

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

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*Ex parte* HAROLD BREM

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Appeal 2007-1151<sup>1</sup>  
Application 10/388,825  
Technology Center 1600

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DECIDED: January 17, 2008

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Before TONI R. SCHEINER, NANCY J. LINCK, and RICHARD M.  
LEBOVITZ, *Administrative Patent Judges*.

SCHEINER, *Administrative Patent Judge*.

**DECISION ON APPEAL**

Appellants appeal under 35 U.S.C. § 134 from a final rejection of claims 1, 3, 10-14, and 19-21, all the claims remaining in the application. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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<sup>1</sup> Heard October 23, 2007.

### STATEMENT OF THE CASE

The claims on appeal are directed to compositions comprising the angiogenic molecule, Vascular Endothelial Growth Factor (VEGF), and administration of VEGF “directly to diabetic wound ulcers, in an effective amount for a sustained period of time effective to promote [wound] closure” (Spec. 1: 4-6, and 2: 28-30).

Claims 1, 3, 10-14, and 19-21 stand rejected under 35 U.S.C. § 102(b) as anticipated by Tischer<sup>2,3</sup> (Answer 4).

Appellant presents separate arguments for the following groups of claims: claims 1 and 14 (Group I); claim 3 (Group II); claims 10-12 and 19-21 (Group III); and claim 13 (Group IV). We select claims 1, 3, 10, 13, and 14 as representative of their respective groups for the purpose of deciding this appeal. 37 C.F.R. § 41.37(c)(1)(vii) (2006).

Claims 1, 3, 10, 12, 13, and 14 read as follows:

1. A method for treating a diabetic ulcer comprising administering to the wound an effective amount of VEGF for a sustained period of time of at least two weeks to enhance the rate of closure of the wound.
3. The method of claim 1 wherein the VEGF is effective to treat bacterial contamination of the wound in a patient with a diabetic ulcer.
10. The method of claim 1 wherein the VEGF is administered by a sustained delivery pump.

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<sup>2</sup> U.S. Patent 5,194,596 to Tischer et al., issued March 16, 1993.

<sup>3</sup> A rejection under 35 U.S.C. § 112, first paragraph, was withdrawn (Answer 2).

12. The method of claim 11 wherein the device is formed of a biodegradable polymer in the form of microspheres, slabs, disks, or gels.
13. The method of claim 1 wherein the VEGF is released over a period of between two and six weeks.
14. A composition for treating a diabetic ulcer comprising an effective amount of VEGF administered for a sustained period of time of at least two weeks to enhance the rate of closure of the wound.

#### FINDINGS OF FACT<sup>4</sup>

1. Tischer teaches that Vascular Endothelial Growth Factor (VEGF) “is useful as a wound healing agent, particularly in applications where it is desired to re-endothelialize vascular tissue, or where the growth of a new capillary bed (angiogenesis) is important” (Tischer, col. 10, ll. 63-68). VEGF “can, therefore, be used in the treatment of full-thickness wounds such as dermal ulcers, including the categories of pressure sores, venous ulcers and *diabetic ulcers*” (Tischer, col. 11, ll. 1-4 (emphasis added)).
2. “In cases where . . . [VEGF] is being used for topical wound healing, . . . it may be administered by any of the routes described . . . for the re-endothelialization of vascular tissue, . . . preferably by topical means” (Tischer, col. 11, ll. 26-30). “Slow release devices directing . . . [VEGF] to the injured site will also be used” (Tischer, col. 11, ll. 33-35).
3. Topical administration of VEGF includes administration “as either a solution, spray, gel, cream, ointment or as a dry powder directly to the site of injury . . . applied at a concentration ranging from 50 to 1,000 µg/ml either

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<sup>4</sup> Abbreviated “FF”.

in a single application, or in dosing regimens that are daily or every few days for a period of one to several weeks. Generally, the amount of topical formulation administered is that which is sufficient to apply from about 0.1 to 100  $\mu\text{g}/\text{cm}^2$  of . . . [VEGF] based on the surface area of the wound” (Tischer, col. 11, ll. 30-43).

4. One of ordinary skill in the art would have understood that wound closure is part of wound healing.
5. An ordinary meaning of the word “several”, appropriate to the context in which Tischer uses it above, is “consisting of a number more than two but not very many” (definition available at <http://www.webster-dictionary.net>, accessed January 10, 2008).
6. Routes of administration suitable for re-endothelialization (and therefore, for topical administration (FF 3)) include direct application in a thickened carrier material, intravenous administration, and delivery “to the site by a micrometering pump” (Tischer, col. 11, l. 65 to col. 12, l. 19).
7. Tischer also teaches that VEGF “is particularly useful in the treatment of abdominal wounds with a high risk of infection” (Tischer, col. 11, ll. 20-22), because “[a]ngiogenesis is also important in keeping wounds clean and non-infected” (*id.* at col. 11, ll. 16-17).
8. According to the present Specification, “almost all patients with diabetic foot ulcers have some degree of . . . bacterial contamination” (Spec. 21: 11-12), and treatment with VEGF “may reverse bacterial contamination” (Spec. 21: 9-10).
9. Thus, the Examiner found that an inherent effect of administration of VEGF to diabetic ulcers is treatment of bacterial contamination (Answer 4).

10. Tischer describes “[a] parenteral solution suitable for administration intravascularly via catheter to a wound site”; “[a]n aqueous gel, suitable for topical application to a wound site”; and “[a] dry powder, suitable for dusting onto a wound site”; each of which comprises 0.05-1.0 mg/ml VEGF (Tischer, col. 35, l. 55 to col. 36, l. 6).

11. As Tischer discloses a range of dosages and treatment times, one of ordinary skill in the art would have recognized that the appropriate dosage and duration of treatment for a given wound would vary within the parameters outlined by Tischer, given the severity and size of the wound, at the very least.

#### ISSUE ON APPEAL

The Examiner rejected claims 1, 3, 10-14, and 19-21 under 35 U.S.C. § 102(b) as anticipated by Tischer based on Tischer’s explicit teaching that VEGF can be used to treat diabetic ulcers (Answer 4), Tischer’s description of administering “amounts encompass[ing] Appellant’s amounts” (*id.* at 6), and Tischer’s teaching of “prolonged administration[ ]” of VEGF (*id.* at 7).

Appellant concedes that Tischer’s discloses “everything, including the specific disorder to be treated” (Br. 9). Nevertheless, Appellant contends that Tischer “does not demonstrate the relationship between VEGF and . . . enhancement of the rate of closure of a diabetic ulcer” (Br. 10), and Tischer’s disclosure is so broad “that one skilled in the art would have absolutely no guidance on how to arrive at the method and composition as defined by the claims . . . and is therefore not enabling” (*id.* at 8).

“Anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure.” *Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1380 (Fed. Cir. 2003) (citing *In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985)). “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. . . . 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). Thus, “a presumption arises that both the claimed and unclaimed disclosures in a prior art patent are enabled” (*id.*).

Given the fact that Tischer explicitly teaches that diabetic ulcers can be treated with VEGF (FF 1), that one skilled in the art would understand that wound closure is part of wound healing (FF 4), and that Tischer’s teachings encompass effective dosages and treatment durations (FF 2, 3, 6, 10), we find that the Examiner has set forth sufficient evidence to establish *prima facie* anticipation of the claimed invention by Tischer.

As discussed above, Tischer is presumed to be enabling. Therefore, the issue raised by this appeal is whether Appellant has met his burden of establishing that Tischer’s disclosure is not enabling.

#### ANALYSIS

##### *Claims 1 and 14*

With respect to method claim 1 and composition claim 14, Appellant argues that Tischer “does not demonstrate the relationship between VEGF and wound closure; much less enhancement of the rate of closure of a

diabetic ulcer” (Br. 10), “does not recognize the difference between chronic wounds such as diabetic ulcers and wounds in general” (*id.* at 9), and “fails to appreciate the importance of an effective amount during the entire two weeks or more of treatment that appellant has determined is critical to success” (*id.*). Appellant argues that “the angiogenic response in wound healing is time dependent . . . therefore it is not sufficient to just have some VEGF at the site for two weeks, it is imperative to have an *effective* amount at the site for that *entire* period of time” (Reply Br. 3 (citing as evidence Spec. 15: 24-30)). Finally, Appellant cites Margolis<sup>5</sup> as evidence “of the lack of adequate treatment in the art at the time of filing” (Reply Br. 6).

These arguments are not persuasive. Tischer explicitly teaches that diabetic ulcers can be treated with VEGF, e.g., topically (FF 1, 2). There is no dispute that Tischer’s disclosure encompasses dosages and durations effective to treat diabetic ulcers (FF 3, 6). Appellant has provided no evidence to show that it would have required undue experimentation<sup>6</sup> for one skilled in the art to work within the dosage and duration parameters disclosed by Tischer to treat diabetic ulcers, or that two weeks or more of treatment would be critical to success.

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<sup>5</sup> D.J. Margolis et al., *Healing diabetic neuropathic foot ulcers: are we getting better?*, 22 *Diabetic Medicine* 172-176 (2005).

<sup>6</sup> Enablement for the purposes of anticipation requires that the reference “teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation. *Elan Pharmaceuticals, Inc. v. Mayo Foundation*, 346 F.3d 1051, 1054-55 (Fed. Cir. 2003).

While the Specification does teach that “[a]ngiogenesis occurs in a time-dependent manner in relation to the wound healing process” (Spec. 15: 24-25), the time-dependency referred to is not the duration of treatment. Rather, the time period referred to is the period between “wound creation” and initiation of angiogenic therapy (“If the angiogenesis inhibitor [TNP-470] is given before or 5 days after wound creation, there is no delay in wound closure, but if it is given in the first 5 days after wounding a sharp delay in closure is noted” (Spec. 15: 27-30)).

Margolis describes “[a] cohort study within a multicentre wound care network of individuals with diabetic neuropathic foot ulcer who were treated by a standard wound care algorithm” (Margolis, Abstract). The study concluded that the improvement observed in healing diabetic ulcers was primarily due to “individuals . . . seeking care when their wounds are most easily treated and . . . more likely to heal” (*id.*). Margolis does not discuss treatment with VEGF at all, and is not relevant to whether it would have required undue experimentation to work within Tischer’s disclosure.

On this record, Appellant has not met his burden of rebutting the presumption of Tischer’s enablement.

Moreover, claim 14 is simply directed to a composition comprising VEGF in an amount effective to enhance closure of a diabetic ulcer over a period of at least two weeks. Appellant has not identified anything tangible about the claimed preparation which would distinguish it from the VEGF preparations described by Tischer (FF 10).

The Examiner’s rejection is affirmed with respect to claims 1 and 14.

*Claim 3*

With respect to claim 3, Appellant argues that “Tischer discloses a broad genus of applications of VEGF, but does not disclose or suggest administration of VEGF . . . to enhance the rate of closure of a diabetic wound and treat bacterial contamination of the wound” (Br. 12).

This argument is not persuasive. “[W]hen considering a prior art method, the anticipation doctrine examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure.” *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1378 (Fed. Cir. 2005).

As discussed above, Tischer’s disclosure encompasses dosages and durations effective to treat diabetic ulcers (FF 3, 6), and therefore anticipates the claimed invention. According to Appellant, an amount of VEGF effective to treat diabetic ulcers is also effective to treat bacterial contamination (FF 8). Thus, we agree with the Examiner’s finding that treatment of bacterial contamination is an inherent result of administration of VEGF in an amount effective to treat diabetic ulcers (FF 9), regardless of whether it was recognized by Tischer. In any case, Tischer teaches that VEGF is useful in the treatment of wounds with a high risk of infection because angiogenesis is important in keeping wounds clean and non-infected (FF 7).

Again, Appellant has provided no evidence to show that undue experimentation would have been required to work within Tischer's disclosure to treat infected wounds or wounds at risk of infection, including diabetic ulcers. On this record, Appellant has not met his burden of rebutting the presumption of enablement of the Tischer reference.

The Examiner's rejection is affirmed with respect to claim 3.

*Claims 10-12 and 19-21*

Appellant argues that "Tischer does not disclose biodegradable polymers in the form of microspheres, slabs, disks, or gels as defined by claims 12 and 21" (Br. 13). Appellant also argues that "Tischer discloses pumps for delivery of drug only to the vascular system . . . , not directly to a wound" (Br. 13), as required by claims 10, 11, 19 and 20 (*id.*).

This argument is not persuasive. Tischer explicitly teaches that VEGF can be administered to topical wounds, including diabetic ulcers "by topical means . . . as a solution, spray, gel, cream, ointment or as a dry powder" (Tischer, col. 11, l. 4, 26-28, and 30-33; FF 1, 2, 3). In addition, Tischer teaches "[i]n cases where . . . [VEGF] is being used for topical wound healing, . . . it may be administered by any of the routes described . . . for the re-endothelialization of vascular tissue" (Tischer, col. 11, ll. 26-30; FF 2), and "[s]low release devices directing . . . [VEGF] to the injured site will also be used" (Tischer, col. 11, ll. 33-35; FF 2). The routes described for the re-endothelialization of vascular tissue include administration of VEGF in "a thickened carrier material . . . for example, 1-5% carbopol", a polymeric gel, and "deliver[y] to the site by a micrometering pump" (Tischer, col. 11, ll. 64-65, and col. 12, ll. 10-13, and 17-18; FF 6).

Appellant asserts that “it is well known that a 1-5% carbopol gel would not provide release over a period of at least two weeks” (Br. 13).

Appellant has provided no evidence to support this assertion. Attorney argument is not evidence. *In re Pearson*, 494 F.2d 1399, 1405 (CCPA 1974). Nor can it take the place of evidence lacking in the record. *Meitzner v. Mindick*, 549 F.2d 775, 782 (CCPA 1977). In any case, Tischer teaches that gels containing VEGF may be applied (i.e., reapplied) daily or every few days for a period of one to several weeks (FF 3).

The Examiner’s rejection is affirmed with respect to claims 10-12 and 19-21.

*Claim 13*

Appellant argues that “Tischer does not disclose administration of VEGF for a *sustained* period of time of between *two to six weeks* to *enhance* the rate of closure of a diabetic ulcer” as required by claim 13 (Br. 14).

This argument is not persuasive. As discussed above, Tischer teaches that VEGF can be administered “daily or every few days for a period of one to several weeks” (FF 3). An ordinary meaning of the word “several” is “consisting of a number more than two but not very many” (FF 5). Thus, we agree with the Examiner that Tischer anticipates the method of claim 13. Again, Appellant has provided no evidence establishing that it would have required undue experimentation for one skilled in the art to work within the dosage and duration parameters disclosed by Tischer to treat diabetic ulcers.

The rejection is affirmed with respect to claim 13.

SUMMARY

We agree with the Examiner that Tischer discloses the limitations of the claimed invention. Tischer is presumed to be enabled, and the presumption of enablement has not been successfully rebutted. We therefore affirm the Examiner's anticipation rejection of claims 1, 3, 10-14, and 19-21 under 35 U.S.C. § 102(b) as anticipated by Tischer.

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) (2006).

AFFIRMED

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