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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/621,782	06/13/2017	Thomas B. Ottoboni	092459-0213/8026.US06	9963

108547 7590 09/02/2020

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EXAMINER	
LIU, TRACY	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
09/02/2020	ELECTRONIC

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte THOMAS B. OTTOBONI and
LEE ANN LYNN GIROTTI[1]

Appeal 2020-001510
Application 15/621,782
Technology Center 1600

Before ERIC B. GRIMES, JOHN G. NEW, and MICHAEL A. VALEK, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] We use the term "Appellant" to refer to the "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies Heron Therapeutics, Inc. 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 1–8, 15–19, 25–35, 40–45, 47, and 53–59. Specifically, claims 1–8, 15–19, and 25–33 stand rejected as unpatentable under 35 U.S.C. § 103 as being obvious over the combination of Ng et al. (US 2012/0283253 A1, November 8, 2012) ("Ng") and Wohabrebbi (US 2010/0015049 A1, January 21, 2010) ("Wohabrebbi").

Claims 34, 35, 40–45, 47, and 53–59 stand rejected as unpatentable under 35 U.S.C. § 103 as being obvious over the combination of Ng, Wohabrebbi, and Dadey et al. (US 2008/0299168 A1, December 4, 2008) ("Dadey").

Claims 1–8, 15–19, 25–35, 40–45, 47, and 53–59[2] also stand rejected as unpatentable under the nonstatutory doctrine of obviousness-type double patenting as being obvious over claims 1, 6, and 7 of US 9,744,163 B2; August 29, 2017 (the "'163 patent"), claim 1 of US 9,592,227 B2; March 14, 2017 (the "'227 patent"), and claims 1 and 8 of US 9,913,909 B2; March 13, 2018 (the "'909 patent"), Ng, and Wohabrebbi.

Claims 1–8, 15–19, 25–35, 40–45, 47, and 53–59 stand further provisionally rejected as unpatentable under the nonstatutory doctrine of obviousness-type double patenting as being obvious over claim 1 of copending US Ser. No. 14/691,491 (the "'491 application") and claims 1 and

[2] Appellant states that claims 1–8, 15–19, 25–35, and 40–59 are rejected as unpatentable in both obviousness-type double patenting rejections. App. Br. 3. However, claims 46 and 48–52 have been canceled. *See* App. Br. 18–19 (Claims Appendix).

9 of copending US Ser. No. 15/457,545 (the "'545 application"), Ng, and Wohabrebbi.[3]

Claims 1–8, 15–19, 25–35, 40–45, 47 and 53–59 are provisionally rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1–40 of copending US Ser. No. 15/331,759 (the "'759 application").

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

We REVERSE.

NATURE OF THE CLAIMED INVENTION

Appellant's claimed invention is directed to compositions comprising a delivery vehicle or delivery system and an active agent dispersed within the delivery vehicle or system, wherein the delivery vehicle or system contains a polyorthoester polymer and a polar aprotic solvent. The compositions include an amide- or anilide-type local anesthetic of the "caine" classification, and a non-steroidal anti-inflammatory drug ("NSAID"). Abstr.

REPRESENTATIVE CLAIM

Claim 1 is representative of the claims on appeal and recites:

> 1. A composition, comprising: an amide local anesthetic, an enolic-acid non-steroidal anti-inflammatory drug (NSAID) and a delivery vehicle, wherein the enolic-acid non-steroidal NSAID is the sole NSAID comprised in the composition.

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[3] The Examiner also rejected claims 33 and 58 as unpatentable under 35 U.S.C. § 112(b) as being indefinite. Final Act. 2. The Examiner has withdrawn this rejection. Ans. 5.

App. Br. 13.

ISSUES AND ANALYSES

We decline to adopt the Examiner's findings, reasoning, and conclusion that the claims on appeal are *prima facie* obvious over the cited prior art. However, we do not reach the rejection of claims 1–8, 15–19, 25–35, 40–45, 47 and 53–59 over the '759 application. We address the arguments raised by Appellant below.

A. Rejection of claims 1–8, 15–19, 25–35, 40–45, 47, and 53–59 under 35 U.S.C. § 103

Issue 1

Appellant argues that the Examiner erred in finding that a person of ordinary skill in the art would have been motivated to combine the teachings of the cited prior art references to arrive at Appellant's claimed compositions. App. Br. 4.

Analysis

The Examiner finds that Ng teaches, *inter alia*, compositions comprising active agents including any compound or mixture of compounds which produces a beneficial or useful result. Final Act. 4. The Examiner finds that Ng teaches examples of these active agents, including anti-inflammatory agents and amide-type local anesthetics such as bupivacaine. *Id.* (citing Ng ¶ 23). The Examiner finds that Ng also teaches that the concentration of the active agent in the semi-solid polyorthoester composition can vary over a wide range (e.g., 0.1–80 wt%), depending on a

variety of factors, such as the release profile of the composition, the therapeutically effective dose of the active agent, and the desired length of the interval during which the active agent is released. *Id.* (citing Ng ¶ 75).

The Examiner acknowledges that Ng neither teaches nor suggests that its compositions comprise an enolic-acid non-steroidal anti-inflammatory drug ("NSAID"). Final Act. 5. However, the Examiner finds, Wohabrebbi teaches methods and compositions for reducing, treating or preventing post-operative pain and/or inflammation comprising administration of one or more biodegradable drug depots comprising a therapeutically effective amount of diclofenac and/or ketoprofen to a target tissue site. Final Act. 5 (citing Wohabrebbi Abstr.). The Examiner finds that Wohabrebbi also teaches the inclusion in its compositions of other therapeutic agents including meloxicam, as an NSAID, and bupivacaine as an analgesic agent. *Id.* at 6 (citing Wohabrebbi ¶¶ 45, 47).

The Examiner concludes that it would have been obvious for a person of ordinary skill in the art to incorporate meloxicam into the compositions taught by Ng, because it was a known anti-inflammatory agent, as taught by Wohabrebbi. Final Act. 6.

Appellant argues that Ng neither teaches nor suggests an enolic-acid non-steroidal anti-inflammatory drug as the active agent, much less a combination of an amide local anesthetic and an enolic-acid non-steroidal anti-inflammatory drug as recited in the claims. App. Br. 5. Appellant acknowledges that Ng teaches a composition comprising an active agent and a semi-solid delivery vehicle. *Id.* (citing Ng ¶ 9). Appellant also notes that Ng teaches that the active agent includes any compound or mixture of compounds, which produces a beneficial or useful result, and teaches a

"laundry list" of active agents. *Id.* (citing Ng ¶ 23). Appellant argues that Ng teaches anti-inflammatory agents only as an example of an active agent, and does not distinguish enolic-acid non-steroidal anti-inflammatory drugs from other anti-inflammatory agents, nor does it list any enolic-acid non-steroidal anti-inflammatory drugs among the exemplified anti-inflammatory agent (e.g., aspirin, ibuprofen, naproxen, ketorolac, COX-1 inhibitors, COX-2 inhibitors, etc.). *Id.*

Appellant contends that, other than Ng's broad teaching that the active agent can include any compound or a mixture of compounds which produces a beneficial or useful result, Ng neither teaches nor exemplifies a composition comprising a mixture of any particular compounds. App. Br. 6. Therefore, argues Appellant, Ng does not teach or suggest a composition comprising an amide local anesthetic and an enolic-acid non-steroidal anti-inflammatory drug, as recited in the claims. *Id.* Appellant asserts that "[t]he fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness." *Id.* at 7 (citing *In re Jones*, 958 F.2d 347, 350 (Fed. Cir. 1992) (holding that "We decline to extract from *Merck* the rule … that regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it"); *see also* MPEP§ 2144.08)). Appellant also points to our reviewing court's holding that the disclosure of an active ingredient that can be contained in a formulation is insufficient by itself to invalidate a claim directed to a formulation comprising the active ingredient. *Id.* at 8 (citing *Impax Labs., Inc. v. Lannett Holdings Inc.*, 893 F.3d 1372, 1379 (Fed. Cir. 2018)).

Turning to Wohabrebbi, Appellant argues that the reference teaches compositions comprising diclofenac and/or ketoprofen that have analgesic and anti-inflammatory effect, used in single or multiple drug depots. App. Br. 9 (citing Wohabrebbi ¶ 10). Appellant notes, and it is not disputed by the Examiner, that diclofenac and ketoprofen are both NSAIDs and, furthermore, are both carboxylate, and not enolate, NSAIDs. *Id.* (citing Wohabrebbi ¶¶ 4, 5).

Appellant acknowledges that Wohabrebbi further teaches that, in addition to diclofenac and/or ketoprofen, the compositions may comprise one or more additional therapeutic agents, including anti-inflammatory agent and analgesic agents. App. Br. 9 (citing Wohabrebbi ¶¶ 42, 49). Among these, Appellant notes, are meloxicam (an enolic acid-based NSAID) as an anti-inflammatory agents and bupivacaine as an amide analgesic agent. *Id.* at 9–10 (citing Wohabrebbi ¶¶ 45, 47).

Appellant contends that the Examiner has provided no rationale with respect to why a person of ordinary skill in the art would have chosen meloxicam, an optional NSAID, over diclofenac and/or ketoprofen, both required by Wohabrebbi for analgesic and anti-inflammatory effect, or over any of the other optional NSAIDs taught in paragraph [0045], and then to have incorporated it into the compositions taught by Ng. App. Br. 10. Appellant contends that Wohabrebbi teaches, at most, combining meloxicam as an optional agent with diclofenac, and provides no suggestion to combine meloxicam with a local amide anesthetic. *Id.* at 11.

The Examiner responds that it is, generally, *prima facie* obvious to select a known material for incorporation into a composition, based on its recognized suitability for its intended use. Ans. 6 (citing MPEP § 2144.07).

The Examiner therefore concludes that it would have been obvious to a person of ordinary skill in the art to have incorporated meloxicam (i.e., an enolic-acid non-steroidal anti-inflammatory drug) into the composition of Ng, because Wohabrebbi teaches that meloxicam is well known in the art as an anti-inflammatory agent. *Id.*

We are not persuaded by the Examiner's reasoning. As an initial matter, we agree with Appellant that the teachings of Ng are too broad to adequately describe a genus of which a person of ordinary skill in the art would recognize the claimed compositions to be a member. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010):

> [A] sufficient description of a genus instead requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can "visualize or recognize" the members of the genus.

Ng teaches that an "active agent":

> [I]ncludes any compound or mixture of compounds which produces a beneficial or useful result. Active agents are distinguishable from such components as vehicles, carriers, diluents, lubricants, binders and other formulating aids, and encapsulating or otherwise protective components. Examples of active agents and their pharmaceutically acceptable salts, are pharmaceutical, agricultural or cosmetic agents.

Ng ¶ 23. Ng elaborates that:

> Suitable pharmaceutical agents include locally or systemically acting pharmaceutically active agents which may be administered to a subject by topical or intralesional application (including, for example, applying to abraded skin, lacerations, puncture wounds, etc., as well as into surgical incisions) or by injection, such as subcutaneous, intradermal, intramuscular, intraocular, or intra-articular injection. Examples of these agents

> include, but not limited to, anti-infectives (including antibiotics, antivirals, fungicides, scabicides or pediculicides), antiseptics (e.g., benzalkonium chloride, benzethonium chloride, chlorhexidine gluconate, mafenide acetate, methylbenzethonium chloride, nitrofurazone, nitromersol and the like), steroids (e.g., estrogens, progestins, androgens, adrenocorticoids, and the like), therapeutic polypeptides (e.g.[,] insulin, erythropoietin, morphogenic proteins such as bone morphogenic protein, and the like), analgesics and *anti-inflammatory agents (e.g., aspirin, ibuprofen, naproxen, ketorolac, COX-1 inhibitors, COX-2 inhibitors, and the like)*, cancer chemotherapeutic agents (e.g., mechlorethamine, cyclophosphamide, fluorouracil, thioguanine, carmustine, lomustine, melphalan, chlorambucil, streptozocin, methotrexate, vincristine, bleomycin, vinblastine, vindesine, dactinomycin, daunorubicin, doxorubicin, tamoxifen, and the like), narcotics (e.g., morphine, meperidine, codeine, and the like), *local anesthetics (e.g., the amide- or anilide-type local anesthetics such as bupivacaine, dibucaine, mepivacaine, procaine, lidocaine, tetracaine, and the like)*, antiemetic agents such as ondansetron, granisetron, tropisetron, metoclopramide, domperidone, scopolamine, and the like, antiangiogenic agents (e.g., combrestatin, contortrostatin, anti-VEGF, and the like), polysaccharides, vaccines, antigens, DNA and other polynucleotides, antisense oligonucleotides, and the like. The present invention may also be applied to other locally acting active agents, such as astringents, antiperspirants, irritants, rubefacients, vesicants, sclerosing agents, caustics, escharotics, keratolytic agents, sunscreens and a variety of dermatologics including hypopigmenting and antipruritic agents. The term "active agents" further includes biocides such as fungicides, pesticides, and herbicides, plant growth promoters or inhibitors, preservatives, disinfectants, air purifiers and nutrients. Prodrugs of the active agents are included within the scope of the present invention.

Id. (emphasis added). We quote this lengthy passage in full to illustrate the very considerable breadth of the genus of "active agents" taught by Ng. We agree with Appellant that it would not have been obvious from this teaching

of Ng to select a composition "comprising[ ] an amide local anesthetic, an enolic-acid non-steroidal anti-inflammatory drug (NSAID)," as recited in the claims.

However, we also note that Ng is primarily directed to a "semi-solid delivery vehicle which comprises a polyorthoester and an excipient. The excipient is readily miscible with the polyorthoester and the resulting semi-solid delivery vehicle has a smooth and flowable texture" (*see* Ng ¶ 8). We surmise, the Examiner's stated findings and Appellant's arguments in this appeal notwithstanding, that it is upon this teaching of a polymeric and, specifically, a polyorthoester, delivery vehicle that the Examiner relies upon Ng as teaching. *See, e.g.*, dependent claim 15, which recites, "wherein the sustained-release delivery vehicle is a polymeric formulation in the form of a semi-solid polymer formulation comprising a polymer, the amide local anesthetic and the enolic-acid NSAID"; *see also* claim 18, which recites, "wherein the polymer is selected from the group consisting of polylactides, polyglycolides, poly(lactic-co-glycolic acid) copolymers, polycaprolactones, poly-3-hydroxybutyrates, and *polyorthoesters*" (emphasis added).

With respect to Wohabrebbi, the reference is directed to "methods and compositions comprising administering one or more biodegradable drug depots comprising a therapeutically effective amount of diclofenac and/or ketoprofen or pharmaceutically acceptable salt thereof to a target tissue site." Wohabrebbi Abstr. Specifically, Wohabrebbi teaches "diclofenac and/or ketoprofen compositions and methods are provided that have long acting analgesic and anti-inflammatory effects over periods of 3 to 15 days in a single drug depot or multiple drug depots." *Id.* at ¶ 10.

Wohabrebbi further teaches that:

> In addition to diclofenac and/or ketoprofen, the drug depot may comprise one or more additional therapeutic agents.
> ….
> Specific examples of therapeutic agents suitable for use include, but are not limited to an anti-inflammatory agent, analgesic agent, or osteoinductive growth factor or a combination thereof. Anti-inflammatory agents include, but are not limited to, salicylates, diflunisal, sulfasalazine, indomethacin, ibuprofen, naproxen, tolmetin, ketorolac, fenamates (mefenamic acid, meclofenamic acid), *enolic acids (piroxicam, meloxicam)*
> ….
> Suitable analgesic agents include, but are not limited to, acetaminophen, *lidocaine, bupivicaine*….

Id. at ¶¶ 42, 45, 47 (emphases added). Wohabrebbi thus teaches that, *inter alia*, an amide local anesthetic (e.g., bupivacaine) and an enolic-acid non-steroidal anti-inflammatory drug, as recited in claim 1 may be optional constituents of its disclosed compositions in addition to diclofenac and/or ketoprofen, which are carboxylate-based NSAIDs (*see* App. Br. 9, this is not disputed by the Examiner).

Independent claim 1 recites: "A composition, comprising: an amide local anesthetic, an enolic-acid non-steroidal anti-inflammatory drug (NSAID) and a delivery vehicle, wherein *the enolic-acid non-steroidal NSAID is the sole NSAID comprised in the composition*" (emphasis added). Claim 40, the only other independent claim on appeal, also recites the limitation in italics quoted above. We construe that limitation as a negative limitation, because it serves to exclude any additional NSAIDs (enolate- and carboxylate-based alike) from Appellant's claimed composition.

Appellant's Specification supports this negative limitation, disclosing that:

> Interestingly, it appears that not all NSAIDs are effective in enhancing the effect of a locally administered amide-type anesthetic. As described in Example 7, an illustrative composition comprising a polyorthoester as a delivery vehicle and bupivacaine and 7.5 wt% diclofenac (having a proton-donating carboxylic acid group) failed to regain its short-term efficacy after about 1 day following application or more, and provided significantly less pain relief over the time frame of 1 to 5 days following application when compared to its early, short-term efficacy up to about 5 hours post-application. This is in distinct contrast to the bupivacaine-meloxicam [an enolate-based NSAID] composition.

Spec. ¶ 177; *See Santarus, Inc. v. Par Pharm. Inc.*, 694 F.3d 1344 (Fed Cir. 2012) (holding that: "Negative claim limitations are adequately supported when the specification describes a reason to exclude the relevant limitation").

Appellant's claims thus expressly exclude the carboxylate-based NSAIDs diclofenac and/or ketoprofen from its compositions. The Examiner has articulated no reason or motivation with respect to why a person of ordinary skill in the art would have been motivated to select the amide local anesthetic and enolic-acid NSAID constituents from the lists of additional, and optional, elements of the compositions taught by Wohabrebbi, and simultaneously exclude the required carboxylate NSAIDs diclofenac and/or ketoprofen from the composition. Absent any such reasoning articulated by the Examiner, we are not persuaded that the Examiner has established a *prima facie* case of obviousness, and we reverse the Examiner's rejection. Furthermore, because we reverse the Examiner's rejection in this respect, we do not reach Appellant's additional arguments with respect to this rejection.

B. Rejection of claims 1–8, 15–19, 25–35, 40–45, 47, and 53–59 under the nonstatutory doctrine of obviousness-type double patenting

Appellant relies upon essentially the argument presented *supra*, arguing that both the obviousness-type double patenting and the provisional obviousness-type double patenting rejection are based on the Examiner's allegedly improper conclusion that Ng and Wohabrebbi render obvious the claimed composition. App. Br. 11; *see also* Final Act. 13–14. Because we reverse the Examiner's conclusion that the claims on appeal are obvious under 35 U.S.C. § 103 over Ng and Wohabebbi, we conclude that the provisional and non-provisional obviousness-type double patenting rejections that also cite Ng and Wohabrebbi[4] must similarly be reversed.

We do not reach the provisional rejection of claims 1–8, 15–19, 25–35, 40–45, 47 and 53–59 over the '759 application. Neither Appellant's Brief, nor the Examiner's Answer, have provided arguments on the merits directed to the claims of the '759 application. However, because we have reversed Examiner's other rejections and "[t]he only remaining rejection is a provisional non-statutory double patenting rejection," we determine it is "premature" to address this rejection and consequently do not reach it. *In re Moncla*, 95 USPQ2d 1884 (BPAI 2010) (precedential).

[4] That is, the rejection of claims 1–8, 15–19, 25–35, 40–45, 47, and 53–59 as unpatentable over claims 1, 6, and 7 of the '163 patent, claim 1 of the '227 patent, and claims 1 and 8 of the '909 patent, Ng, and Wohabrebbi, and the provisional rejection of claims 1–8, 15–19, 25–35, 40–45, 47, and 53–59 over claim 1 of the copending '491 application and claims 1 and 9 of the '545 application, Ng, and Wohabrebbi.

CONCLUSION

The Examiner's rejection of claims 1–8, 15–19, 25–35, 40–45, 47, and 53–59 under 35 U.S.C. § 103 is reversed.

The Examiner's rejection of claims 1–8, 15–19, 25–35, and 40–59 under the nonstatutory doctrine of obviousness-type double patenting is reversed.

REVERSED

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1–8, 15–19, 25–33	103	Ng, Wohabrebbi		1–8, 15–19, 25–33
34, 35, 40–45, 47, 53–59	103	Ng, Wohabrebbi, Dadey		34, 35, 40–45, 47, 53–59
1–8, 15–19, 25–35, 40–45, 47, 53–59		Non-statutory Double Patenting: '163 patent, '227, patent, '909 patent, Ng, Wohabrebbi		1–8, 15–19, 25–35, 40–45, 47, 53–59
1–8, 15–19, 25–35, 40–45, 47, 53–59		Provisional Non-statutory Double Patenting: '491 application, '545 application, Ng, Wohabrebbi		1–8, 15–19, 25–35, 40–45, 47, 53–59
1–8, 15–19, 25–35, 40–45, 47, 53–59		Provisional Non-statutory Double Patenting: '759 application[5]		

[5] As explained above, we do not reach this rejection per *Ex parte Moncla,* 95 USPQ2d 1884 (BPAI 2010) (designated precedential).

Overall Outcome				**1–8, 15–19, 25–35, 40–45, 47, 53–59**