using oxymorphone in a controlled release delivery

system to overcome the difficulties associated with immediate release formulations of opioids.

Claims 8-27 are pending and on appeal. Because the '859 Application was filed under the Accelerated Examination Program, Endo was limited to arguing the patentability of the independent claims and only argued independent claims 8 and 21 before the Board. Thus, the claims of the '859 Application stand or fall with independent claims 8 and 21.

Claim 8 of the '859 Application is directed to a method for treating pain by administering oxymorphone in a controlled release formulation that (1) provides at least 12 hours of sustained pain relief and (2) results in a "Cmax" (maximum concentration) at least about 50% higher when administered to fed versus fasting patients. Claim 8 reads as follows (relevant terms emphasized):

> 8. A method for treating pain in a human subject in need of acute or chronic pain relief, comprising the steps of:
>
> (a) Providing a solid oral dosage form comprising about 5 mg to about 80 mg oxymorphone or a pharmaceutically acceptable salt thereof in a controlled release delivery system with a release rate profile designed to provide an adequate blood plasma level over *at least 12 hours to provide sustained pain relief* over this same period, the system comprising a filler and a hydrophilic material, wherein oxymorphone is the sole active ingredient; and,
>
> (b) administering the dosage form to the subject, wherein the oxymorphone *Cmax is at least about 50% higher when the dosage form is administered to the subject under fed versus fasted conditions.*

Claim 21 additionally requires, among other limitations, that the controlled release formulation include a hydrophobic material. Claim 21 reads as follows (relevant terms emphasized):

> 21. A method for treating pain in a human subject in need of acute or chronic pain relief, comprising the steps of
>
> (a) Providing a solid oral dosage form comprising about 5 mg to about 80 mg oxymorphone or a pharmaceutically acceptable salt thereof in a controlled release delivery system with a release rate profile designed to provide an adequate blood plasma level over *at least 12 hours to provide sustained pain relief* over this same period, the system comprising:
>
> (i) a hydrophilic material
>
> (ii) *a hydrophobic material*
>
> (iii) a cationic cross-linking agent, and
>
> (iv) a filler,
>
> wherein oxymorphone is the sole active ingredient; and
>
> (b) administering the dosage form to the subject, wherein the oxymorphone *Cmax is at least about 50% higher when the dosage form is administered to the subject under fed versus fasted conditions.*

The examiner rejected claims 8 and 21 as obvious in view of, among other references, Maloney. The examiner found that Maloney "teaches oral sustained release preparations of opioid analgesics" with the use of oxymorphone as a preferred opioid.

On appeal, the Board affirmed the examiner's rejection, relying exclusively on Maloney. The Board found that Maloney discloses a controlled release formulation with an opioid in amounts of 5-100 mg and that oxymorphone is a preferred opioid. The Board found that Maloney further teaches using calcium sulfate (a cross linking agent), lactose (a filler), and hydrogenated vegetable oil (a hydrophobic material) in his formulation. Based on these disclosures, the Board determined that it would have been obvious to a person of ordinary skill in the art to formulate the claimed oral dosage form and to administer the form to the subject as claimed in the '859 Application.

The Board then turned to the evidence of secondary considerations. Just as it did with the '432 Application, it assumed that the evidence of commercial success and unexpected results presented by Endo was sufficient to overcome a prima facie case of obviousness with respect to the commercial embodiment but agreed with the examiner that the evidence was not commensurate with the scope of the claims and, therefore, failed to overcome the rejections.

III. The '740 Application

The '740 Application was likewise filed under the Accelerated Examination Program; so only the independent claims 21, 25, and 30 are potentially at issue. For reasons that will become clear below, we limit our discussion to claim 21.

Independent claim 21 reads:

> 21. A method of providing extended pain relief to patients in need thereof, comprising:

> providing information that the average bioavailability of oxymorphone in an oral extended release formulation designed to have a 12 hour dosing cycle is increased by at least about 26% for subjects with renal impairment compared to that for healthy subjects, and
>
> providing a therapeutically effective amount of such an extended release oral dosage form of oxymorphone or its pharmaceutically acceptable salt thereof.

'740 Application.

The Office rejected claim 21 as obvious over three different combinations. We need focus on only one: Maloney in view of United States Patent Publication No. 2002/0032581 ("Reitberg"). The examiner found that "Maloney teaches a controlled-release dosage form comprising oxymorphone," that Reitberg teaches a clinical evaluation kit for measuring the effectiveness of treatment of a specific individual comprising a medication and instructions, and that it would have been obvious to combine the two. Ahdieh argued to the Board that it would not have been obvious to a person of ordinary skill to combine the two references because the correlation between renal impairment and bioavailability of controlled release oxymorphone was not previously known, and because, in any case, evidence of commercial success and unexpected results compel a determination of nonobviousness.

DISCUSSION

A claimed invention is unpatentable "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was

made to a person having ordinary skill in the art." 35 U.S.C. § 103(a). Whether an invention is obvious is a question of law based on underlying facts. *In re Kotzab*, 217 F.3d 1365, 1369 (Fed. Cir. 2000). This court reviews the Board's ultimate determination of obviousness de novo and the Board's fact findings for substantial evidence. *In re Gartside*, 203 F.3d 1305, 1316 (Fed. Cir. 2000). "Substantial evidence is such relevant evidence as a reasonable mind might accept as adequate to support a conclusion." *In re Kumar*, 418 F.3d 1361, 1366-67 (Fed. Cir. 2005) (quotation omitted).

I. The '432 Application

A. Obviousness

Endo contends that the examiner failed to present a prima facie case of obviousness because there is no evidence that substituting oxymorphone for oxycodone in Maloney's Formula 6 would result in a formulation that satisfies the claimed dissolution profile. Endo claims that the Board improperly relied on speculation and hindsight to conclude otherwise.

The Office argues that the Board correctly concluded that replacing oxycodone with oxymorphone in Formula 6 would result in the claimed invention. The Office asserts that Maloney provides ample reason for one of skill in the art to alter Formula 6 as suggested by the Board and teaches that Formula 6 can relieve pain for twelve hours. It claims that the Board reasonably concluded that there is a correlation between the claimed dissolution test (the USP Paddle Method) and the test disclosed by Maloney (the USP Basket Method), and applying this correlation demonstrates that Formula 6 has the claimed dissolution profile.

Before turning to the merits of Endo's appeal, we first consider the Office's contention that only claim 1, and not claim 20, is properly before us on appeal. The Office contends that Endo did not present separate arguments concerning claim 20 to the Board, and that claim 20 therefore stands or falls with claim 1. Endo responds by pointing to various portions of the record where it contends it separately argued the patentability of claim 20.

We agree with the Office that Endo waived the right to have the Board separately consider claim 20. Under 37 C.F.R. § 41.37(c)(1)(vii), "the failure of appellant to separately argue claims which appellant has grouped together shall constitute a waiver of any argument that the Board must consider the patentability of any grouped claim separately." The portions of the record cited by Endo merely mention claim 20 and lack any type of separate, substantive argument concerning the claim as required by 37 C.F.R. § 41.37(c)(1)(vii). *See also In re McDaniel*, 293 F.3d 1379, 1383 (Fed. Cir. 2002) ("[T]he Board is free to select a single claim from each group of claims subject to a common ground of rejection as representative of all claims in that group and to decide the appeal of that rejection based solely on the selected representative claim" in the absence of a clear statement asserting separate patentability of the claims.).

On the merits, this court agrees with Endo that the Board relied on erroneous reasoning in making the factual determinations that underlie its conclusion that claim 1 is obvious, and that its factual findings are therefore unsupported by substantial evidence. However, because the evidence of record may yet satisfy the required substantial evidence standard, the Board's determination will be vacated and remanded.

An examiner bears the initial burden of presenting a prima facie case of obviousness. *See In re Glaug*, 283 F.3d

1335, 1338 (Fed. Cir. 2002). Once the examiner establishes a prima facie case of obviousness, the burden shifts to the applicant to rebut that case. "The prima facie case is a procedural tool, and requires that the examiner initially produce evidence sufficient to support a ruling of obviousness; thereafter the burden shifts to the applicant to come forward with evidence or argument in rebuttal." *In re Kumar*, 418 F.3d at 1366. However, once the applicant has come forward with rebuttal evidence, the examiner must consider the totality of the evidence to determine whether the obviousness rejection should stand. "When rebuttal evidence is provided, the prima facie case dissolves, and the decision is made on the entirety of the evidence." *Id*.

The Board first observed that Maloney discloses specific controlled release formulations of oxycodone, that Maloney states that oxymorphone can also be used in a controlled release formulation, and that it is indeed a preferred compound. Based on these observations, the Board concluded that it would have been obvious to substitute oxymorphone in Maloney's Formula 6 (that being one of the controlled release oxycodone formulations disclosed in Maloney). The Board then observed that while Maloney does not disclose the dissolution rate of Formula 6 as measured by the Paddle Method, it does disclose that rate as measured by the Basket Method. To support that observation, the Board relied upon the Second Chang declaration to find a correlation between Paddle Method and Basket Method measurements for Opana® ER after one hour of dissolution. Applying that correlation to the Basket Method measurements of the oxycodone Formula 6 disclosed in Maloney, the Board concluded that oxycodone Formula 6 fell within the dissolution rate range of claim 1. On the basis of these factual determinations, the Board concluded that "the product made obvious by Maloney [i.e. Formula 6 with an oxymorphone substitute] would have a dissolution rate

between 15% and 50% after one hour when measured by the USP Paddle Method."

Accepting that it would be obvious to substitute oxymorphone in Maloney's Formula 6, the Board's reasoning nonetheless does not pass the substantial evidence threshold as to whether such a substitution would indeed fall within the dissolution profile of pending claim 1. As an initial matter, it should be clear that it makes no difference, a priori, to the question of obviousness whether the hypothetical person of ordinary skill in the art would have understood the claimed dissolution profile in terms of a Paddle-Method or a Basket-Method test range, just as it would make no difference whether the hypothetical person of skill in the art preferred to think in English or Metric units. The claimed subject matter is not presumed to change as a function of how one elects to measure it. The reason this "correlation" appears to matter on the Board's formulation of the present case is that there is a lack of direct factual support in the record for the view that the claimed range of dissolution rates actually overlaps with the dissolution rate disclosed in Maloney, a premise upon which the Board's reasoning is founded. Thus, while it matters not whether the hypothetical skilled artisan would have *appreciated* the "correlation" at issue here, it matters greatly whether anything the skilled artisan would be prompted by the prior art to do is *in fact* within the scope of the pending claim.

The declaration relied upon by the Board does not provide substantial evidence for its finding of a correlation between the Basket and Paddle Methods. The Board relied on four data points from an exhibit correlating the dissolution rates of Opana® ER, when tested by both methods, and Maloney's Formula 6, tested only by the Basket Method, and concluded, without any reasoning, that because the Basket Method dissolution in the first hour for Opana® ER was 1.3 times faster than the disso-

lution rate of the Paddle Method for Opana® ER, this correlation would also hold for Maloney's Formula 6. Moreover, the declarant responsible for the exhibit expressly stated that there is no general correlation between the Basket and Paddle Methods and cited prior art literature that supported this conclusion. The Board has not provided any reason, apart from its own statement to the contrary, to question this conclusion. The Board's own conjecture does not supply the requisite substantial *evidence* to support the rejections, i.e., "such evidence as a reasonable mind might accept as adequate to support a conclusion." *Consol. Edison Co. v. Nat'l Labor Relations Bd.*, 305 U.S. 197, 229 (1938). For these reasons, the Board's reliance on its own conjecture regarding whether a direct substitution of oxymorphone in Formula 6 would satisfy the claimed range of dissolution rates is improper.

While the Board did not base its factual conclusions regarding the correlation of the two ranges on substantial evidence, the importance, or lack thereof, of the claimed range to the alleged nonobviousness of the invention is a question we leave for the Board to consider on remand. *See, e.g.*, *Ormco Corp. v. Align Technology, Inc.*, 463 F.3d 1299, 1311 (Fed. Cir. 2006) (explaining that overlap between claimed range and prior art gives rise to a presumption of obviousness; where claimed range and prior art value are insubstantially different, prima facie obviousness rejection is proper).

The Board's decision is vacated and remanded so that the Board can consider whether, under the proper analysis, the evidence of record is sufficient to maintain an obviousness rejection. As the Supreme Court has explained:

> When there is. . . market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in

> the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

KSR Intern. Co. v. Teleflex Inc., 550 U.S. 398, 402-403 (2007). Thus, while the Board should neither rely upon conclusory reasoning nor its own conjecture in assessing the weight of evidence, the Board may, or may not, still find that the evidence supports the examiner's rejection.

B. Secondary Considerations

Endo argues that it submitted evidence of unexpected results and commercial success sufficient to rebut a *prima facie* showing of obviousness. The Office contends that the Board correctly discounted the secondary considerations evidence submitted by Endo because the evidence was not commensurate with the scope of the claims. Endo is correct that the Board erred by failing to give the evidence of secondary considerations its due weight. But there were nonetheless other defects in at least the presentation of this evidence.

To start, when secondary considerations are present, though they are not always dispositive, it is error not to consider them. *See Stratoflex v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983) ("[E]vidence rising out of the so-called 'secondary considerations' must always when present be considered en route to a determination of obviousness."); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007) ("Although secondary considerations must be taken into account, they do not necessarily control the obviousness conclusion.").

Evidence of secondary considerations must be reasonably commensurate with the scope of the claims. *See*

In re Tiffin, 448 F.2d 791, 792 (CCPA 1971); *In re Hiniker*, 150 F.3d 1362, 1369 (Fed. Cir. 1998). This does not mean that an applicant is required to test every embodiment within the scope of his or her claims. If an applicant demonstrates that an embodiment has an unexpected result and provides an adequate basis to support the conclusion that other embodiments falling within the claim will behave in the same manner, this will generally establish that the evidence is commensurate with scope of the claims. *See In re Greenfield*, 571 F.2d 1185, 1189 (CCPA 1978) (concluding that evidence of secondary considerations was not commensurate with the scope of the claims where that evidence related to a single compound and there was no adequate basis to conclude that other compounds included within the scope of the claims would exhibit the same behavior); *In re Cescon*, 474 F.2d 1331, 1334 (CCPA 1973) (concluding that, although not every compound within the scope of the claims was tested, the evidence of secondary considerations was sufficient where evidence showed a correlation and there was no factual basis to expect the compounds to behave differently in different environments).

But there is a more fundamental requirement that must be met before secondary considerations can carry the day. "For objective evidence of secondary considerations to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the *claimed invention*." *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1246 (Fed. Cir. 2010) (quotation omitted). Where the offered secondary consideration actually results from something other than what is both claimed and *novel* in the claim, there is no nexus to the merits of the claimed invention. *Tokai Corp. v. Easton Enters., Inc.*, 632 F.3d 1358, 1369 (Fed. Cir. 2011) ("If commercial success is due to an element in the prior art, no nexus exists."); *Ormco Corp.*, 463 F.3d at 1312 ("[I]f the feature that creates the commercial success was known in

the prior art, the success is not pertinent."); *In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990) ("The law is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims . . . . [and] in such a situation, the applicant must show that the particular range is *critical*, generally by showing that the claimed range achieves unexpected results relative to the prior art range." (citations omitted)).

1. Unexpected Results

The Board acknowledged applicant's evidence that, unlike immediate release formulations, ingesting a particular disclosed controlled-release formulation resulted in unexpected multiple peaks in oxymorphone blood concentration. Despite assuming that this evidence was sufficient to overcome the *prima facie* case of obviousness for that formulation, the Board disregarded this evidence because, in its view, the evidence was not commensurate with the scope of the claims.

The Board noted that the '432 Application disclosed that a particular controlled release formulation caused unexpected multiple peaks in oxymorphone blood concentration, while immediate release formulations did not. In light of this, the Board concluded that this unexpected property must be caused by some component of that particular disclosed controlled-release formulation. This is unsupported by the record. The only evidence of record indicates that the unexpected in vivo characteristics of oxymorphone controlled release compositions did not result from properties unique to any specific commercial embodiment. Endo supplied a declaration from one of its experts stating that, after reviewing clinical studies and scientific literature, it appeared that extended release formulations of oxymorphone—not limited to formulations

with any specific excipient—cause multiple peaks in oxymorphone blood concentration. The Board did not challenge this conclusion. Because the Board ignored the evidence of record and relied instead upon its own conjecture, its treatment of Endo's argument regarding unexpected results was improper.

On remand, the Board, in considering the evidence of unexpected results, should determine whether there is a nexus between the unexpected in vivo concentration profile and aspects of the claimed invention not already present in the prior art. More specifically, for the unexpected in vivo concentration profile of the applicant's product to have substantial weight, there must be a nexus to some aspect of the claim not already in the prior art, such as the claimed range of dissolution rates, as against other unclaimed prior-art dissolution rates.

2. Commercial Success

The Board also discounted Endo's evidence of commercial success of Opana® ER on the grounds that it was not commensurate with the scope of the claims. But an applicant "need not sell every conceivable embodiment of the claims in order to rely upon evidence of commercial success, so long as what was sold was within the scope of the claims." *In re DBC*, 545 F.3d 1373, 1384 (Fed. Cir. 2008). *See also Applied Materials, Inc. v. Advanced Semiconductor Materials Am. Inc.*, 98 F.3d 1563, 1570 (Fed. Cir. 1996) ("[A] patentee need not show that all possible embodiments within the claims were successfully commercialized in order to rely on the success in the marketplace of the embodiment that was commercialized."). As this court recently explained, "[i]t seems unlikely that a company would sell a product containing multiple, redundant embodiments of the patented invention . . . . Under the [Office's] logic, there would never be

commercial success evidence for a claim that covers more than one embodiment." *In re Glatt Air Techniques, Inc.*, 630 F.3d. 1026, 1030 (Fed. Cir 2011). The Board's refusal to credit the applicant's evidence of commercial success because it was not proven across the entire claimed range of dissolution rates was improper.

Nonetheless, the record is nearly silent on whether the commercial success was caused by the merits of the invention as distinct from the prior art. In short, if it is not established that the claimed and novel range for a controlled release oxymorphone formulation causes commercial success where the prior art range would not, then it will be difficult to show the required nexus. Applicants' expert opined that the unexpected in vivo concentration was likely responsible for the commercial success of the embodying product. Applicants' expert further opined that the amelioration of analgesic tolerance to which Applicants attribute commercial success "is precisely the practical impact [he] would expect from the biphasic and triphasic pK behavior" of the commercial embodiment. But if the same behavior would be observed in any oxymorphone controlled release formulation, then there is no necessary nexus between the commercial success and the claimed formulation. On remand, the Board, in considering the commercial success argument, should make a factual determination as to whether the commercial success of the embodying product resulted from the merits of the claimed invention as opposed to the prior art or other extrinsic factors.

II. The '859 Application

A. Obviousness

Endo advances three main arguments in challenging the Board's finding of obviousness. First, Endo argues

that Maloney fails to disclose the claimed food effects. Second, Endo argues that Maloney fails to disclose the 12-hour effectiveness of the claimed controlled release formulation of oxymorphone. Third, Endo argues that Maloney fails to disclose the claimed combination that includes a hydrophobic material. We address each argument in turn.

1. Food Effects Limitation

Endo argues that Maloney does not expressly disclose the "food effect" limitation: "wherein the oxymorphone Cmax is at least about 50% higher when the dosage form is administered to the subject under fed versus fasted conditions." Endo asserts that the Board erroneously relied on the teaching in the specification of the '859 Application that the claimed "food effect" was a property of oxymorphone and that Maloney inherently disclosed the limitation. Endo argues that an obviousness rejection can only be based on what is known by those of skill in the art at the time of the invention, and there is no evidence in the record that anyone recognized the claimed food effect at that time.

The Office responds that substantial evidence supports the Board's finding of inherency. The Office further responds that the Board's reliance upon the specification of the '859 Application to support this conclusion is entirely proper. Further, the Office responds that inherency is indeed a part of the obviousness inquiry.

This court agrees with the Office. Substantial evidence supports the Board's finding, based upon the specification, which confirms that the claimed "food effect" is an inherent property of oxymorphone itself, present both in controlled release and immediate release formulations of that drug. *See In re Kubin*, 561 F.3d 1351, 1357 (Fed.

Cir. 2009) (stating "[e]ven if no prior art of record explicitly discusses the [limitation], [applicant's] application itself instructs that [the limitation] is not an additional requirement imposed by the claims on the [claimed invention], but rather a property necessarily present in [the claimed invention]"); *see also King Pharmaceuticals, Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1275-76 (Fed. Cir. 2010) (stating that "merely discovering and claiming a new benefit of an old process cannot render the process again patentable" (citations omitted)). This is not a case where the Board relied on an unknown property of prior art for a *teaching*. Rather, Maloney's express teachings render the claimed controlled release oxymorphone formulation obvious, and the claimed "food effect" adds nothing of patentable consequence.

2. 12-Hour Effectiveness Limitation

Endo argues that Maloney does not expressly disclose the recited 12-hour effectiveness limitation. Endo asserts that it provided evidence that one of skill in the art would not have expected that oxymorphone could be substituted for oxycodone because (1) oxymorphone has a much lower bioavailability than oxycodone and (2) oxymorphone is subject to the "first-pass effect."

The Office responds that the Board found that Maloney expressly teaches using oxymorphone in the disclosed formulations. Although Endo's experts essentially stated their view that Maloney did not enable the disclosed oxymorphone formulation, their statements were based on various "concerns" that fall short of establishing that the Maloney reference was non-enabling. *See In re Merck & Co., Inc.,* 800 F.2d 1091, 1097 (Fed. Cir. 1986) (concluding that obviousness does not require absolute predictability, only a reasonable expectation that the beneficial result will be achieved).

This court agrees with the Office. Substantial evidence supports the Board's finding. The Board found that Maloney teaches a controlled release opioid formulation comprising an opioid compound in amounts of 5-100 mg. Maloney further discloses that oxymorphone is a preferred opioid compound. Finally, Maloney discloses that its dosage form provides a dissolution rate of 60%-80% active agent released after 12 hours. Based on these findings, the Board reasonably concluded that Maloney's active agent would still be effective after 12 hours because it is still being released from Maloney's dosage form at 12 hours. Notwithstanding the "concerns" expressed by Endo's experts, Endo has failed to provide record evidence showing that Maloney's disclosure fails to provide a reasonable expectation of obtaining the plasma levels of oxymorphone suggested by Maloney and required by claims 8 and 21. *See Merck*, 800 F.2d at 1097. Substantial evidence supports the Board's conclusion that the oxymorphone formulation disclosed in Maloney would satisfy the claimed 12-hour effectiveness limitation.

3. Hydrophobic Limitation

Endo argues that Maloney fails to teach a controlled release formulation including both a hydrophilic and a hydrophobic material. According to Endo, although Maloney discloses an example using a hydrophobic lubricant, the example describes this hydrophobic material as "optional" and it is used as a lubricant, not as part of the release formulation.

The Office responds that substantial evidence supports the Board's finding that Maloney teaches the use of hydrophilic polymers with lubricants, such as hydrogenated vegetable oil, a hydrophobic material. Claim 21 simply requires the inclusion of a hydrophobic material, irrespective of its function. That Kao's alleged purpose for incorporating a hydrophobic material into the claimed

formulation differs from Maloney's is irrelevant when Kao's alleged purpose is not a limitation of claim 21.

This court again agrees with the Office. Substantial evidence supports the Board's finding that Maloney teaches a controlled release formulation using both hydrophobic and hydrophilic materials, as required by claim 21. Kao's argument is wholly without merit because Maloney expressly recites adding hydrogenated vegetable oil to the formulation, which Kao's own specification states is a hydrophobic material.

B. Secondary Considerations

Endo argues that it presented sufficient evidence of secondary considerations to overcome the Board's finding of obviousness. Endo's evidence of secondary considerations and the Board's response are identical between each of the three patent applications related to controlled-release tablets containing the drug oxymorphone and are addressed more fully above. Here, as with the '432 Application, the Board erred by failing to consider Endo's evidence of secondary considerations. Unlike the '432 Application, however, the Board, in this appeal, presented a strong showing of obviousness. Indeed, the only claim element not expressly disclosed in the prior art was the previously-unknown, yet inherent, food-effect property. As stated above, merely discovering and claiming a new benefit of an old process cannot render the process again patentable. Endo's evidence of secondary considerations was insufficient to overcome this strong showing of primary considerations that rendered the claims at issue invalid. *See, e.g.*, *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007).

II. The '740 Application

The Board determined that Ahdieh failed to separately argue the patentability of claims 25 and 30 of the '740 Application, and so it determined the patentability of all claims based on claim 21. Ahdieh cites three statements in his brief to the Board as showing a separate patentability argument regarding claims 25 and 30. Reply Br. of Ahdieh at 20 n.7. Far from showing distinct arguments for each claim, these fragments show that Ahdieh argued all the claims together. Because Ahdieh failed to argue to the Office that claim 25 is separately patentable, and fails to argue here that claim 30 is separately patentable, the only relevant claim before this court in this appeal is independent claim 21.

A. Obviousness

It is undisputed that Maloney discloses a method of providing extended pain relief by the provision of a therapeutically effective amount of controlled release oxymorphone. Ahdieh's asserted novel contribution is "providing information" about a previously undiscovered correlation between renal failure and bioavailability. Ahdieh argues that the Board and the examiner erred in holding his claim obvious because there was not substantial evidence that the correlation was known in the prior art.

This court squarely rejected a similar argument in *King Pharmaceuticals*. There, the claim at issue recited "a method of increasing the oral bioavailability of metaxalone" by "administering to the patient a therapeutically effective amount of metaxalone in a pharmaceutical composition with food," and "informing" the patient that taking metaxalone with food will increase the drug's bioavailability. *King Pharms.*, 616 F.3d at 1270-71. This court stated that the relevant question in determining

whether the method claims were patentable was "whether the additional instructional limitation of claim 21 has a 'new and unobvious functional relationship' with the known method of administering metaxalone with food." *Id.* at 1279 (citing *In re Ngai*, 367 F.3d 1336, 1338 (Fed. Cir. 2004)). We held that there was no functional relationship between the informing step and the administering step, because "[i]nforming a patient about the benefits of a drug in no way transforms the process of taking the drug with food," and therefore the claim was invalid as anticipated by the prior art. *Id.*

This case is not meaningfully distinct. Though the correlation between the renal impairment and bioavailability was not known, informing someone of the correlation cannot confer patentability absent a functional relationship between the informing and administering steps. *In re Ngai*, 367 F.3d at 1338; *see also General Elec. Co. v. Jewel Incandescent Lamp Co.*, 326 U.S. 242, 249 (1945) ("It is not invention to perceive that the product which others had discovered had qualities they failed to detect."). Just as in *King Pharmaceuticals*, the informing step does not "transform[] the process of taking the drug." 616 F.3d at 1279. This is because there is no requirement in the claim that the dosage be adjusted in response to the informing step. Indeed, because there is no indication of who is to be informed or to whom the drug is to be administered, the claim would presumably cover a situation where a doctor informs patient A of the correlation and administers a therapeutically effective dose of controlled release oxymorphone to patient B. Because there is no functional relationship between the two steps in the method, and because the administration of controlled release oxymorphone is squarely present in the prior art, Ahdieh's claim must fail. We agree with our predecessor court that to allow such a claim would effectively "remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior

art." *In re Wiseman*, 596 F.2d 1019, 1023 (CCPA 1979); *see also In re Ngai*, 367 F.3d at 1339 (noting that allowing claims where the printed matter was the only novel contribution would allow "anyone [to] continue patenting a product indefinitely provided that they add a new instruction sheet to the product").

Endo attempts to limit *King Pharmaceuticals* to the anticipation context, and distinguish it because the "informing" step was itself in the prior art, unlike the "providing information" step here. The *King Pharmaceuticals* analysis is not so limited. Claim 5 of United States Patent Number 6,683,102 was rejected as obvious in *King Pharmaceuticals*, though it depended upon a claim that was rejected for anticipation under the above reasoning. 616 F.3d at 1280-81. Moreover, it is simply not true that the correlation in *King Pharmaceuticals* was itself known in the prior art. *See id.* at 1278 ("Eon tacitly concedes that the district court never expressly found the 'informing' limitation disclosed in the prior art.").

Endo also argues that the "providing information" step and the administration step are functionally related because the step of "providing a therapeutically effective amount" "of necessity, requires adjusting the dosage as appropriate in accordance with the information provided in the prior step in light of the patient's renal condition." Br. of Appellant at 29. However, nothing *in the claim* requires that the dosage be adjusted in response to the providing of the information. Indeed, there is nothing in the claim even referencing the actual condition of the patient's renal system, which would presumably be the basis of any adjustment. Endo invites this court to import from the specification into the claim the limitation that the dosage be adjusted as a result of the informing step. This court declines Endo's invitation. The claim calls merely for informing someone of the noted correlation, and administering an effective dose of controlled release

oxymorphone to someone. There is no functional relationship between the two steps.

B. Secondary Considerations

Endo argues that the commercial success and unexpected results of Endo's Opana® ER product overcome the showing of obviousness. There is no dispute that Opana® ER is an embodiment of the claimed invention.

The Board assumed that the secondary considerations would be enough to overcome a prima facie case of obviousness but held that because Opana® ER was a single embodiment of the broad claim, the secondary considerations were not commensurate with the scope of the claim.

As discussed above, the Board's application of so strict a commensurateness requirement was improper. However, here, this error was harmless because there was no nexus between the secondary considerations presented and the claimed invention. *See Tokai*, 632 F.3d at 1369.

The only limitation not expressly recited in the prior art of record is the informing step. Endo does not contend that the evidence of unexpected results in the form of the multiple peaks is at all related to the informing step of the claim. Likewise, there is no indication that Opana® ER's commercial success is attributable to the informing step, particularly because, as discussed above, the claim does not require that the informing step have any appreciable effect on the administration of the drug.

Because here Endo has not provided any evidence of secondary considerations with a nexus to the novel components of claim 21, the secondary considerations do not compel a holding of nonobviousness.

CONCLUSION

For the foregoing reasons, this court vacates the decision of the Board in Appeal No. 2010-1307 regarding the '432 Application and remands for further proceedings consistent with this opinion, and affirms the decisions of the Board in Appeal No. 2010-1308 regarding the '859 Application and in Appeal No. 2010-1309 regarding the '740 Application.

VACATED AND REMANDED AS TO THE '432 APPLICATION

AFFIRMED AS TO THE '859 AND '740 APPLICATIONS

COSTS

Each party shall bear its own costs.