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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SUZANNE MARIE MITHIEUX and
ANTHONY STEVEN WEISS[1]

Appeal 2018-003696
Application 14/347,512
Technology Center 1600

Before ERICA A. FRANKLIN, JAMES A. WORTH, and
ROBERT A. POLLOCK, *Administrative Patent Judges*.

POLLOCK, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellants appeal under 35 U.S.C. § 134(a) from the final rejection of claims 2–9 and 14–20. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

STATEMENT OF THE CASE

According to the Specification, "[a]geing and tissue injury are associated with degeneration of the extracellular matrix leading to loss of tissue structure and/or function. Loosened skin, relaxed subcutaneous tissue, loss of density of the extracellular matrix, wrinkling, stretch marks and

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[1] Appellants identify the Real Party in Interest as Elastagen Pty Ltd. App. Br. 3.

fibrosis are the physical manifestations of the degeneration." *Id.* at 1. "About 20 years ago, the research effort sought to use the various molecules of the extracellular matrix in a range of clinical and cosmetic interventions for correcting loss of tissue structure and function." *Id.* "Elastin was considered by some as advantageous for this work because . . . it could be used to form elastic implants and fillers. The early work focused on synthesis of recombinant forms of tropoelastin which would then be coacervated and chemically or enzymatically cross linked, either before or after delivery to an individual, so that an elastic implant or filler would be formed either *ex* vivo or *in* vivo for filling tissue voids or for augmenting or re-shaping tissue." *Id.* But "while an implant with elastic properties could be provided to tissue, the nature of the implant and its elastic properties was not suggestive of that normally ascribed to the tissue. . . . [And] while elasticity could be imparted to a tissue by the implantation of a material with properties that include elasticity, a return to a physical appearance or function resembling normal could not." *Id.* at 3.

"The initiation of a process that is like elastogenesis (i.e. one whereby the tissue synthesises an elastic fiber *de novo* from a common set of factors) in adult tissue is a desirable goal because it is believed that such a process would restore an elastic profile to a tissue." *Id.* "The widely considered hypothesis for explaining the absence of elastic fiber formation *de novo* in an adult is that adult cells or the relevant tissue in which they are contained lack one or more of the necessary factors and processes required for elastogenesis." *Id.* "It follows that the provision of tropoelastin alone to adult tissue should not in itself be sufficient to restore the elastic profile of

the tissue, because without the relevant factors required for elastogenesis, the tissue cannot utilise the tropoelastin to form an elastic fiber." *Id.* at 5.

Appellants disclose an assay system that uses adult human cells to form elastic fiber in vitro. *Id.* at 11. Appellants report that "repeat administration of tropoelastin to the system demonstrates an ongoing capacity to form elastic fiber, indicating that the tropoelastin is the limiting factor to elastic fiber formation." *Id.* at 12. According to Appellants, subsequent clinical trial data "establishes the importance of maintaining tropoelastin in tissue for enough time for cells to engage with the tropoelastin." *Id.* In light of these findings, Appellants disclose "methods of restoring elasticity in tissue using tropoelastin containing compositions." *Id.* at Abstract, 14–17. The disclosed methods include "administering tropoelastin to the individual according to a treatment regime that has been selected to maintain the administered tropoelastin in the tissue for a period of time that enables factors expressed in the tissue for formation of an elastic fiber to engage with the administered tropoelastin for synthesis of elastic fiber therefrom." *Id.* at 6.

Claim 20, the sole independent claim before us, recites:

> 20. A method of restoring the elastic profile of skin tissue of an individual, the method including the following steps:
>
> - providing an individual in whom restoration of elastic profile of skin tissue is required;
>
> - defining a treatment area on the skin of the individual, wherein the treatment area is an area of skin in which the elastic profile is to be restored;
>
> - injecting a tropoelastin composition having a concentration of 0.5 mg/ml to 200 mg/ml tropoelastin into skin tissue in a volume of 10 µl to 100 µl within the treatment area to enable elastic fiber formation in the treatment area;

> wherein the tropoelastin composition is injected into skin tissue within the treatment area according to a predetermined treatment schedule, to establish an amount of tropoelastin within the treatment area that is increased relative to skin outside the treatment area, said treatment schedule defining a specified number of treatments, each treatment in the form of an injection at a specified time point; and
>
> wherein at least one treatment of the treatment schedule includes multiple injections, each injection made at an injection site that is spaced apart from other injection sites by a predetermined distance,
>
> - thereby maintaining an amount of tropoelastin within the treatment area for a predetermined period of time over the treatment schedule to enable elastic fiber formation and thereby restoring the elastic profile in the skin of the individual.

The Examiner rejects claims 2–4, 6–9, and 14–20 under pre-AIA 35 U.S.C. § 103(a) as unpatentable over the combination of Weiss,[2] Bénédicte Le Bris,[3] and Smith.[4] Fin. Rej. 5–16.

The Examiner rejects claims 2–9 and 14–20 under pre-AIA 35 U.S.C. § 103(a) as unpatentable over the combination of Weiss, Bénédicte Le Bris, Smith, Guillen,[5] and Sommer-Knudsen.[6] *Id.* at 16–17.

We have reviewed Appellants' contentions that the Examiner erred in rejecting claims 2–9 and 14–20 as obvious over the cited art. App. Br. 5–14.

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[2] Weiss et al., WO 2010/102337 Al, published Sept. 16, 2010.
[3] Le Bris, et al., WO 2009/034559 A2, published Mar. 19, 2009.
[4] S. Smith et al., *Duration of wrinkle correction foil owing repeat treatment with Juvederm hyaluronic acid fillers*, 301 Arch Dermatol Res. 757–762 (2010).
[5] Guillen et al., US 2011/0229574 A1, published Sept. 22, 2011.
[6] Sommer-Knudsen, US 2013/0296528 A1, published Nov. 7, 2013.

Because Appellants do not argue the claims individually, we focus our discussion on independent claim 20. We also focus on the rejection in view of Weiss, Benedict Le, and Smith because Appellants make no additional substantive argument with respect to the remaining references. *See* App. Br. 13–14 (arguing that Smith, Guillen, and Sommer-Knudsen "fail to remedy the deficiencies of Weiss, Bénédicte Le Bris and Smith").

We disagree with Appellants' contentions and adopt the findings concerning the scope and content of the prior art set forth in the Examiner's Answer and the Final Rejection dated March 9, 2017. For emphasis, we highlight and address the following:

FINDINGS OF FACT

FF1. Weiss discloses "an injectable composition formed from tropoelastin, the composition including a tropoelastin-containing substance, wherein the substance further includes an agent in an amount effective for providing the substance with properties of flow enabling injection of the composition." Weiss at 2; *see id.* at 37, claim 34. According to Weiss, "when tropoelastin is coacervated and cross linked to form elastin, and/or subjected to alkali polymerisation to form an elastic material . . . at high solids content of tropoelastin, a mass is formed that cannot be passed through a surgical needle." *Id.* at 4. However, "formation of the noninjectable mass at high solids content of tropoelastin may be reduced, if not avoided, by coacervating or polymerising tropoelastin in the presence of a coalescence-controlling agent, resulting in formation of a composition having high solids content and properties of flow required in an injectable composition." *Id.* at 4–5. "The coalescence-controlling agent generally increases the viscosity of the liquid phase in which

coacervation or polymerisation of tropoelastin to form elastin or an elastic material occurs." *Id.* at 7; *see id.* at 10–14 (describing properties and examples of coalescence-controlling agents).

FF2. Weiss teaches intradermal, intracutaneous and/or subcutaneous injection of a tropoelastin composition to correct a tissue defect, ie., to "provide a bulking or filling effect, reducing the appearance of wrinkles or folds." *Id.* a 20. Weiss further defines "correcting a tissue defect' as "refer[ing] to at least partially restoring and/or augmenting tissue structure and/or function, including supporting, enhancing, bulking, or elasticising tissue, or facilitating tissue growth into a tissue defect." *Id.* at 8. The injected composition includes tropoelastin "in an amount from about 1.5 mg/ml to about 400 mg/ml. Preferably . . . in an amount of about 10 mg/ml to about 200 mg/ml." *Id.* at 9. "Typically, the composition is administered at the site of the tissue defect by injection . . . . [and] may be administered over a number of treatments to correct the tissue defect and/or to achieve or maintain the desired result." *Id.* at 20–21.

FF1. Benedict Le Bris teaches mesotherapy "for aesthetic and/or repairing treatment of the skin," including the treatment of wrinkles and fine lines. Benedict Le Bris, Abstract, 20:7–8. "Mesotherapy is a treatment technique by intra-epidermal and/or intradermal and/or subcutaneous injection of active product(s), for instance micronutrients, vitamins and/or hyaluronic acid. The compositions are administered according to this technique by injection in the form of small multiple droplets into the epidermis, the dermo-epidermal junction and/or the dermis in order especially to perform

subcutaneous layering." *Id.* at 4, 19–23; *see* claims 1, 10–12. The droplets may be injected via syringe or injection pistol and "[a]dvantageously . . . have an average volume ranging from 0.01 to 0.2 ml and in particular from 0.05 to 0.15 ml . . . [and] may be performed over several sessions spaced apart by a few days, for example 1, 2, 3, 4, 5 or 6 days to a few weeks, for example 1, 2, 3 or 4 weeks." *Id.* at 19:18–20:19. "The injection points may be spaced apart, for example, by a distance ranging from 5 mm to 1 cm." *Id.* at 20:20–24.

FF1. Smith discloses a study of the effectiveness of repeat injections of Juvederm hyaluronic acid fillers for the treatment of severe nasiolabial folds (smile lines). *See* Smith, Abstract. "An initial treatment and up to two touch-up treatments at 2-week intervals after initial treatment were performed to achieve optimal correction in both [nasiolabial folds] and subjects were followed through 24 weeks after the last treatment. . . . Subjects were offered repeat treatment with the original Juvederm formulation after the 24 week treatment. *Id.* 758. "Investigators determined the appropriate volume of Juvederm needed to obtain optimal correction at the initial, touch-up, and repeat treatments." *Id.*

ANALYSIS

According to the Examiner, "Weiss in view of Bénédicte Le [Bris] and Smith teach the method of the instant claims with the same composition injected at the same concentration and overlapping volumes." Fin. Rej. 3. "Even though Weiss does not teach specifically that the tropoelastin will increase elasticity of the skin . . . increasing elastin fiber formation would be

inherently achieved." *Id.* "Furthermore, there is a reasonable expectation of success given that Weiss specifically teaches increasing elasticity of the skin, treating wrinkles and that elastin is formed from tropoelastin with a coalescence controlling agent and that the tropoelastin/coalescence controlling agent can be injected into the skin for correcting tissue defects." Ans. 17.

Further, and upon considering the Declaration of Anthony Steven Weiss under 37 C.F.R. § 1.132, the Examiner finds that "Applicants have failed to show unexpected results with regards to the specific concentration range, volume range and treatment schedule." *Id.*; *see* Ans. 16–17. "In the absence of unexpected results or criticality of a claimed range, it would have been obvious for one of ordinary skill to discover the optimum workable ranges (frequency of the injections, location and distance of the injections and volume of the injections) of the methods disclosed by the prior art by normal optimization procedures known in the pharmaceutical arts for improving appearance of the skin." Fin. Rej. 4.

Appellants contend that "the cited references fail, individually and in combination, to teach or suggest a method of enabling elastic fiber formation in the treatment area as claimed, let alone a method of administering a tropoelastin composition to enable elastic fiber formation." App. Br. 6. "Rather, the methods of the prior art are merely directed to methods of injecting an elastic material derived from tropoelastin for the purpose of plumping or bulking skin tissue." *Id.* at 6–7.

We do not find Appellants' arguments persuasive and agree with the Examiner that Weiss teaches the injection of tropoelastin compositions into the skin for "correcting a tissue defect," which

> refers to a least partially restoring and/or augmenting tissue structure and/or function, including supporting, enhancing, bulking, **or elasticizing tissue, or facilitating tissue growth into a tissue defect** (see page 8, fourth paragraph). Thus, Weiss teaches injecting tropoelastin into [the] skin to improve the appearance of the skin via elasticizing the tissue or facilitating growth which would meet the limitations of 'restoring elastic profile' and that the compositions were not just for a "bulking effect."

Ans. 18. We further agree with the Examiner's conclusion that "[e]ven though Weiss does not teach specifically that the tropoelastin will increase elasticity via increased elastic fiber formation per se . . . Weiss in view of Bénédicte Le Bris and Smith teach the method of the instant claims with the same composition injected at the same concentration and overlapping volumes." *Id.* at 11. Accordingly, "the result of increasing elastin fiber formation would inherently be achieved." *Id.*

We further agree with the Examiner that one of ordinary skill in the art would have been motivated to combine the teachings of Weiss, Bénédicte Le Bris, and Smith "to achieve uniform distribution and the desired visual effect" or appearance of the skin. *Id.* at 13. We find no error in the Examiner's conclusion that "[i]t would have been obvious to optimize the injection protocol to create a layer so that the composition of the invention is uniformly distributed in the cutaneous area to be treated and optimize the number of treatments to obtain the desired therapeutic effect." *Id.* at 14–15. In this respect, we agree with the Examiner that the claimed ranges are result effective variables such that it would have been obvious for one of ordinary skill in the art to discover through routine experimentation, the optimum ranges for injection frequency, location, and distance as claimed. *See id.* at 9, 14; *see also id.* at 16 ("based on the teachings of Weiss of increasing

elasticity of the skin via injection of tropoelastin compositions, the Examiner disagrees that the finding of increased elastic fibre formation is unexpected"). Nevertheless, to the extent Appellants results might have been unexpected, they do not overcome the Examiner's evidence of obviousness. *See, e.g., Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 1372 (Fed. Cir. 2007). ("Here, the record establishes such a strong case of obviousness that Pfizer's alleged unexpectedly superior results are ultimately insufficient.").

For the above reasons, and as set forth in the Examiner's Answer and Final Rejection, we affirm the rejection of claim 20 in view of Weiss, Benedict Le Bris and Smith. Claims 2–4, 6–9, and 14–19, which Appellants do not separately argue, fall with claim 20. 37 C.F.R. § 41.37(c)(1)(iv). The rejections of claims 2–9 and 14–20 in view of Weiss, Benedite Le Bris and Smith, further in view of Guillen, and Sommer-Knudsen are affirmed for the same reasons.

SUMMARY

For the reasons above, we affirm the Examiner's decision rejecting claims 2–4, 6–9, and 14–20.

TIME PERIOD FOR RESPONSE

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

AFFIRMED