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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte MARKUS RAST, PETER SKUFCA, WOLFRAM STEINHILBER, GERHARD BECKER, JURGEN VOLZ, and WOLFGANG ISE

Appeal 2018-007643
Application 14/068,074
Technology Center 1600

Before DEBORAH KATZ, JOHN G. NEW, and JOHN E. SCHNEIDER, *Administrative Patent Judges*.

KATZ, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellant[1] seeks our review[2], under 35 U.S.C. § 134(a), of the Examiner's decision to reject claims 1–6, 8, and 9.[3] (Appeal Br. 1.) We have jurisdiction under 35 U.S.C. § 6(b). We AFFIRM.

Appellant's Specification is directed to methods for preparing high concentration liquid formulation of an antibody. (Specification ("Spec.") 1:3.)

Appellant's claim 1 recites:

> A method for preparation of a high concentration liquid formulation of a veltuzumab antibody or a fragment thereof, having a concentration C^H of the antibody, comprising the steps of:
> a) providing a solution containing the antibody in a starting concentration C^S;
> b) ultrafiltering the solution of step (a) in order to obtain a solution having an intermediate concentration C^1 of the antibody, wherein C^1 is at least about 260 mg/mL; and
> c) diluting the solution of step (b) to a concentration C^H of the antibody in order to obtain the high concentration liquid formulation.

(App. Br. 15.)

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[1] We use the word "Appellant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party-in-interest as TAKEDA GMBH. (Appeal Br. 3.)
[2] We consider the Final Office Action issued August 11, 2017 ("Final Act."), the Appeal Brief filed January 18, 2018 ("Appeal Br."), the Examiner's Answer issued on May 23, 2018 ("Ans."), the Reply Brief filed July 12, 2018 ("Reply Br.") and the oral argument held on September 17, 2019, in reaching our decision.
[3] Appellant canceled claims 7, 24 and 25 and withdrew claims 10–23, 26, and 27 during prosecution. (*See* Appeal Br. 15–17.)

The Examiner provisionally rejected claims 1–6, 8, and 9 under the doctrine of obviousness-type double-patenting over claims 1–9 of copending application 14/437,902 in view of Goldenberg[4]. (*See* Final Act. 3.) Because none of the claims of application 14/437,902 have been determined to be allowable, review of this rejection is premature. *See Ex parte Moncla*, Appeal No. 2009-006448 (BPAI June 22, 2010) (precedential).

The Examiner also rejected claims 1–6, 8, and 9 as being obvious under 35 U.S.C. § 103(a) over Yang[5] and Goldenberg. (Final Act. 4–7.) Appellant does not present arguments for the separate patentability of any of these claims. Accordingly, we focus on claim 1 in our analysis. *See* 37 C.F.R. § 41.37(c)(1)(iv).

Findings of Fact

1. Yang teaches using filtration methods to obtain concentrated antibody preparations. (*See* Yang abstract and 15:21–26.)

2. Yang teaches ultrafiltration of an anti-CD20 antibody to obtain a formulation of antibody with a concentration in the range of 25–350 mg/ml. (*See* Yang 13:12–14.)

3. Yang teaches concentrating antibodies through ultrafiltration as a final step before formulating the pharmaceutical to be administered. (*See* Yang 15:21–24; 21:5–28; claims 22–41.)

4. Yang teaches that effective treatment with therapeutic antibodies typically requires administration of doses concentrated to 100

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[4] Goldenberg et al. International Patent Application Publication WO 2010/011697 A1, published January 28, 2010 ("Goldenberg").
[5] Yang et al., International Patent Application Publication WO 2004/001007, published December 31, 2003 ("Yang").

mg/ml or greater and that the concentration of antibodies in pharmaceutical preparations is desirably between 100 and 300 mg/ml. (*See* Yang 2:15–32.)

5. Goldenberg teaches that the antibody veltuzumab was a known antibody with improved efficacy compared to other anti-CD20 antibodies such as rituximab. (*See* Goldenberg ¶¶ 180–180, Example 14.)

Analysis

Appellant's claim 1 is drawn to providing an antibody solution of one concentration, ultrafiltering it to achieve an intermediate concentration (at least about 260 mg/ml), and diluting that intermediate concentration solution to solution with a third concentration. (*See* Appeal Br. 15.) If it was known in the art to use utrafiltration to achieve an antibody solution of at least 260 mg/ml and it would have been obvious to do so with veltuzumab, the only other step in Appellant's claim is diluting the antibody solution.

The Examiner finds that Yang teaches ultrafiltering an antibody solution to obtain a concentration of up to 350 mg/ml. (*See* Final Act. 4 and 5, citing Yang 13.) The Examiner finds that Yang teaches antibodies can be used therapeutically at lower concentrations: from 100 to 300 mg/ml. (*See* Final Act. 4, citing Yang 2.) The Examiner finds further that Goldenberg teaches the desirable attributes of veltuzumab. (*See* Final Act. 5.) We find that the record supports these findings. (*See* FFs 1–5.)

The prior art shows that one of ordinary skill would have known how to concentrate an antibody such as veltuzumab, to concentrations of at least about 260 mg/ml by ultrafiltration. Appellant does not argue otherwise. Thus, the issue before us is whether it would have been obvious to one of ordinary skill in the art to dilute a solution of antibody concentrated by ultrafiltration.

The Examiner determines that because antibodies could be produced at the higher concentration of 350 mg/ml and these antibodies could be used at lower concentrations (100-300 mg/ml), it would have been obvious to dilute these antibodies for therapeutic use. (*See* Final Act. 4–5.) We agree with the Examiner.

Appellant argues that the "Examiner expressly acknowledges that Yang does 'not teach [the dilution] step c) of claim 1,' or the use of veltuzumab" and "cites nothing to fill this acknowledged gap in the cited prior art." (*See* Appeal Br. 8) But, Appellant also acknowledges that formulating a preparation at the highest needed concentration and then diluting it to prepare any lower concentrations needed "may be a reasonable approach." (Reply Br. 5.) We agree that such an approach would be reasonable. It also would have been obvious.

Appellant's argument that the rejected claims are directed to production of one concentration of antibody at concentration "C^H" and that there is no need for antibody at any other concentration does not persuade us to the contrary. (*See* Reply Br. 5.) If it is obvious to dilute a solution of concentrated antibody, it does not matter what C^H is or how it is used, as long as it is lower to at least some extent than "at least about 26 mg/ml."

We are not persuaded by Appellant's argument that because the Examiner stated that "Yang et al. do not teach step c) of claim 1 . . . ." (Appeal Br. 8.) In *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), the Supreme Court explained:

> In many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends. Granting patent protection to advances that

> would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility.

(*Id.* at 419.) The Examiner's reasoning that from the express teachings of Yang it would have been obvious to dilute ultrafiltered formulations of antibody is reasonable because there would be no other way to obtain therapeutic concentrations from the highest ultrafiltered concentrations.

We disagree with Appellant's argument that Yang does not teach initially "over-concentrating" the formulation to a concentration higher than ultimately desired. (Appeal Br. 10.) We also disagree with Appellant that Yang focuses on providing the desired concentration directly. (*See id.* at 11–12.) Yang teaches ultrafiltering antibody solutions to achieve a concentration of up to 350 mg/ml. (*See* FF 2.) Yang also teaches that antibodies can be administered at lower concentrations: between 100 and 300 mg/ml. (*See* FF 4.) Thus, even if Yang does not use the word "diluting," those of ordinary skill in the art would know that the most concentrated antibody formulations taught by Yang using ultrafiltration would have to be diluted to obtain pharmaceutical formulations.

Appellant argues that "the claims clearly contemplate that **the highest needed concentration** - the desired 'high concentration liquid formulation of a veltuzumab antibody or a fragment thereof - **is at concentration c^{H}**.'" (Reply Br. 4–5.) We are not persuaded by this argument because there is no limitation to a "needed" concentration in Appellant's claims. Appellant's claims recite on a starting concentration, an intermediate concentration, and

a high concentration. Neither of them is recited to be "needed" or otherwise therapeutic.

We are also not persuaded by Appellant's argument questioning the truth of the statement in Yang that concentrations as high as 350 mg/ml may be prepared because there are no express teachings or examples of being prepared and maintained. (Reply Br. 5.) "[B]oth claimed and unclaimed materials disclosed in a patent are presumptively enabling." *In re Antor Media Corp.*, 689 F.3d 1282, 1287 (Fed. Cir. 2012) (citing *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed.Cir.2003)). Appellant fails to present evidence to rebut this presumption. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1355 (Fed. Cir. 2003) ("The applicant, however, can then overcome that rejection by proving that the relevant disclosures of the prior art patent are not enabled.").

Appellant fails to persuade us that the Examiner erred. Accordingly, we affirm the rejection under 35 U.S.C. § 103(a).

Conclusion

Upon consideration of the record and for the reasons given, we affirm the Examiner's rejection.

In summary:

Claims Rejected	**Basis**	**Affirmed**	**Reversed**
1–6, 8, and 9	Obviousness-type double-patenting[6]		
1–6, 8, and 9	§ 103 over Goldenberg and Yang	1–6, 8, and 9	
Overall Outcome		1–6, 8, and 9	

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

AFFIRMED

[6] As explained above, we do not reach this rejection per *Ex parte Moncla*, Appeal No. 2009-006448 (PTAB June 22, 2010) (holding that it is premature to address a provisional rejection) (designated precedential).