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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* NIBALDO C. INESTROSA and
JUAN L. HANCKE OROZCO[1]

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Appeal 2019–000509
Application 14/761,824
Technology Center 1600

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*Before:* JEFFREY N. FREDMAN, JOHN G. NEW, and JAMIE T. WISZ, *Administrative Patent Judges.*

NEW, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] We use the word "Appellant" to refer to the "applicant" as defined in 37 C.F.R. § 1.142. Appellant identifies InnoBiosciences LLC as the real party-in-interest. App. Br. 1.

## SUMMARY

Appellant files this Appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 9, 10, and 12–17 as unpatentable under 35 U.S.C. § 103(a) as being obvious over Hancke Orozco et al. (US 2006/0063831 A1, March 23, 2006) ("Hancke Orozco").

Claims 1–9 also stand rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over 和记黄 et al. (CN 1666985 A, March 14, 2005) ("CN '985").[2]

Claims 1, 2, 5–7, and 11 stand rejected as unpatentable under 35 U.S.C. § 103(a) as being obvious over Bombardelli et al. (WO 2011/086007 A1,July 21, 2011) ("Bombardelli").

We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

## NATURE OF THE CLAIMED INVENTION

Appellant's claimed invention is directed to a method of using andrographolide (the claimed composition) and its derivatives in the treatment of Alzheimer's disease. Spec. Abstr.

## REPRESENTATIVE CLAIM

Independent claim 1 is representative of the claims on appeal and recites:

> 1. Administering to human diagnosed with dementia, a therapeutically effective amount of a compound of Formula (I):

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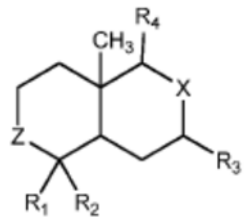
[2] A machine translation of CN '985 provided by Google Patents is of record. Neither Appellant nor the Examiner dispute its accuracy.




(I)

wherein

$R_1$ is selected from the group consisting of hydrogen, alkyl or hydroxyl,

$R_2$ is selected from the group consisting of hydroxyalkyl or alkyl-O-$L_1$, wherein $L_1$ is a carbohydrate moiety,

$R_3$ is selected from the group consisting of hydrogen or hydroxyl,

X is selected from the group consisting of C(=$CH_2$), CH(OH), or a spirooxirane-2 moiety,

Z is selected from the group consisting of $CH_2$, CH(OH) or C(=O), and

$R_4$ is selected from the group consisting of an optionally substituted $L_2$ alkyl or $L_2$ alkenyl, wherein $L_2$ is an optionally substituted 3-furanyl or 3-fur-3-enyl moiety,

or a pharmaceutically acceptable salt, ester, ether or prodrug thereof.

App. Br. 21.

## ISSUES AND ANALYSES

We agree and adopt, the Examiner's findings, reasoning, and conclusion that the claims on appeal are obvious over the combined cited prior art. We address the arguments raised sequentially by Appellant below.

### A. Rejection of the claims 9, 10, and 12–17 over Hancke Orozco

*Issue*

Appellant argues that the Examiner erred in disregarding a different Examiner's finding in a prior examination that Hancke Orozco does not enable treating dementia. App. Br. 10.

*Analysis*

The Examiner finds that Hancke Orozco teaches an andrographolides[3] composition that reduces proinflammatory cytokines and exemplifies its use in treating Alzheimer's disease and multiple sclerosis. Final Act. 6 (citing Hancke Orozco ¶¶ 38, 69, 149, and 153–158 claims 53, 54, 57, 64). The Examiner finds that Example 9 of Hancke Orozco teaches the andrographolides composition used in the treatment of Alzheimer's disease and multiple sclerosis. *Id.* (also citing Hancke Orozco Exs. 11, 15, ¶¶ 149, 153–156). The Examiner finds that these treatments comprise 24.6% andrographolide, 4.8% 14-deoxyandrographoilide, and 0.6%

[3] Andrographolides are labdane diterpenes extracted from, and a major component of, the plant *Andrographis paniculata* (family Acanthaceae). *See* Spec. 1. Appellant and the Examiner do not dispute that Appellant's claimed compositions are andrographolides.

neoandrographolide and further suggests a pharmaceutical form with dosages of 1–5 mg/kg andrographolide, 0.2–1 mg/kg 14-deoxyandrographoilide, and 0.02–0.12 mg/kg neoandrographolide. *Id.* (citing Hancke Orozco 144–147).

The Examiner finds further that Hancke Orozco teaches that the method of treating Alzheimer's disease includes diagnosing patients with appropriate neuropsychological tests, such as the MMSE, BNT, and TT. Final Act. 6 (citing Hancke Orozco ¶¶ 153, 154). The Examiner finds that Hancke Orozco differs from the present claims 9, 10, and 12–17 in that Hancke Orozco at least explicitly suggests the methods now claimed but fails to describe or contemplate an embodiment beyond the general teaching and prophetic examples. *Id.*

Appellant argues that, in a prior examination, the Examiner found that, given the unpredictability of pharmaceutical science, Hancke Orozco does not enable treating dementia. App. Br. 10 (citing Office Act. re US Appl. No. 10/516,500 at 6 (March 16, 2006) (the "'500 Examination")). Appellant contends that the Examiner in the present appeal can reject the earlier fact finding in the '500 Examination, but that, to do so, the Examiner must first demonstrate evidence showing why the fact finding in the ''500 Examination was clearly error. *Id.* Appellant argues that the Examiner has not done so. *Id.* Appellant therefore asserts that the Examiner must accept the fact findings of the '500 Examination, because Examiner Barker has not provided any evidence showing clear error in that finding. *Id.* at 11 (citing MPEP §§ 704.01, 706.04).

Appellant argues further that federal administrative procedure distinguishes between fact findings and legal conclusions. App. Br. 11.

According to Appellant, an Agency's legal conclusions in one case do not bind it in a later case with different facts, but Agency fact findings bind the Agency in subsequent proceedings. *Id.* (citing, e.g., *U.S. v. Utah Constr. & Mining Co.*, 384 U.S. 394, 422 (1966) (holding that when a Federal agency "resolve[s] disputed issues of fact properly before it which the parties have had an adequate opportunity to litigate, the courts have not hesitated to apply *res judicata*")).

Appellant contends that, in the '500 Examination, the Examiners found that Hancke Orozco provides such limited disclosure, in an unpredictable art, that Hancke Orozco failed to enable the artisan to treat either dementia or AIDS. App. Br. 12. Appellant asserts that this is a finding of fact, and not a legal conclusion. *Id.* Appellant argues that the present Examiner's rejection must be reversed as a matter of law because the '500 Examination already found that Haneke Orozco fails to enable treating dementia, and the Examiner in the present appeal provides no new evidence showing that the '500 Examination's finding was clearly error. *Id.*

Appellant argues further that the Examiner's alleged disregard of the '500 Examination's findings are in violation of the Federal Administrative Procedure Act (the "APA"). App. Br. 12 (citing, e.g., *Dickinson v. Zurko*, 527 U.S. 150, 152 (1999)). Appellant alleges that the Examiner's disregard of the fact finding of the '500 Examination, without providing evidence to support a contrary position, is arbitrary and capricious in violation of 57 U.S.C. § 706(2)(A).

Appellant further argues that the APA requires the Examiner to give "full faith and credit" to the findings of fact of the '500 Examination. App. Br. 13 (citing M.P.E.P. §§ 704.01; 706.04). Appellant therefore contends

that the Examiner's disregard of the '500 Examination's prior fact finding is thus "without observance of procedure required by law." *Id.* (citing 57 U.S.C. § 706(2)(D)).

We are not persuaded by Appellant's argument. As an initial matter, we disagree with Appellant's contention that the '500 Examiner's conclusion that: "Hancke [Orozco] failed to enable the artisan to treat either dementia or AIDS," is a finding of fact, rather than a conclusion of law. App. Br. 12. "Invalidity for lack of enablement is a conclusion of law and must be supported by facts proved by clear and convincing evidence." *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990). The '500 Examination's conclusion that Hancke Orozco does not enable the treatment of dementia is therefore, Appellant's argument notwithstanding, a conclusion of law that is not controlling in our analysis in the present appeal.

Furthermore, Appellant's characterization of the Examiner's initial Final Rejection of the '500 application does not withstand scrutiny. Although the Examiner initially rejected the claims under 35 U.S.C. § 112, first paragraph, as failing to enable a "method of diagnosing in a patient a disease selected from the group consisting of: Alzheimer's disease; Immune deficiency syndrome; and autoimmune disease," this rejection was subsequently withdrawn by the Examiner in a subsequent rejection. *See* '500 Exam., Final Act., March 16, 2006 at 10–11; '500 Exam., Final Act., January 19, 2007 at 2–3.

Furthermore, the claims at issue in the present appeal are not directed to "a method of diagnosing a patient," as claimed in the '500 application, or in Hancke Orozco, but rather to "[a] method comprising: administering to a

human diagnosed with dementia…" (dependent claims 9, 10 (which depend from claim 2)) or "[a]dministering to a human a test" and "Administering to said human, … a daily dosage (claims 12–17). Whether the Hancke Orozco claims enabled "diagnosing" is consequently entirely irrelevant to our present inquiry and, in any case, that rejection was withdrawn by the Examiner. Appellant makes no argument on the merits that the claims of Hanck Orozco were not enabled by the Specification.

The question at hand, rather, is whether the claims are obvious over the prior art reference cited by the Examiner. Appellant makes no substantive argument on the merits of the Examiner's obviousness rejection beyond the argument that the prior art is not enabled. Because we conclude that Appellant's argument is not persuasive in this respect, we affirm the Examiner's rejection of claims 9, 10, and 12–17 upon this ground.

B. Rejection of the claims 1–9 over CN '985

*Issue*

Appellant argues that the Examiner erred because the Specification of CN '985 does not enable the claimed treatment of dementia. App. Br. 15.

*Analysis*

Appellant acknowledges that CN '985 teaches that andrographolide affects IL-1β and TNF-α expression *in vitro*, and that, based upon this data, CN '985 teaches that andrographolide can be used to treat Alzheimer's-related dementia. App. Br. 13 (citing CN '985 2, Figs. 1–2). However, Appellant argues that CN '985 also teaches that andrographolide can also be used to treat a large number of other diseases that are associated with IL-1β

and TNF-α expression. *Id.* at 13–14 (citing CN '985 2, 5). Appellant argues that the wide range of diseases that can thus be treated with andrographolide is consequently and inherently unbelievable. *Id.* at 14.

Appellant argues, therefore, that CN '985 is not enabled, and cannot therefore stand as prior art to the present application. App. Br 15 (citing MPEP § 2121(1); *In re Morsa*, 713 F.3d 104, 110 (Fed. Cir. 2013)). Appellant points to the unpredictability of the art as further substantiating their conclusion that CN '985 is not enabled. *Id.* at 15. Appellant contends that, given this unpredictability, the Board has already concluded that, generally speaking, limited *in vitro* data standing alone does not enable treating human dementia. *Id.*

We are not persuaded by Appellant's argument. The question before us is whether CN '985 is enabling for the claims of the CN '985 patent. The claims of CN '985 are not directed to a method of "treating human dementia," as argued by Appellant, but are primarily composition claims directed to andrographolide. *See* CN '985 claim 1: "A compound of the following general formula or a prodrug thereof"; claim 5: "[t]he compound or prodrug thereof of the following formula…."; claim 8: "[a]ndrographolide preparing [sic] IL-1β inhibitor use…."; claim 9: "[a] compound or prodrug thereof of the following formula"; claim 11: "the pharmaceutical composition of claim 10…."

Claim 4 of CN '985 recites: "Andrographolide preparation TNF-α inhibitor use, wherein the TNF-a inhibitors useful for treating disorders selected from the group of one or more of [various diseases including Alzheimer's]." Claim 10 of the CN '985 patent recites: "A pharmaceutical composition comprising a compound or prodrug thereof a therapeutically

effective amount of a formula selected from the following, in a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers…."

All of the claims of CN '985, with the exception of claim 4, are therefore directed to composition claims and not to a "method of treating human dementia" as argued by Appellant. We acknowledge that certain of the claims of CN '985 also recite some variation of where the claimed compositions "are useful for the treatment of disorders selected from the group of one or more of [various diseases including Alzheimer's]." *See, e.g.*, CN '985 claim 8. However, these limitations recite an intended use of the claimed compositions, and are consequently not limiting upon the claimed composition itself. Therefore, the proper question is whether the Specification of CN '985 is enabling for the compositions recited in the claims, and not whether it is enabling for "treating human dementia," as Appellant argues.

Our reviewing court has held that:

> In patent prosecution the examiner is entitled to reject application claims as anticipated by a prior art patent without conducting an inquiry into whether or not that patent is enabled or whether or not it is the claimed material (as opposed to the unclaimed disclosures) in that patent that are at issue. The applicant, however, can then overcome that rejection by proving that the relevant disclosures of the prior art patent are not enabled.

*Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1355 (Fed. Cir. 2003) (Internal citation omitted). Appellant has made no argument that the CN '985 Specification is not enabled for the *compositions* recited in the claims of the CN '985 patent.

Claim 10 of CN ’985 recites: “A pharmaceutical composition comprising a compound or prodrug thereof a therapeutically effective amount of a formula selected from the following, in a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers….” The Specification of the CN ’985 patent discloses:

> A therapeutically effective amount of the compound of the present invention, a prodrug thereof or a pharmaceutically acceptable salt thereof and a pharmaceutical composition is between 0.001–100mg/kg/d. Between any of the above range of the amount of an effective amount of the present invention are all between 0.001 mg/kg/d and 99.999 mg/kg/d which is between the lower dose, higher doses ranged from 0.002 mg /kg/ d and between 100 mg/kg/d.

*See* CN ’985, 12. We therefore conclude that, contrary to Appellant’s argument, the CN ’985 patent is enabled for administering a therapeutically effective dose of andrographolide.

Claim 4 of the CN ’985 patent recites: “Andrographolide preparation TNF-α inhibitor use, wherein the TNF-α inhibitors useful for treating disorders selected from the group of one or more of [various diseases including Alzheimer’s].” We interpret this language to mean that the claim recites using andrographolide as a TNF-α inhibitor, with the intended purpose (“useful for”) of the treatment of various diseases, including Alzheimer’s-related dementia. The CN ’985 patent discloses, in Figure 1: “[T]he formula shown [sic] andrographolide and its derivatives, analogs *in vitro* significantly inhibited the expression of precursor inflammatory cytokines TNF-α and IL-1β….” CN ’985, 6. We therefore conclude that the Specification of CN ’985 is enabling for its use as a TNF-α inhibitor. *Id.* at 7. Furthermore, CN ’985 also discloses that it was well known in the art that

TNF-α inhibitors are useful in the treatment of TNF-α-related diseases, including Alzheimer's dementia. *See* CN '985, 2. We consequently conclude that the CN '985 is enabling for claim 4.

We conclude that Appellant has failed to meet the burden of showing that CN '985 is not enabled. Because Appellant makes no substantive argument addressing the Examiner's conclusion that the claims on appeal are obvious over CN '985, we affirm the Examiner's rejection of claims 1–9 on that ground.

C. Rejection of the claims 1, 2, 5–7, and 11 over Bombardelli

*Issue*

Appellant argues that: (1) Bombardelli fails to enable the artisan to treat dementia; and (2) Bombardelli expressly teaches away from the claimed method. App. Br. 18–19

*Analysis*

With respect to argument (1), Appellant argues that Bombardelli, like the instant inventors, evaluates the behavior of transgenic mice in a Morris Water Maze. App. Br. 16 (citing Bombardelli). According to Appellant, Bombardelli teaches that treatment improved learning in the transgenic mice, similarly to that found by the instant inventors. *Id.* However, argues Appellant, Bombardelli does not provide examples of any further studies, unlike the inventors of the present application. *Id.* Appellant therefore argues that Bombardelli teaches how to improve learning, but not how to treat dementia, because, Appellant asserts, water maze data alone does not

"reasonably correlate" to efficacy in treating dementia in humans. *Id.* (citing MPEP § 2107.03(1)).

With respect to argument (2), Appellant contends that the administration of andrographolide without *Gingko biloba* extract and phospholipids fails to "fully satisfy the therapeutic requirements." App. Br. 19 (quoting Bombardelli 4). Appellant acknowledges the Examiner's finding that Appellant's claims 1 and 2 allow for additional ingredients. *Id.* However, argues Appellant, the issue is not whether a skilled artisan, starting from claim 1, would find it obvious to add *Gingko biloba* extract and phospholipids to claim 1 so as to replicate Bombardelli. *Id.* Rather, Appellant asserts, the proper question is whether a skilled artisan, starting from Bombardelli would have found it obvious to remove *Gingko biloba* extract and phospholipid from the method taught by Bombardelli to arrive at the method of claim 1. *Id.*

Appellant asserts that Bombardelli expressly admonishes the reader to not do so, warning that andrographolide without *Gingko biloba* extract and phospholipid fails to "fully satisfy the therapeutic requirements." App. Br. 19 (quoting Bombardelli 4). Therefore, Appellant contends, Bombardelli teaches away from Appellant's claims on appeal. *Id.*

We are not persuaded by Appellant's arguments. With respect to Appellant's argument (1) *supra*, Bombardelli expressly teaches that:

> [T]he APPswe/PS1 transgenic mouse.…expresses the human gene presenilin 1 (delta E9) and the chimeric mouse/human gene of amyloid precursor protein (APP), which in turn contains the Swedish mutation.
>
> It has previously been demonstrated that this animal model is characterized by abnormal amyloid deposition, with progressive

> memory loss, thus demonstrating one of the most predictive models for the study of drugs designed to treat Alzheimer's disease.

*See* Bombardelli 8 (internal reference omitted). We agree with the Examiner that Bombardelli thus teaches or suggests to the person of ordinary skill in the art that the transgenic mice in question are recognized in the art as being an accepted model for studying drugs designed to treat dementia, such as that caused by Alzheimer's disease, and that an aspect of this transgenic mouse model of Alzheimer's disease is progressive memory loss. *See id.*

Bombardelli further teaches that:

> Treatment of 20 transgenic mice per group with the composition described in example 1 *and the individual ingredients* demonstrates that the composition according to the invention significantly reduces memory loss induced by amyloid accumulation in the transgenic mouse, as demonstrated in the Morris water maze paradigm test (Morris R, J. Neurosci. Methods 1984; 11:47-60).

Bombardelli 8 (emphasis added). Bombardelli does not thus merely teach that treatment with its compositions improves learning, as argued by Appellant, but rather teaches that administration of the composition, *or its individual ingredients*, "significantly reduces memory loss induced by amyloid accumulation in the transgenic mouse." *Id.* We therefore agree with the Examiner that a person of ordinary skill, comprehending the teachings of Bombardelli, would have found it obvious to administer andrographolide, one of the individual ingredients of Bombardelli's composition, to a human diagnosed with dementia.

For the same reason, we are not persuaded that Bombardelli teaches away from Appellant's invention. A "teaching away" requires a reference to

actually criticize, discredit, or otherwise discourage the claimed solution. *See In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004). As we have explained, Bombardelli expressly teaches that andrographolide, one of the individual ingredients of Bombardelli's composition, "significantly reduces memory loss induced by amyloid accumulation in the transgenic mouse." Bombardelli 8. The passage of Bombardelli quoted by Appellant reads, in its entirety: "Not all the mixtures described in the literature and present on the market fully satisfy the therapeutic requirements." Bombardelli 4. This sentence is presented subsequent to a review of certain prior art compounds, and *not* to the compositions taught by Bombardelli, which, as we have explained, demonstrates that andrographolide, one of the individual ingredients of Bombardelli's composition, "significantly reduces memory loss induced by amyloid accumulation in the transgenic mouse." *Id.* at 8. We do not, therefore, find persuasive Appellant's argument that Bombardelli teaches away from Appellant's claimed invention.

Finally, in a footnote, Appellant also argues that Bombardelli is not enabled because it does not teach dosage. App. Br. 18, fn.3. According to Appellant, Bombardelli teaches making 600 mg cellulose oral capsules, which, Appellant argues, has approximately the volume of a chick pea. *Id.* (citing Bombardelli 7). Appellant argues that such capsules would be too large for a mouse to swallow, and that Bombardelli therefore teaches administering, not capsules, but "the composition," Bombardelli, without teaching how much composition is to be administered. *Id.*

We are not persuaded. Even if we accept Appellant's unsupported assertion with respect to the volume of a 600 mg oral capsule, Bombardelli expressly teaches "[t]reatment of 20 transgenic mice per group with the

composition described in example 1." *See* Bombardelli 8. Example 1 of Bombardelli teaches preparation of containing:

1. *Andrographis paniculata* extract (35% andrographolides) 150 mg
2. *Ginkgo biloba* extract complexed with phospholipid 250 mg
3. Evening primrose oil *q.s. for 600 mg*.

*Id.* Although Example 4 of Bombardelli is silent with respect to the means of administration of the composition of Example 1, Bombardelli teaches that administration of andrographolide alone, at 150 mg, "significantly reduces memory loss induced by amyloid accumulation in the transgenic mouse." *Id.* at 8, 9, Table 1. We are consequently not persuaded by Appellant's argument that Bombardelli is not enabled as prior art to Appellant's claims.

## CONCLUSION

The Examiner's rejection of claims 1–17 under 35 U.S.C. § 103(a) is affirmed.

## AFFIRMED

| Claims Rejected | 35 U.S.C. § | Reference(s)/Basis | Affirmed | Reversed |
|---|---|---|---|---|
| 9, 10, 12–17 | 103(a) | Hancke Orozco | 9, 10, 12–17 | |
| 1–9 | 103(a) | CN '985 | 1–9 | |
| 1, 2, 5–7, 11 | 103(a) | Bombardelli | 1, 2, 5–7, 11 | |
| **Overall Outcome** | | | 1–17 | |