



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

Table with 5 columns: APPLICATION NO., FILING DATE, FIRST NAMED INVENTOR, ATTORNEY DOCKET NO., CONFIRMATION NO.
13/207,864 08/11/2011 Thomas STIEFEL 708766 6869

23460 7590 12/02/2016
LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER

FISHER, ABIGAIL L

ART UNIT PAPER NUMBER

1616

NOTIFICATION DATE DELIVERY MODE

12/02/2016

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte THOMAS STIEFEL¹

Appeal 2015-001022
Application 13/207,864
Technology Center 1600

Before DONALD E. ADAMS, ULRIKE W. JENKS, and
TAWEN CHANG, *Administrative Patent Judges*.

JENKS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims directed to a method of treating sepsis, systemic inflammatory response syndrome, and/or septic shock in a patient. The Examiner rejects the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

¹ According to Appellant, the real party in interest is Biosyn Arzneimittel GmbH. (App. Br. 2.)

STATEMENT OF THE CASE

Claims 1–20 are on appeal, and can be found in the Claims Appendix of the Appeal Brief. Claim 1 is representative of the claims on appeal, and reads as follows:

1. A method of treating sepsis, systemic inflammatory response syndrome (SIRS), and/or septic shock in a patient, which method comprises administering to the patient (a) a pharmaceutical composition comprising a selenium containing active substance comprising 100-2035 µg of selenium, (b) a pharmaceutical composition comprising a corticoid-containing active substance, and (c) a pharmaceutical composition comprising insulin, whereby the patient is treated for sepsis, SIRS, and/or septic shock.

Appellant requests review of the Examiner rejection of claims 1–20 under 35 U.S. C. § 103(a) as unpatentable over Van den Berghe,² Briegel,³ and Forceville.⁴

Issue

Does the preponderance of the evidence of record support the Examiner’s conclusion that the combination of references renders the method of treating sepsis obvious? And if so, has Appellant provided sufficient rebuttal evidence or evidence of unexpected results to overcome the prima facie showing of obviousness?

² Van den Berghe et al., *Intensive Insulin Therapy in Critically Ill Patients*, 345 New England J. Med. 1359–1367 (2001) (“Van den Berghe”).

³ Briegel et al., *Low dose hydrocortisone infusion attenuates the systemic inflammatory response syndrome*, 72 Clin. Investig. 782–787 (1994) (“Briegel”).

⁴ Forceville, WO 00/12101, published Mar. 9, 2000 (“Forceville”).

Findings of Fact

We adopt the Examiner's findings concerning the scope and content of the prior art (Ans. 2–6), and provide the following findings for reference convenience.

- FF1. Van den Berghe teaches that “[g]lycemic control is a preventive approach that is more broadly applicable to critically ill patients and that reduced mortality during intensive care by more than 40 percent” (Van den Berghe 1364). The goal of “intensive insulin therapy [is] to maintain blood glucose at a level that did not exceed 110 mg per deciliter” in critically ill patients (*id.* at 1363; *see also* 1360 (“Study Design”)). Teaching that insulin therapy reduced “deaths from multiple organ failure with sepsis regardless of whether there was a history of diabetes or hypoglycemia” (*id.* at 1364).
- FF2. Briegel teaches that “low-dose hydrocortisone infusion in patients with septic shock decreased the febrile response and heart rate, and increased the mean arterial pressure” (Briegel 785). “Infusion was started with a loading dose of (100 mg in 30 min) and continued with a constant infusion of 10 mg per hour” (*id.* at 783). “The infusion of hydrocortisone at a dose of 10 mg/hr corresponds to the maximum secretory rate achieved in corticotropin simulated healthy humans” (*id.* at 786, *see* 784–785).
- FF3. Forceville teaches the application of “2 to 40 mg, even 80 mg of atomic selenium equivalent” for treating severe systemic inflammatory response syndrome (Forceville, Abstract; *see col. 2* 165 to *col. 3, l. 4*).

Principle of Law

It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art.

In re Kerkhoven, 626 F.2d 846, 850 (CCPA 1980)(citations omitted).

Analysis

Based on the combination of Van den Berghe, Briegel, and Forceville, the Examiner concludes that, at the time Appellant's inventions was made, it would have been prima facie obvious to combine "selenium, insulin and hydrocortisone to treat sepsis. One of ordinary skill in the art would have been motivated to utilize these three components together as they are all individually taught as being effective for the treatment of sepsis" (Ans. 4, 9; FF1–FF3).

Appellant contends that the experimental data shown in the Specification "demonstrates synergistic effects for patients treated with 2035 µg of selenium on day 1 and 1035 µg of selenium per day after day 1, which tested dosages span[ning] a significant portion of the claimed range of 100-2035 µg of selenium" (App. Br. 10; Reply Br. 3⁵). Relying on ¶8 of Dr. Stiefel's Declaration⁶, Appellant contends that the claimed combination therapy achieves substantially superior results than with selenium alone,

⁵ We note that the Reply Brief makes a correction to the table shown on page 10 of the Appeal Brief, specifically indicating that the control group A is treated with insulin to control blood sugar. (Reply Br. 3).

⁶ Declaration under 35 U.S.C. § 1.132 by Dr. Stiefel signed May 24, 2013.

further citing *Angstwurm*⁷ in support (App. Br. 11). In particular, Appellant notes that “*Angstwurm* reports a reduction in mortality of only 14.3% with selenium alone, whereas the claimed combination therapy results in a reduction in mortality of 80%, such that the claimed combination therapy is substantially superior to a selenium-only therapy” (*id.*).

We are not persuaded by Appellant’s contention. We note that the reliance on *Angstwurm* in Dr. Stiefel’s Declaration ignores the contribution made by insulin therapy and corticosteroid therapy in similarly situated patients, each of which would be expected to contribute a beneficial effect when applied as a combination therapy. We agree with the Examiner that the data shown in the Specification and represented in table form in both the Appeal Brief and Reply Brief show an improved mortality rate for the combination; however, this is not sufficient to overcome *prima facie* showing of obviousness (*see* App. Br. 10 and Reply Br. 3; *see* Ans. 10). Specifically, the Examiner explains that the improved mortality rate is shown for a single data point presented, but there is insufficient evidence in the Specification or the Stiefel Declaration to establish an expectation that this improvement in mortality rate would translate to the entire claimed range (*see* App. Br. 10; Reply Br. 3; *see also* Ans. 10 (stating that “appellants have only presented data at the highest data point claimed; they have not established that the surprising unexpected results occur over the entire claimed range”)). We agree with the Examiner’s position that each of

⁷ *Angstwurm et al., Selenium in Intensive Care (SIC): Results of a prospective randomized, placebo-controlled, multiple-center study in patients with severe systemic inflammatory response syndrome, sepsis, and septic shock, 35 Crit. Car. Med. 118–126 (2007), submitted with Form 1049 on July 18, 2013.*

the cited references individually shows that each claimed component results in a reduction in mortality; therefore, the combination would be expected to achieve at least an additive effect (*see* FF1–FF3). Because the data presented in the Specification is at the upper limit of the claimed range for each of the components there is insufficient evidence in the record to establish that lower concentration in any one of the components would produce the same effect, i.e., improvement in the mortality rate for septic patients. Accordingly, we agree with the Examiner that disclosure of “one data point [] is not commensurate in scope with the claimed invention. While the declaration may argue one of skill in the art could reasonably conclude [that the synergistic effects of combination therapy extend beyond the particular dosage used in the study described in the Specification], there is no evidence to support such a statement” (Ans. 10; *see* Stiefel Decl. ¶ 9).

The preponderance of the evidence of record supports the Examiner’s conclusion of obviousness and Appellant has not sufficiently rebutted the Examiner’s prima facie case. We affirm the rejection of claim 1 based on the combination of Van den Berghe, Briegel, and Forceville references. Claims 2–20 were not separately argued and fall with claim 1.

SUMMARY

We affirm the rejection of all claims.

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