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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* SEAN D. MCALLISTER and PIERRE-YVES DESPREZ

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Appeal 2017-003707  
Application 14/587,831  
Technology Center 1600

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Before TAWEN CHANG, JOHN E. SCHNEIDER, and  
TIMOTHY G. MAJORS, *Administrative Patent Judges*.

MAJORS, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellants<sup>1</sup> submit this appeal under 35 U.S.C. § 134 involving claims to a method of treating glioblastoma multiforme with a therapeutically effective amount of a combination of cannabidiol (CBD) and tetrahydrocannabinol (THC). The Examiner rejected the claims as anticipated and obvious<sup>2</sup>. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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<sup>1</sup> Appellants identify the Real Party in Interest as Sutter West Bay Hospitals. App. Br. 2.

<sup>2</sup> We herein refer to the Specification, filed Dec. 31, 2014 (“Spec.”); Final Office Action, mailed Jun. 22, 2015 (“Final Act.”); Appeal Brief, filed Mar.

### STATEMENT OF THE CASE

Appellants’ “invention relates to methods and compositions for treating cancer.” Spec. ¶ 3. In embodiments, “the cancer is brain cancer, such as glioblastoma multiforme.” *Id.* ¶5. More specifically, the Specification describes treating cancer in a subject by administering “a therapeutically effective amount of a composition comprising a combination of the cannabinoids cannabidiol (CBD) and tetrahydrocannabinol (THC).” *Id.* ¶ 8. According to the Specification, “[t]he disclosure demonstrates that the addition of CBD to  $\Delta^9$ -THC improves the overall potency and efficacy of  $\Delta^9$ -THC in the treatment of cancer (e.g., glioblastoma multiforme ‘GBM’)” and that, in some aspects, this combination “synergistically inhibits GBM cell growth and induces apoptosis.” *Id.* ¶¶ 13–14.

Claims 16–18 are on appeal.<sup>3</sup> Those claims are reproduced below:

16. A method of treating glioblastoma multiforme in a human, consistent essentially of administering to said human in need of such treatment a therapeutically effective amount of a combination comprising cannabidiol (CBD) and a tetrahydrocannabinol (THC).

17. The method of claim 16, wherein the CBD and THC are in a ratio of 1:1.

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21, 2016 (“App. Br.”); Examiner’s Answer, mailed Oct. 7, 2016 (“Ans.”); and the Reply Brief, filed Dec. 6, 2016 (“Reply Br.”).

<sup>3</sup> Claim 19 was rejected under 35 U.S.C. § 112, second paragraph (*see* Final Act. (dated June 22, 2015) 16–18), but later canceled in an after-final amendment. *See* Interview Summary dated Dec. 22, 2015 (“The amendment [canceling claim 19] is hereby entered and only claims 16-18 are pending.”). The § 112 rejection of claim 19 is, thus, moot.

18. The method of claim 16, wherein the treatment of the glioblastoma multiforme in a human in need thereof is to reduce cell growth.

App. Br. 27 (Claims App'x).

The claims stand rejected as follows:

- I. Claims 16–18 under 35 U.S.C. § 102(b) as anticipated by Guzman Pastor<sup>4</sup> as evidenced by AANS<sup>5</sup> (“Rejection I”).  
Ans. 2–3.
- II. Claims 16–18 under 35 U.S.C. § 103(a) as obvious over Guzman Pastor as evidenced by AANS (“Rejection II”).  
Ans. 3–4.

An oral hearing before the Board was held on November 1, 2018, and a record of the hearing will be provided in the prosecution record.

#### REJECTION I – ANTICIPATION

##### *Issue*

The Examiner finds that “Guzman Pastor teaches that cannabidiol (CBD) and tetrahydrocannabinol (THC) are both used to treat glioblastomas,” (known as glioblastoma multiforme per AARC). Ans. 2. The Examiner focuses on Guzman Pastor’s claims, finding that “it is made clear that cannabinoids (plural) are used and in claim 3 it is specified that the

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<sup>4</sup> Guzman Pastor et al., US 2004/0039048 A1, published Feb. 26, 2004.

<sup>5</sup> American Association of Neurological Surgeons, Glioblastoma Multiforme (April 3, 2015) (.pdf of web pages of record) (“AANS”); *see also* <https://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Glioblastoma-Multiforme> (last visited Nov. 5, 2018).

cannabinoids can be CBD and THC.” *Id.* Thus, the Examiner asserts, “it would have been inevitable that both CBD and THC were used in the same composition since cannabinoids (plural) are used in the claims.” *Id.* at 2–3.

Appellants argue Guzman Pastor does not describe *combination* therapy, much less describe “administering of CBD in *combination* with THC” as required in claim 16. App. Br. 5. Appellants argue the Examiner misinterprets the term “cannabinoids” in Guzman Pastor’s claims as describing a combination of CBD and THC when, in fact, Guzman Pastor “consistently used ‘cannabinoids’ (plural) to refer to [administering] only a single type of cannabinoid.” *Id.* at 7–10 (citing numerous disclosures in Guzman Pastor). Appellants also contend that claim 3 of Guzman Pastor, which the Examiner principally relies on, uses *Markush*-style claim language to list the cannabinoids: THC ( $\Delta^9$ -tetrahydrocannabinol),  $\Delta^8$ -tetrahydrocannabinol, cannabiniol, and cannabidiol (CBD). *Id.* at 10; Guzman Pastor (claim 3). If anything, Appellants argue, this *Markush* language signals a listing of *alternative* cannabinoids — not combinations of them. App. Br. 10 (citing MPEP 2173.05(h) (“A ‘Markush’ claim recites a list of **alternatively** useable species . . . .”)) (emphasis by Appellants). Insofar as the Examiner is invoking inherency by asserting that combination therapy with THC and CBD would have been “inevitable,” Appellants argue the Examiner’s position is legally and factually flawed. App. Br. 11–14.<sup>6</sup>

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<sup>6</sup> Appellants’ contentions related to a potential interference between the presently claimed subject matter and claims in U.S. Patent No. 8,632,825 are not germane to resolution of this appeal. App. Br. 25.

The issue on appeal is whether a preponderance of the evidence on this record supports the Examiner’s determination that Guzman Pastor (as evidenced by AANS) describes the subject matter of the appealed claims.

*Analysis*

To show anticipation, each and every claim element, arranged as in the claim, must be found in a single prior art reference. *Net MoneyIN, Inc. v. Verisign, Inc.*, 545 F.3d 1359, 1369–71 (Fed. Cir. 2008) (holding “it is not enough that the prior art reference . . . includes multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention.”).

We are unpersuaded that Guzman Pastor describes administration of a therapeutically effective amount of a *combination* of CBD and THC to treat glioblastoma multiforme as claimed. Appellants’ reading of Guzman Pastor is more persuasive on this record. The use of plural “cannabinoids” in claim 3 does not require or describe the administration of *combinations* of the four natural cannabinoids listed as suggested by the Examiner. When read in light of Guzman Pastor’s entire description — including the copious citations and text pointed out by Appellants (App. Br. 7–10) — claim 3 suggests picking *one* of the listed cannabinoids for treatment. The use of the plural “cannabinoids” does not override the entire description of Guzman Pastor, none of which expressly describes treatment with combinations of cannabinoids. The use of *Markush*-style claim format in claim 3 also reinforces Appellants’ interpretation of Guzman Pastor, reflecting that the cannabinoids listed are contemplated as *alternatives*, not combinations.

The Examiner’s assertion that combination therapy is “inevitable” from Guzman Pastor fares no better in establishing that the pending claims

are anticipated.<sup>7</sup> From a reading of Guzman Pastor, it is not necessarily or inevitably the case that compositions comprising a combination of CBD and THC are administered to a subject. To the contrary, as Appellants note, there are no examples, experiments, or data described where any combination was administered and no instance where CBD was given even by itself. App. Br. 11–15. Hence, Appellants contend, Guzman Pastor “clearly and unequivocally shows that the ‘inevitable’ did not in-fact happen.” App. Br. 11. “Probabilities or possibilities” do not suffice to show that a claim limitation is present. *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981) (“The mere fact that a certain thing may result from a given set of circumstances is not sufficient.”).

Inasmuch as the Examiner meant to assert that the ordinarily skilled person would immediately “envisage” treatment with combinations of CBD and THC because both agents are in a preferred list, we disagree. Ans. 17. It is true that anticipation may sometimes be found even when specific subject matter is not explicitly combined in the reference if the person of ordinary skill in the art would “at once envisage” that subject matter from the reference’s description. *See In re Petering*, 301 F.2d 676, 681 (CCPA 1962). We are not, however, persuaded that is the case here. We reject the Examiner’s interpretation of the plural “cannabinoids” as indicating combination therapy for reasons discussed above. Also, this is not a case

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<sup>7</sup> For claim 17, the Examiner asserts that “[i]t is also inevitable that a ratio of 1:1 was used with respect to both CBD and THC since they were both noted to have equal importance in the claims [of Guzman Pastor].” Ans. 3. As Appellants point out, the Examiner provides no legal or scientific basis for this assertion. App. Br. 9–10.

where combination therapy using certain active agents is expressly set out in a working example, with a short list of substitute active agents also listed — a fact pattern more in line with the notion that a skilled artisan would at once envisage a substitute agent being used in place of an exemplified agent. Here, as already explained, there is simply no therapy using combinations of natural cannabinoids described whatsoever in Guzman Pastor. That change to Guzman Pastor, to the extent it could or would be made, raises the issue of obviousness, not anticipation.<sup>8</sup>

### *Conclusion*

For the above reasons, we conclude that the preponderance of the evidence on this record does not support the Examiner’s finding that Guzman Pastor anticipates claims 16 (or dependent claims 17 and 18).

## REJECTION II – OBVIOUSNESS

### *Issue*

The Examiner alternatively concludes that claims 16–18 would have been obvious over Guzman Pastor. Ans. 3–4. According to the Examiner:

In the event it is seen that it would not have been inevitable that both CBD and THC were used at the same time in the same composition . . . then it would have been obvious for one having

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<sup>8</sup> Appellants also contend the ordinarily skilled person would not have “envisaged” therapy with CBD in combination with THC because CBD was (contrary to Guzman Pastor’s suggestion) a known antagonist of the CB<sub>1</sub> and CB<sub>2</sub> receptors that Guzman Pastor was seeking to agonize with THC and synthetic agents. App. Br. 15–17; *see, e.g.*, Guzman Pastor ¶¶ 20, 34, 36; McAllister Decl. (dated Sept. 21, 2015) ¶¶ 4–7 (“CBD and THC work in conflict (really, opposite to each other) on CB1 and CB2 receptors”). We address this evidence below related to the rejection for obviousness.

ordinary skill in the art at the time the invention was made to use both CBD and THC at the same time to treat glioblastomas since the claims clearly state that both CBD and THC can be used to treat glioblastomas.

*Id.* at 4; *see also* Final Act. 14–15 (“It would have been obvious to one of ordinary skill in the art . . . to combine the components for their known benefit since each is well known in the art for the same purpose”) (citing *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007) and *In re Kerkhoven*, 626 F.2d 846, 850 (CCPA 1980)).

Although we agree with Appellants that Guzman Pastor does not expressly or inherently describe combination therapy with THC and CBD, that is not dispositive for the obviousness inquiry. Guzman Pastor teaches or suggests that cannabinoids including either THC or CBD can be used to treat glioblastomas. *See, e.g.*, Guzman Pastor, ¶¶ 2, 20, claims 1–3. This is true regarding Guzman Pastor’s disclosure even under the interpretation advanced by Appellants — where “cannabinoids” should be interpreted as requiring a selection of one of the cannabinoid agents in Guzman Pastor’s claim 3, for example, which lists both THC and CBD. App. Br. 7–11.

Given that Guzman Pastor suggests that compositions including either THC or CBD may provide treatment for glioblastomas, it follows from logic and the law that it is generally obvious to combine such compositions to form a third composition used for the same purpose. *In re Kerkhoven*, 626 F.2d 846, 850 (CCPA 1980) (“It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for

the very same purpose. . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art.”).

But that analysis also does not end the inquiry, because Appellants have provided further evidence that directly bears on the issues of a skilled person’s motivation for giving combination therapy and the reasonable expectation of success with such therapy. In order to sustain the § 103 rejection, the preponderance of the evidence must demonstrate that the ordinarily skilled person would have been motivated to administer combinations of CBD and THC to subjects with a reasonable expectation of success in treating glioblastoma. On these issues, and notwithstanding Guzman Pastor’s disclosure, the evidence on this record tilts in Appellants’ favor.

As discussed above, Guzman Pastor describes no examples, experiments, or data to back up its suggestion that CBD is capable of treating glioblastoma. That suggestion is provided in Guzman Pastor’s claims. Guzman Pastor, claims 2–3. The only other mention of CBD (“cannabidiol”) is in paragraph 20, where it states that the invention is applicable to CBD and suggests that CBD will behave like other natural cannabinoids (i.e., THC) — as an *agonist* of the CB<sub>1</sub> and CB<sub>2</sub> receptors. Guzman Pastor ¶ 20.

Evidence submitted by Appellants, however, demonstrates that this may be scientifically inaccurate in that CBD is not a CB<sub>1</sub> and CB<sub>2</sub> agonist. App. Br. 20–21. Rather, it was apparently well known prior to the invention that CBD was a potent *antagonist* to CB<sub>1</sub> and CB<sub>2</sub> activation. McAllister Decl. ¶¶ 4–7 (“CBD does not efficiently interact nor activate CB1 and CB2

receptors, and therefore would antagonize the effects of drugs activating CB1 and CB2 receptors.”); Schowalter<sup>9</sup> (showing that CBD’s affinity for CB1 and CB2 receptors is approximately 100-fold lower than those receptors affinity for THC). Indeed, in a study by Thomas,<sup>10</sup> the researchers found that cannabidiol (CBD) displays unexpectedly high potency as an antagonist of CB<sub>1</sub> and CB<sub>2</sub> receptor agonists. So, as one of the inventors testifies:

[O]ne of ordinary skill in the art in 2007 would not have used CBD in combination with THC as alleged by the Office, as the two compounds were recognized as having opposite effects on the antiproliferative effects of CB1 and CB2 receptors identified as being important for the methods of Guzman Pastor.

McAllister Decl. ¶ 7. When other CB<sub>1</sub> and CB<sub>2</sub> antagonists were administered in Guzman Pastor “an effective prevention was observed of the cell death induced by THC (FIG. 5a).” Guzman Pastor ¶ 16; *see also id.* ¶ 36 (describing THC’s antiproliferative and cell-death inducing effect, which effect was prevented upon the addition of CB<sub>1</sub> and CB<sub>2</sub> antagonists); Reply Br. 8. Put differently, because killing the cancer cells with THC is desired in Guzman Pastor, this antagonist activity is the opposite of the effect desired. Appellants therefore argue that “one of skill in the art,

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<sup>9</sup> Vincent M. Schowalter et al., *Evaluation of Binding in a Transfected Cell Line Expressing a Peripheral Cannabinoid Receptor (CB2): Identification of Cannabinoid Receptor Subtype Selective Ligands*, 278:3 THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS 989–96 (1996).

<sup>10</sup> A Thomas et al., *Cannabidiol displays unexpectedly high potency as an antagonist of CB<sub>1</sub> and CB<sub>2</sub> receptor agonists in vitro*, 150 BRITISH JOURNAL OF PHARMACOLOGY 613–23 (2007).

knowing that CBD is an antagonist and reading the fact that Guzman Pastor *et al.* teach antagonists inhibit cancer cell death caused by THC would not have combined CBD with THC as posed by the Examiner.” *Id.* (bold font deleted). When balanced against Guzman Pastor’s unsubstantiated suggestion that CBD is a CB<sub>1</sub> and CB<sub>2</sub> receptor agonist for treating glioblastoma, Appellants’ argument and cited evidence is more persuasive.<sup>11</sup> And, on this record, the Examiner has not established a sufficient evidentiary basis to support the finding that the ordinarily skilled person would have been motivated to administer combination therapy with both CBD and THC with a reasonable expectation of success.

Because we find the evidence on the issues of motivation to modify the prior art and the reasonable expectation of success insufficient to support a *prima facie* conclusion of obviousness, we decline to reach Appellants’ evidence of alleged unexpected synergy with the claimed combination therapy.

### *Conclusion of Law*

The preponderance of the evidence on this record fails to support the Examiner’s conclusion that claims 16–18 would have been obvious over Guzman Pastor (as evidenced by AANS).

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<sup>11</sup> The Examiner never squarely rebuts this evidence beyond reiterating Guzman Pastor’s teachings. Ans. 36–38 (“That teaching [in Guzman Pastor] is not negated because of what others may teach about the activities of the two cannabinoids in a different context”). But, as noted, the lack of supporting detail in Guzman Pastor is outweighed by the testimony and multiple publications in the scientific literature cited by Appellants.

Appeal 2017-003707  
Application 14/587,831

SUMMARY

We reverse the rejections for anticipation and obviousness on appeal.

REVERSED