NOTE: This disposition is nonprecedential.

# United States Court of Appeals for the Federal Circuit

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**IN RE: RAGHAVAN RAJAGOPALAN,**
*Appellant*

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2020-1956

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Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 14/499,191.

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Decided: May 18, 2021

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ROBERT FRITZ GREEN, Green, Griffith & Borg-Breen LLP, Chicago, IL, argued for appellant Raghavan Rajagopalan.

ROBERT MCBRIDE, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, argued for appellee Andrew Hirshfeld. Also represented by KAKOLI CAPRIHAN, THOMAS W. KRAUSE, AMY J. NELSON, FARHEENA YASMEEN RASHEED.

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Before TARANTO, BRYSON, and CHEN, *Circuit Judges*.

TARANTO, *Circuit Judge*.

Raghavan Rajagopalan is the named inventor on U.S. Patent Application No. 14/499,191, entitled "Prevention of

Illicit Methamphetamine Manufacture from Pseudoephedrine Using Food Flavor Excipients." The Patent and Trademark Office's Patent Trial and Appeal Board rejected claims 1–3 and 10 for obviousness based on two prior-art references and rejected claims 12 and 13 for obviousness based on those references together with a third. We affirm the Board.

## I

### A

The '191 application describes a composition that "prevent[s] [the] illicit manufacture of methamphetamine" from pseudoephedrine, a common pharmaceutical ingredient in over-the-counter allergy medication. J.A. 22. The application explains the basic two steps in the manufacture of methamphetamine from such available medications. The first step is isolation, or extraction, of the pseudoephedrine from the available medications, which contain other components. The second step is a chemical "reduction" reaction, involving reducing agents that donate electrons to the pseudoephedrine to produce methamphetamine. J.A. 23.

The application discloses a pseudoephedrine composition that impedes the second (reduction) step of that conversion process. Specifically, it discloses a combination of pseudoephedrine with a food-flavoring excipient (an additive), J.A. 23, in which the "excipient may capture the electrons from the reducing agent . . . at a much higher rate than pseudoephedrine . . . thereby blocking the formation of methamphetamine," J.A. 25. These food-flavoring excipients are referred to in the '191 application as "organoleptic agents." J.A. 23.

Independent claim 1 is representative and recites:

> 1. A pharmaceutically acceptable composition for deterring illicit manufacture of methamphetamine, said composition comprising:

> (a) an active pharmaceutical ingredient, wherein the active pharmaceutical ingredient is ephedrine or pseudoephedrine; and
>
> (b) an effective amount of an organoleptic excipient, wherein the organoleptic excipient is selected from the group consisting of pyrazines, pyrimidines, thiazolines, thiazolidines, and thiazoles; wherein said organoleptic excipient inhibits the chemical reduction of said active pharmaceutical ingredient to methamphetamine with reducing agents; and wherein said reducing agents comprise alkali metals, zinc, or phosphorous.

J.A. 455; *see also Ex parte Rajagopalan*, No. 2018-007283, 2020 WL 2126720, at *4 (P.T.A.B. Apr. 29, 2020) (Board finding claim 1 representative).

B

The examiner and the Board relied on three prior-art references—Giamalva, Adams, and Takakura—for rejecting claims 1–3, 10, 12, and 13 of the '191 application, invoking the first two references for all claims and adding Takakura for claims 12 and 13.

Giamalva is a published patent application, U.S. Patent Application Publication No. 2007/0243140, entitled "Pharmaceutical Composition Containing Sympathomimetic Amine Salt and Co-Distillable Additive." Giamalva recognizes that over-the-counter medications containing pseudoephedrine (which is a sympathomimetic amine) may be used to illicitly manufacture methamphetamine. *See* Giamalva ¶¶ 3–4. And Giamalva notes that

> [i]t has thus been found desirable to formulate sympathomimetic amine-containing products in order to render *isolation* of the sympathomimetic amine more difficult *or otherwise interfere with efforts to produce illegal drugs from common [over-the-counter] medications, e.g., by altering reactants*

> *used to convert sympathomimetic amine to methamphetamine*.

*Id.* ¶ 5 (emphases added).

The reference teaches including an additive in the compound to "inhibit[] reduction of the sympathomimetic amine and/or its derivatives." *Id.* ¶ 17. The additive, Giamalva teaches, should have properties sufficiently similar to the pseudoephedrine to prevent separation of the two when distillation is used to isolate pseudoephedrine before chemical reduction to methamphetamine. *See id.* ¶ 43. The additive may be an odorant, *i.e.*, a compound that "exhibit[s] a characteristic odor, and in some cases, a characteristic flavor as well, particularly during purification and/or conversion of sympathomimetic amines in illegal drug synthesis, or in the product of the illegal synthesis itself." *Id.* ¶ 47. The odor can be unpleasant and, if released during preparation, "render such preparation distasteful and/or serve as a recognizable signal to law enforcement." *Id.* ¶ 48. Critically, inclusion of the additive can also "interfere[] with the reduction to methamphetamine by competing with pseudoephedrine for the reducing agent." *Id.* ¶ 46.

Giamalva elaborates on the odorant's role at each of the two steps involved in the process of manufacturing methamphetamine. At the first step of the methamphetamine-production process, where the pseudoephedrine is isolated, "an odorant can deter misuse of commercially available sympathomimetic amines by imparting a very strong odor to a material, even after multiple attempts to isolate" it. *Id.* ¶ 52. At the second step of the production process, where the pseudoephedrine is chemically converted into methamphetamine, "specific odorants" that are "present at sufficiently high levels" (higher than those required to simply create the odor) "can inhibit one or more of the reactions, e.g., *reduction*, used to convert the sympathomimetic amine to an illegal drug." *Id.* (emphasis added).

Giamalva further explains that a "specific odorant" may be a "standard flavorant." *Id.* And it adds that embodiments include odorants that "contain nitrogen, e.g., as a volatile amine." *Id.* ¶ 53.

Adams is a journal article: T.B. Adams et al., *The FEMA GRAS Assessment of Pyrazine Derivatives Used as Flavor Ingredients*, 40 Food and Chemical Toxicology 429 (2002). It teaches that pyrazines are nitrogen-containing compounds that are used as flavoring agents in foods. *Id.* at 430. It explains that acetylpyrazine is the most commonly used pyrazine flavoring ingredient in the United States, and it discloses the structure of acetylpyrazine. *Id.* at 430, 434.

Takakura is a published patent application, U.S. Patent Application Publication No. 2012/0052177, entitled "Flavoring Material." Takakura teaches that thiazoles are known organoleptic compounds. *See* Takakura ¶¶ 26, 30, 45–48. Takakura further teaches that 5-acetyl-2,4-dimethylthiazole "impart[s] a particularly favorable livestock meat stock flavor." *Id.* ¶ 48.

C

On September 29, 2017, the examiner issued a final rejection of independent claim 1 and dependent claims 2, 3, 10, 12, and 13 of the '191 application. J.A. 403–28 (Final Rejection). On April 29, 2020, the Board affirmed the examiner's rejections of the claims as obvious in light of Giamalva combined with Adams or with Adams and Takakura. *Rajagopalan*, 2020 WL 2126720, at *4–7. Because Mr. Rajagopalan has not argued that the Board adopted new grounds of rejection and denied him a required opportunity to respond, we limit our description to the Board's decision.

The Board set forth the findings of fact that were key to its decision. It found that "Giamalva teaches the preparation of a pharmaceutical composition comprising

pseudoephedrine and a volatile amine odorant." *Id.* at *3 (citing Giamalva Abstract). It found, too, that Giamalva teaches what Giamalva paragraph 5 expressly states—the desirability of formulating a product containing a sympathomimetic amine such as pseudoephedrine so as to "'interfere with efforts to produce illegal drugs from common [over-the-counter] medications, e.g., by altering reactants used to convert sympathomimetic amine to methamphetamine.'" *Id.* (quoting Giamalva ¶ 5). The Board further found that Giamalva teaches what Giamalva paragraph 47 states—use of odorants as codistillable additives "'that interfere with subsequent chemical reactions for converting sympathomimetic amine compounds to illegal drugs.'" *Id.* (quoting Giamalva ¶ 47). The Board added that Adams teaches aroma-producing pyrazine-based flavoring ingredients, including acetylpyrazine, which is among the structures covered by claim 1, as made explicit in Formula I of the '191 application's specification. *Id.* at *3 (citing Adams 429–30).

The Board also "adopt[ed] the [e]xaminer's findings as [its] own, including with regard to the scope and content of, and motivation to modify or combine, the prior art." *Id.* at *3. One of the examiner's findings was that "'[i]t would have been obvious to one of ordinary skill in the art to combine the teachings of Giamalva . . . with the organoleptic agents disclosed by Adams'" and that, with that combination, "'conversion of any pure pseudoephedrine to methamphetamine [would be] hindered with a reasonable expectation of success.'" *Id.* at *2 (quoting J.A. 420–21). That finding, as the examiner made explicit to the Board, is a finding of "motivation to combine . . . with a reasonable expectation of success." J.A. 497 (examiner's answer).

The Board summarized: "Giamalva teaches a composition comprising pseudoephedrine and an amine[-]based odorant which interferes with the conversion of pseudoephedrine. Adams teaches that pyrazines[,] including those having a chemical structure meeting the

requirements of [F]ormula I in the Specification, exhibit aromas. We agree with the [e]xaminer that it would have been obvious to substitute the pyrazines of Adams for the odorants of Giamalva." *Rajagopalan*, 2020 WL 2126720, at *5 (citations omitted).

The Board considered and rejected Mr. Rajagopalan's arguments against the examiner's obviousness rejections. *Id.* at *4–7. The Board first rejected the contention that the invention claimed in the '191 application satisfies a long-felt need—a contention, the Board concluded, that was only attorney argument, unsupported by any "objective evidence . . . that there was a long-felt need and that the present invention satisfied that need." *Id.* at *4. The Board next rejected Mr. Rajagopalan's argument that the prior art taught away from the combination that the Board found the art actually taught. *Id.* Mr. Rajagopalan also contended that the cited prior art "does not enable the claimed composition" because "the compositions taught by Giamalva do not inhibit the chemical conversion of pseudoephedrine to methamphetamine," *id.* at *5, but the Board concluded otherwise. The Board reasoned that because "the composition resulting from the combination of Giamalva and Adams matches the claimed composition," Mr. Rajagopalan had the burden to show that the Giamalva-Adams combination composition "would not possess the same property" as the claimed composition, but Mr. Rajagopalan had "not offered any persuasive evidence" to make that showing. *Id.* Similarly, the Board concluded, Mr. Rajagopalan had "not offered any evidence of unexpected results." *Id.* at *6.

Mr. Rajagopalan did not make separate arguments as to the examiner's rejection of claims 12 and 13 for obviousness based on the combination of Giamalva, Adams, and Takakura, so the Board likewise affirmed that rejection. *See id.* at *4, *7.

Mr. Rajagopalan timely appealed under 35 U.S.C. § 141(a). We have jurisdiction. *See* 28 U.S.C. § 1295(a)(4).

II

Obviousness is a question of law that we review de novo, with underlying factual determinations reviewed for substantial evidence. *PersonalWeb Techs., LLC v. Apple, Inc.*, 917 F.3d 1376, 1381 (Fed. Cir. 2019). Factual findings include "the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, the presence or absence of a motivation to combine or modify with a reasonable expectation of success, and objective indicia of non-obviousness." *Ariosa Diagnostics v. Verinata Health, Inc.*, 805 F.3d 1359, 1364 (Fed. Cir. 2015). On substantial-evidence review, we ask "'whether a reasonable fact finder could have arrived at the agency's decision' and require[] examination of the 'record as a whole, taking into account evidence that both justifies and detracts from an agency's decision.'" *Intelligent Bio-Systems, Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1366 (Fed. Cir. 2016) (quoting *In re Gartside*, 203 F.3d 1305, 1312 (Fed. Cir. 2000)).

In this case, obviousness follows readily from the Board's key factual findings if those findings are supported by substantial evidence. As described above, the Board, in its expressly stated findings and in its adoption of the examiner's findings, found that Giamalva teaches using an amine-based odorant to interfere with the chemical conversion of pseudoephedrine to methamphetamine; that Adams discloses particular odorants, namely, pyrazines, which come within claim 1 of the '191 application and its specification; and that a relevant artisan had a motivation to use the Adams-disclosed compositions as odorants in the Giamalva composition with a reasonable expectation of success of hindering the chemical conversion. Those findings are supported by substantial evidence.

Some of the support is found in evidence the Board expressly quoted or cited. *See*, *e.g.*, Giamalva ¶ 5 ("It has thus been found desirable to formulate sympathomimetic amine-containing products [like pseudoephedrine] in order to render isolation of the sympathomimetic amine more difficult or otherwise interfere with efforts to produce illegal drugs from common [over-the-counter] medications . . . ."), ¶ 47 (teaching codistillable additives "that interfere with subsequent chemical reactions for converting sympathomimetic amine compounds to illegal drugs"); *see also* Adams 429–30. Additional supporting evidence is found on the face of Giamalva at paragraphs 17, 43, 46, 48, 52, and 53 (all quoted above). Those paragraphs, among other things, disclose the motive to inhibit the reduction reaction, the use of odorants to achieve that inhibition, the inclusion of "standard flavorants" among the "specific odorants" described as inhibiting reduction, and the use of nitrogen-containing odorants like volatile amines. *See id.* Adams, for its part, adds that pyrazines are commonly used amine (nitrogen-containing) odorants and that one type of pyrazine (acetylpyrazine) is the most commonly used pyrazine flavorant in the United States. Adams 430. The '191 application itself makes clear that acetylpyrazine falls within the group of amine odorants recited in the claims because acetylpyrazine has the structure of Formula I set forth in the application. *Compare* J.A. 20 (Formula I), *with* Adams 434 (acetylpyrazine).

This is sufficient evidence of a motivation to use the Adams pyrazine, a standard flavorant amine, as an odorant in the Giamalva formulation, creating a composition that, as a prima facie matter, Giamalva indicates would be reasonably expected to have the claimed inhibition-of-reduction property. In this circumstance, "the burden shifts to the patentee to provide evidence" to rebut the examiner's prima facie case—here, specifically, to show that the claimed inhibition of reduction would not result. *See In re Brandt*, 886 F.3d 1171, 1176 (Fed. Cir. 2018); *ACCO*

*Brands Corp. v. Fellowes, Inc.*, 813 F.3d 1361, 1365–66 (Fed. Cir. 2016); *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977). Mr. Rajagopalan has not undermined the Board's determination that he did not rebut the prima facie case.

Mr. Rajagopalan argues that the prior-art references do not teach using the organoleptic excipient in an "effective amount," which the '191 application defines as an amount that sufficiently inhibits the formation of methamphetamine to be "less than about 25%" of the formed composition. J.A. 26; Rajagopalan Opening Br. at 11–12, 32. But the Board adopted the examiner's findings, which include a finding that the claimed "effective amount" in the '191 application is taught in Giamalva's disclosure of the most preferred amount of odorant to add. *See* J.A. 410. Giamalva supports that finding. It teaches that the ratio of additive to pseudoephedrine should "preferably" be "from about 10:1 to about 1:10," "[m]ore preferably" "from about 3:1 to about 1:3," and "[m]ost preferably" "from about 2:1 to about 1:2." Giamalva ¶ 56. The '191 application teaches that if the ratio of the excipient Formula I to pseudoephedrine is roughly 1:1, which is within the range of Giamalva's most preferred ratios, then the amount will be effective, in that methamphetamine will be no more than 6% of the product of the reduction process. *See* J.A. 30–31.

With respect to claims 12 and 13, which depend on claim 1 but specify particular excipients, Mr. Rajagopalan made no separate arguments before the Board that the combination of Giamalva, Adams, and Takakura failed to establish that the claims are unpatentable for obviousness. *See* J.A. 433–62 (Rajagopalan Appeal Brief), 516–27 (Rajagopalan Reply Brief). Such arguments have accordingly been forfeited. *See In re Google Tech. Holdings LLC*, 980 F.3d 858, 863 (Fed. Cir. 2020). In any event, we note that Takakura discloses 5-acetyl-2,4-dimethylthiazole, which, as Mr. Rajagopalan does not dispute, is a thiazole described by the structure of Formula III recited in claims 12 and 13.

*Compare* J.A. 20 (Formula III), *with* Takakura ¶¶ 47–48; *see also* Rajagopalan Opening Br. at 28–30. Takakura further discloses that 5-acetyl-2,4-dimethylthiazole is a flavorant that "impart[s] a particularly favorable livestock meat stock flavor." Takakura ¶ 48; *see also* J.A. 424 (Final Office Action). Thus, for reasons similar to those stated above, substantial evidence supports the finding that a relevant artisan would have been motivated to substitute the flavorant from Takakura for the odorants in Giamalva's teachings. *See* J.A. 424; *cf. Rajagopalan*, 2020 WL 2126720, at *4–5 (explaining why a relevant artisan would combine Giamalva and Adams).

III

We have considered Mr. Rajagopalan's remaining arguments and find them unpersuasive. For the foregoing reasons, we affirm the Board's determination that claims 1–3, 10, 12, and 13 of the '191 application are unpatentable for obviousness.

The parties shall bear their own costs.

**AFFIRMED**