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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte MAKIKO YOSHIMOTO, HIDEO AKIYAMA,
and HITOSHI NOBUMASA

Appeal 2019-004740
Application 15/581,344
Technology Center 1600

Before DONALD E. ADAMS, ULRIKE W. JENKS, and
MICHAEL A. VALEK, *Administrative Patent Judges*.

VALEK, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellant¹ submits this appeal under 35 U.S.C. § 134(a) involving claims to a method for extracting RNA from a biological sample. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

STATEMENT OF THE CASE

Appellant's Specification states that a method "for isolation of RNA frequently employed [is] phenol extraction, precipitation from chaotropic salt solutions and adsorption to silica membranes." Spec. ¶ 2. The

¹ We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies Toray Industries, Inc. as the real party in interest.

Specification refers to two prior art references describing solutions for such methods—one disclosing “a solution for RNA extraction comprising 2 to 5 M guanidine and 40 to 60% phenol” and a second disclosing a solution comprising “a 30 to 50% phenol solution containing 0.5 to 2 M guanidine.” *Id.* ¶¶ 3–4. According to the Specification, “RNA isolated using the solutions and methods described in [these references] still shows contamination with (residual) genomic DNA in an amount which can be detected by the reverse transcription-polymerase chain reaction assay (RT-PCR), leading to problems such as loss of quantitiveness of RNA” and thus an additional step, e.g., treatment with DNase, is required to remove the DNA. *Id.* ¶¶ 6–8. “The present invention aims to solve these problems” based on the “present inventors . . . discover[y] that the phenol concentration has an especially strong relationship with the effect of prevention of contamination with DNA.” *Id.* ¶¶ 10–11.

Claims 7, 8, and 11–17 are on appeal and can be found in the Claims Appendix of the Appeal Brief. Claim 7 is representative of the claims on appeal. It reads as follows:

7. A method for extracting RNA from a biological sample containing RNA and at least DNA, said method comprising the steps of:
homogenizing said biological sample together with a solution comprising:
 - (a) phenol in an amount of not less than 53% by volume based on the total amount of said solution, wherein the amount of phenol does not exceed a percentage that excludes any of components (b)-(e);
 - (b) an aliphatic alcohol having a plurality of hydroxyl groups in an amount of 3 to 10% by volume based on the total amount of said solution;

- (c) a guanidinium salt at a concentration of 0.5 to 2.0 M based on the total amount of said solution;
 - (d) a thiocyanate at a concentration of 0.1 to 0.5 M based on the total amount of said solution;
 - (e) a buffer for maintaining the pH of said solution at 4 to 6;
- centrifuging the obtained mixture; and recovering an RNA-containing aqueous layer produced by the centrifugation.

App. Br. 15.

Appellant seeks review of the following rejections:

- I. Claims 7, 8, and 11–17 under 35 U.S.C. § 102 as anticipated by Chomczynski;² and
- II. Claims 7, 8, and 11–17 under 35 U.S.C. § 103 as obvious over Chomczynski.

App. Br. 5.

Analysis

I. Anticipation Rejection

The issue for this rejection is whether the preponderance of the evidence supports Examiner’s finding that Chomczynski anticipates Appellant’s claims.

Examiner finds that Chomczynski describes a method for isolating substantially pure RNA suitable for PCR using a solution with the same ingredients as in claim 7. *See* Final 5–7. The only difference is that Chomczynski states that the amount of phenol in that solution ranges from “about 30%-50% by volume,” whereas Appellant’s claims recite phenol in “an amount of not less than 53% by volume.” *Id.* at 6 (quoting Chomczynski 4:58). Notwithstanding the foregoing difference in phenol

² US 5,346,994, issued Sept. 13, 1994 (“Chomczynski”).

concentration, Examiner determines Chomczynski anticipates because “[t]he use of the expression ‘about’ is recognized as encompassing values both below and above the recited value.” *Id.*

Appellant contends Examiner erred in finding that Chomczynski anticipates the claimed phenol range because the word “about” in Chomczynski’s stated range of “about 30%-50%” modifies only the lower boundary, i.e., 30%. Appeal Br. 6. Appellant further argues that even if “about” is interpreted to apply to both the “floor and ceiling of the phenol range disclosed by Chomczynski, there is no support in the record to suggest that ‘about’ 50% would include the floor of Appellant’s range, i.e., 53%.” Reply Br. 3.

We are persuaded by Appellant’s argument that Chomczynski does not disclose the solution recited in Appellant’s claims. An amount that is “not less than 53%,” as recited in claim 7, is not the same as Chomczynski’s disclosure of solutions of “about 30%-50%” phenol. Even if “about” modifies the upper limit of Chomczynski’s range, Examiner failed to establish an evidentiary basis on this record to support a finding that about 50% reads on a solution comprising “not less than 53% phenol,” as claimed. Therefore, Chomczynski does not anticipate. *See Titanium Metals*, 778 F.2d at 783 (“[A]nticipation under § 102 can be found only when the reference discloses exactly what is claimed.”).

The ’155 patent,³ which Chomczynski incorporates by reference, does not support the anticipation rejection. *See* Ans. 12 (relying on the phenol range taught in the ’155 patent). The ’155 patent discloses a different

³ US 4,843,155, issued June 27, 1989 (“’155 patent”).

isolation method wherein a solution comprising “about 40% to about 60% phenol” is used in combination with a higher amount of guanidinium (i.e., 2-5 M). *See* ’155 patent, 2:44–46, 3:40. Chomczynski distinguishes the method in the ’155 patent, stating it is not “capable” of achieving the results of the method taught therein. Chomczynski, 2:48–55. Accordingly, Chomczynski and the ’155 patent disclose two distinct methods. Examiner cannot combine aspects of the ’155 patent’s method with Chomczynski’s method to demonstrate anticipation of the present claims. *See Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1083 (Fed. Cir. 2008) (“To anticipate, the reference must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements arranged as in the claim.”) (quotations omitted). Accordingly, we reverse the rejection of claims 7, 8, and 11–17 as anticipated by Chomczynski.

II. Obviousness Rejection

The issue for this rejection is whether the preponderance of the evidence supports Examiner’s finding that Appellant’s claims are obvious over Chomczynski.

Examiner determines that if Chomczynski does not anticipate, Appellant’s claims are “still deemed to have been obvious” over that reference. Final 7. In particular, Examiner determines it would be a matter of routine and obvious optimization for a skilled artisan to “adjust[] the concentrations of a known reactant [phenol] from 50% to 53%,” as claimed. *Id.* at 8.

Appellant argues “even assuming Chomczynski presents a *prima facie* case of obviousness” that case is rebutted by Appellant’s evidence of

“secondary considerations of non-obviousness.” Appeal Br. 5. Specifically, Appellant relies on the Declaration of Ms. Makiko Yoshimoto dated Sept. 5, 2015 (“Yoshimoto Decl.”), which it contends presents “unexpected and surprising results” achieved by using a solution comprising 53% phenol as compared to one with 50% phenol. *Id.* at 13.

Upon considering the record as a whole, we determine that the preponderance of the evidence of record does not support Examiner’s conclusion of obviousness. As discussed below, Appellant’s evidence of unexpected results is sufficient to overcome Examiner’s prima facie showing.

Appellant does not specifically dispute Examiner’s finding it would be routine to adjust the concentration from 50% to 53%. *See* Appeal Br. 11–13. Thus, we find no error in Examiner’s conclusion that Chomczynski supports a prima facie showing of obviousness

What distinguishes Appellant’s claims, however, is the evidence of unexpected results set forth in Appellant’s Specification and the Yoshimoto Declaration.⁴ The Specification provides examples that allow for a

⁴ Examiner states that the Yoshimoto Declaration is not part of the record because it was not “presented prior to the filing of the notice of appeal” on September 30, 2018. Ans. 15. However, as Appellant points out, the Yoshimoto Declaration, which was originally filed in support of the parent application 13/816,792, was also presented in support of the present application in Appellant’s responses filed September 12, 2017 and February 21, 2018. Reply Br. 1–2, n. 1. In each response, Appellant expressly relied on the Yoshimoto Declaration to advance its unexpected results argument, quoted the pertinent data from such, and identified where the declaration appeared in file history for the ’792 application. 9/12/17 Resp. 7–8; 2/21/18 Resp. 8–9. In the first of these responses, Appellant also stated that a copy of the Yoshimoto Declaration was supplied with the response “[f]or

comparison of the solution of the claimed method (e.g., Examples 1–4) to the closest prior art (i.e., a solution with 50% phenol as in Comparative Example 1). *See* Spec. ¶¶ 39–79. The Specification also includes figures showing electropherograms of RNA isolated in these examples. *Id.* at Figs. 1–4. According to the Specification, the solutions in Examples 1–4, which comprise varying amounts of phenol ranging from 53% to 65%, but are otherwise identical to the solution in Comparative Example 1, resulted in RNA with “good” purity. *Id.* at 43, 45 (Tables 1 and 3). In contrast, the purity obtained using the 50% phenol solution in Comparative Example 1 was “not good.” *Id.*

The Yoshimoto Declaration quantifies these results by calculating the relative amounts of the RNA and DNA in each of these examples based on their electropherograms. *See* Yoshimoto Decl. ¶¶ 8–11. According to the Yoshimoto Declaration, the content of contaminating DNA in Comparative Example 1 was 63% of the total nucleic acid isolated, whereas it was only 2–8% in Examples 1–4. *Id.* at ¶ 11. The Specification explains these results are significant because RNA obtained according to the prior art method in Comparative Example 1 requires further purification before it can be amplified via PCR, whereas the claimed method yields RNA that is

convenience.” 9/12/17 Resp. 7, n.1. But it appears that copy was not included with that filing. Notwithstanding that oversight, we agree with Appellant that the Yoshimoto Declaration was presented in support of the present application prior to the date of the notice of appeal and is therefore part of the record before us. In contrast, Appellant appears to concede that it did not present the “Second Yoshimoto Declaration” prior to noticing this appeal and we do not rely on it for our decision here. *See* Appeal Br. 4.

sufficiently free of contaminating DNA to be amplified without additional purification. *See Spec.* ¶¶ 6, 16.

We agree with Appellant that, on this record, the results evidenced by the Specification and Yoshimoto Declaration are unexpected and probative of non-obviousness. Considering “the entire merits of the matter” in light of this evidence, we determine that the preponderance of the evidence does not support the rejection. *See In re Hedges*, 783 F.2d 1038, 1039 (Fed. Cir. 1986). Accordingly, we reverse.

CONCLUSION

The rejection of claims 7, 8, and 11–17 under 35 U.S.C. § 102 as anticipated by Chomczynski is reversed. The rejection of claims 7, 8, and 11–17 under 35 U.S.C. § 103 as obvious over Chomczynski is reversed.

DECISION SUMMARY

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
7, 8, 11–17	102	Chomczynski		7, 8, 11–17
7, 8, 11–17	103	Chomczynski		7, 8, 11–17
Overall Outcome				7, 8, 11–17

REVERSED