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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* THOMAS A. MUSTOE, PETER KIM, JASON KO,  
XIANZHONG DING, and YANAN ZHAO

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Appeal 2015-000549  
Application 12/906,719<sup>1</sup>  
Technology Center 3700

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Before JAMES A. WORTH, CYNTHIA L. MURPHY, and  
KENNETH G. SCHOPFER, *Administrative Patent Judges*.

SCHOPFER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the rejection of claims 1–8, 11–15, 26, 28, and 29. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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<sup>1</sup> According to Appellants, the real party in interest is Northwestern University. Appeal Br. 3.

## BACKGROUND

According to Appellants, the Specification relates to “compositions and methods for preventing or reducing scar formation (e.g., hypertrophic scars) . . . [including] methods of administering HMG-CoA reductase-inhibiting agents for preventing or reducing scar formation.” Spec. 1.

## CLAIMS

Claims 1–8, 11–15, 26, 28, 29 are on appeal. Claim 1 is the only independent claim on appeal and recites:

1. A method for preventing or reducing hypertrophic and/or keloid scar formation in the skin of a subject during wound healing comprising:

administering a HMG-CoA reductase-inhibiting agent locally to a wound site of a subject such that hypertrophic and/or keloid scar tissue formation in said skin is reduced or prevented during said wound healing,

wherein said HMG-CoA reductase-inhibiting agent is administered at a concentration of between 1 and 50  $\mu\text{M}$ .

Appeal Br. 8.

## REJECTIONS

1. The Examiner rejects claims 1–4, 6, 11–15, 26, 28, and 29 under 35 U.S.C. § 103(a) as unpatentable over Rego<sup>2</sup> in view of Ghazizadeh<sup>3</sup> and Leung.<sup>4</sup>
2. The Examiner rejects claim 5 under 35 U.S.C. § 103(a) as unpatentable over Rego in view of Ghazizadeh, Leung, and Avelar.<sup>5</sup>
3. The Examiner rejects claim 7 under 35 U.S.C. § 103(a) as unpatentable over Rego in view of Ghazizadeh, Leung, and Niazi.<sup>6</sup>
4. The Examiner rejects claim 8 under 35 U.S.C. § 103(a) as unpatentable over Rego in view of Ghazizadeh, Leung, and Edell.<sup>7</sup>

## DISCUSSION

With respect to claim 1, the Examiner finds that Rego discloses a method as claimed, except that Rego does not disclose the use of statins to reduce or prevent hypertrophic and/or keloid scar formation and Rego does not disclose the use of a concentration between 1 and 50  $\mu$ M. Final Act. 2–3 (citing Rego 58). The Examiner relies on Ghazizadeh as teaching the use of statins to prevent keloid scars. *Id.* at 3 (citing Ghazizadeh 18). The

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<sup>2</sup> Amália Cíntia Meneses do Rego et al., *Simvastatin improves the healing of infected skin wounds of rats*, 22 *Acta Cirairgic Brasileira* 53 (2007).

<sup>3</sup> Mohammad Ghazizadeh, *Essential Role of IL-6 Signaling Pathway in Keloid Pathogenesis*, 74 *J. Nippon Med. Sch.* 11 (2007).

<sup>4</sup> Bernard P. Leung et al., *A Novel Anti-Inflammatory Role for Simvastatin in Inflammatory Arthritis*, 170 *The Journal of Immunology* 1524 (2003).

<sup>5</sup> Avelar et al., US 2009/0226500 A1, pub. Sept. 10, 2009.

<sup>6</sup> Niazi, US 6,447,820 B1, iss. Sept. 10, 2002.

<sup>7</sup> Edell et al., US 7,241,451 B1, iss. July 10, 2007.

Examiner relies on Leung as disclosing administering a concentration of a statin as claimed. *Id.* (citing Leung 1527–1529). The Examiner concludes:

it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Rego et al. with the method of Ghazizadeh who discloses that statins may be used to reduce inflammation contributing to keloids (page 18, column 2, last 3 paragraphs) [and] it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Rego et al. in view of Ghazizadeh with the dosage as taught by Leung et al. who explicitly teaches that administering 1-50  $\mu\text{M}$  is effective in suppressing an inflammatory response (page 1527 to page 1529, column 1, passage above Discussion heading).

*Id.* Further, in response to Appellants' arguments, the Examiner concludes that one of ordinary skill in the art "would have been motivated to identify the optimum concentration to apply to man because such an endeavor only involves routine skill in the art, and would not have yielded unexpected results since it has been established that applying statins to skin suppresses wound formation." Ans. 8.

Except for certain findings noted below, we agree with and adopt the Examiner's findings and conclusions regarding the scope and content of the prior art with respect to claim 1. *See* Final Act. 2–3; Ans. 8. As discussed below, we are not persuaded of reversible error by Appellants' arguments.

First, Appellants argue that the combination of references does not teach using the claimed concentration in an *in vivo* environment as required by the claims. Appeal Br. 5. In response, the Examiner first finds that the claim "does not exclude *in vitro* environments." Ans. 7. Without further explanation from the Examiner on this issue, we agree with Appellants that because the claim is directed to administering an agent "locally to a wound site *of a subject*" (emphasis added) the claim is limited to *in vivo*

environments. *See* Reply Br. 2. However, we are not persuaded that this rises to the level of reversible error in the rejection for the reasons discussed below.

Next, Appellants argue that Rego and Leung teach away from the claimed concentrations. Appeal Br. 5. However, Appellants only indicate that the references teach away because high concentrations of statins are used. *Id.* “A reference may be said to teach away when a person of ordinary skill, upon reading the reference, . . . would be led in a direction divergent from the path that was taken by the applicant.” *In re Haruna*, 249 F.3d 1327, 1335 (Fed. Cir. 2001) (quoting *Tec Air, Inc. v. Denso Mfg. Mich. Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999)). Without further explanation, Appellants have not shown why the use of a higher concentration in the art would have led a person of ordinary skill in a direction divergent from that of the Appellants.

Appellants also argue that, based on the arguments above, a prima facie case of obviousness has not been established and that there is no motivation or suggestion to combine Leung with Rego and Ghazizadeh. Appeal Br. 5–6. We are not persuaded of error at least because we agree with the Examiner’s conclusion that one of ordinary skill in the art “would have been motivated to identify the optimum concentration to apply to man because such an endeavor only involves routine skill in the art, and would not have yielded unexpected results since it has been established that applying statins to skin suppresses wound formation.” Ans. 8. In *In re Aller*, 220 F.2d 454, 456 (CCPA 1955), the court set forth the rule that the discovery of an optimum value of a variable in a known process is normally obvious. *See also In re Boesch*, 617 F.2d 272, 276 (CCPA 1980).

Exceptions to this general rule include where the parameter optimized was not recognized to be a result effective variable, *In re Antonie*, 559 F.2d 618, 621 (CCPA 1977), and where the results of optimizing a variable, which was known to be result effective, were unexpectedly good. *In re Waymouth*, 499 F.2d 1273, 1276 (CCPA 1974). As discussed below, Appellants have not shown that any exceptions apply to the rejection before us.

We first note that Appellants do not address the Examiner's conclusion that the skilled artisan would have been motivated to optimize the concentration to apply to a human wound. *See* Reply Br. 2–3.<sup>8</sup> We find that, based on the art of record, one of ordinary skill in the art would have recognized that a statin can be used in wound healing applications; to control inflammatory responses; and may be useful in keloid treatment. *See* Rego 58, 62; Leung 1528–1529; Ghazizdeh 18. We also find that one of ordinary skill in the art would have recognized the concentration of statin used to be a result effective variable based on Leung even though Leung teaches the administration of the statins in an *in vitro* environment. *See, e.g.*, Leung, Fig. 6 (showing anti-inflammatory response resulting from application of different concentrations of simvastatin). For these reasons, we find that a preponderance of the evidence on the record before us supports the

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<sup>8</sup> Appellants address two issues in their reply. First, Appellants assert the claim is limited to *in vivo* environments. Reply Br. 2. As discussed herein, we agree but do not find reversible error with respect to the Examiner's findings in this regard. Second, Appellants assert that Rego relates to wound healing and not scar reduction or prevention. *Id.* at 3. However, this argument, raised for the first time in the reply, relates to the Examiner's findings with respect to the obviousness of claims 11–15. We decline to address this argument here. *See* 37 CFR § 41.41(b)(2).

Examiner's conclusion and that one of ordinary skill in the art would have been motivated to optimize the concentration of statin used to treat a human wound and such optimization would only have required routine experimentation. *See In re Aller*, 220 F.2d at 456.

Appellants also argue that the Examiner has ignored the unexpected results described in the Specification. Specifically, Appellants assert example 2 in the Specification shows that “[u]nexpectedly, higher concentrations of the agents (120  $\mu$ M and 400  $\mu$ M), which are 2.4 to 8 times greater than recited in the claims, had no significant effect on scar formation. This, despite the fact that even the highest concentration (400  $\mu$ M) was tolerated by the rats.” Appeal Br. 6 (emphasis omitted).

With respect to showing unexpected results as in the present case, “an applicant may overcome a prima facie case of obviousness by establishing ‘that the [claimed] range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range.’” *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003) (quoting *In re Geisler*, 116 F.3d 465, 1469–70 (Fed. Cir. 1997)). Further, Appellants’ showing of unexpected results must be commensurate in scope with the claimed range, i.e., with a concentration of between 1 and 50  $\mu$ M. *See id.* “Establishing that one (or a small number of) species gives unexpected results is inadequate proof.” *In re Greenfield*, 571 F.2d 1185, 1189, (CCPA 1978); *see also In re Peterson*, 315 F.3d at 1331.

Under this case law, we are not persuaded that Appellants’ alleged evidence of unexpected results is sufficient to rebut the prima facie case of obviousness based on unexpected results. Specifically, the example relied upon relates only to the use of a concentration of 40  $\mu$ Mol of each of

Simvastatin, Lovastatin, and Pravastatin. *See* Spec., 20–26. No other concentrations in the claimed range are provided, and thus, the example provided is not commensurate with the full scope of the claims. Further, we find that the Specification and figures do not clearly show the exact extent to which the results were unexpected or significantly better for these lower concentrations, especially because the claims indicate that keloid formation may be prevented by the method, which does not appear to be the case for any of the examples provided. Further, we also note that in at least one instance (as in Lovastatin, Spec. Fig. 5b), there appears to be a reduction in scar formation at the highest concentrations. Thus, it does not appear to be the case that “higher concentrations . . . had no significant effect on scar formation” as Appellants assert. Appeal Br. 6 (emphasis omitted).

Based on the foregoing, we sustain the rejection of independent claim 1. Appellants do not raise any separate arguments with respect to any of the dependent claims, and thus, we sustain the rejections of claims 2–8, 11–15, 26, 28, and 29 for the same reasons.

#### CONCLUSION

For the reasons set forth above, we AFFIRM the rejections of claims 1–8, 11–15, 26, 28, and 29.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED