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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* MATTHEW T. STONE  
and MIKHAIL KOZLOV

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Appeal 2021-004177  
Application 14/768,267  
Technology Center 1600

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Before ERIC B. GRIMES, RICHARD M. LEBOVITZ, and  
GEORGE C. BEST, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

The Examiner rejected 1, 3, 10, 12, and 26–35 under 35 U.S.C. § 103 as obvious. Pursuant to 35 U.S.C. § 134(a), Appellant<sup>1</sup> appeals from the Examiner’s decision to reject the claims. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

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<sup>1</sup> “Appellant” refers to “applicant” as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as EMD Millipore Corporation. Appeal Br. 3.

STATEMENT OF THE CASE

Claims 1, 3, 10, 12, and 26–35 are rejected by the Examiner in the Non-final Action as follows:

1. Claims 1, 3, 10, 12, 32, and 33 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Lucas et al. (*J. Immunol. Meth.*, 1988, 113:113–122) (“Lucas”), Kaersgaard et al. (WO 97/03092, published January 30, 1997) (“Kaersgaard”), and Wu (Ph.D. Thesis, December 1982) (“Wu”). Non-final Act. 4.

2. Claims 1, 3, 10, 12, 26–29, 32, and 33 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Lucas, Kaersgaard, Wu, and Loos et al. (*Arch. Biochem. Biophys.*, May 23, 2012, 526:167–173) (“Loos”). Non-final Act. 6.

3. Claims 1, 3, 10, 12, and 30–33 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Lucas, Kaersgaard, Wu, and Abe et al. (US 2003/0104586 A1, published June 5, 2003) (“Abe”). Non-final Act. 6.

4. Claims 1, 3, 10, 12, and 32–35<sup>2</sup> under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Lucas, Kaersgaard, Wu, and Lin et al. (*J. Sep. Sci.*, 2011, 34:1696–1702) (“Lin”). Non-final Act. 7.

Claim 1 is the only independent claim on appeal. Claim 1 is reproduced below:

1. A method of selectively removing a proteinaceous impurity from a sample comprising at least an immunoglobulin and the proteinaceous impurity, the method comprising the steps of:

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<sup>2</sup> Claim 35 is pending, but was not included in the statement of the rejection. However, in the Examiner’s Answer, the Examiner stated that Lin was cited only to reject the limitations of claims 34 and 35. Ans. 16.

- (a) providing a sample comprising at least an immunoglobulin and a proteinaceous impurity;
- (b) adjusting the solution pH of the sample, such that the pH is within 2.0 pH units of the isoelectric point of the proteinaceous impurity to be selectively removed;
- (c) contacting the sample with activated carbon, wherein the activated carbon selectively binds the proteinaceous impurity to be selectively removed; and
- (d) removing the activated carbon from the sample, thereby resulting in selective removal of the activated carbon bound proteinaceous impurity from the sample and an increase in the concentration of the immunoglobulin to the proteinaceous impurity in the sample of 70% or more when measured.

#### OBVIOUSNESS REJECTIONS

Claim 1 is directed to a method of “selectively removing a proteinaceous impurity from a sample comprising at least an immunoglobulin and the proteinaceous impurity.” The selective removal is accomplished by “adjusting the solution pH of the sample, such that the pH is within 2.0 pH units of the isoelectric point of the proteinaceous impurity to be selectively removed” and then contacting the sample with activated carbon, which binds to the proteinaceous impurity, and removing the activated carbon along and proteinaceous impurity bound to it.

The Examiner found that Lucas describes the presence of contaminants in monoclonal antibodies. Non-final Act. 4. The Examiner also found that Lucas discloses that the contaminants should be quantitated to ensure that they are removed to produce monoclonal antibodies of the highest purity. *Id.* The Examiner acknowledged that Lucas does not disclose “the solution” to the problem that Appellant claims in claim 1. *Id.* However,

the Examiner found that Kaersgaard describes removing PEG (polyethylene glycol) from immunoglobulins using activated carbon, the same material used in claim 1 to remove the proteinaceous impurity. *Id.* The Examiner additionally found that Wu describes using activated carbon to remove proteinaceous material from a product. *Id.* at 5. The Examiner found that Wu teaches that the maximum adsorption of the proteinaceous material by the activated carbon is at the protein's isoelectric point. *Id.* The Examiner concluded that Wu "teaches that the selectivity of adsorption of polypeptides to activated carbon is based on the relationship between the pH and the isoelectric point." *Id.*

The Examiner determined it would have been obvious to one of ordinary skill in the art at the time of the invention "to remove the impurities of Lucas" by Wu's method, "motivated by the desire for highest purity, described by Lucas." Non-final Act. 5. The Examiner further reasoned that because Kaersgaard "teach[es] using very similar methods for purifying immunoglobulins, and explicitly discuss[es] using the methods to remove other impurities, an artisan in this field would attempt this process with a reasonable expectation of success." *Id.*

Appellant argues that none of the references cited by the Examiner describe the selective removal of a protein impurity from other proteins. Appellant identifies the deficiencies in the cited references. Specifically, Appellant argues that Kaersgaard removes PEG, and not a protein impurity, from immunoglobulins. Appeal Br. 9. Wu, Appellant argues, removes protein from corn syrup, but does not teach selectively removing a proteinaceous impurity from other proteins based on the isoelectric point of the impurity as required by claim 1. *Id.* at 10–11. For these reasons,

Appellant contends that the combination of cited references does not suggest claim 1 nor provide the motivation to combine Wu with Lucas and Kaersgaard. *Id.* at 11.

#### DISCUSSION

In *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), although the Supreme Court emphasized “an expansive and flexible approach” to the obviousness question, *id.* at 415, it also reaffirmed the importance of determining “whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue.” *Id.* at 418.

Thus, as the Federal Circuit has since explained, “obviousness concerns whether a skilled artisan not only *could have made* but *would have been motivated to make* the combinations or modifications of prior art to arrive at the claimed invention.” *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1073 (Fed. Cir. 2015).

Here, the claimed invention is directed to a method of “selectively removing a proteinaceous impurity from a sample comprising at least an immunoglobulin and the proteinaceous impurity.” As explained above, the selective removal is accomplished by “adjusting the solution pH of the sample, such that the pH is within 2.0 pH units of the isoelectric point of the proteinaceous impurity to be selectively removed” and then contacting the sample with activated carbon, which binds to the proteinaceous impurity. Lucas describes the problem that monoclonal antibodies, a type of immunoglobulin, may be contaminated by protein A and bovine IgG, but does not teach how to remove them. Lucas 113 (“These methods should quantitate the contaminants most likely to occur at each isolation step to

ensure that they are removed.”). The Examiner relied on Wu for teaching how to selectively remove contaminating proteins. Non-final Act. 5. However, as argued by Appellant, Wu does not describe selective removal of proteins from a product.

Wu discloses that “[i]n products such as corn syrup, table sugar and wine, protein is an undesired ingredient and it must be removed.” Wu 1. Wu teaches that activated carbon can be used as a protein adsorbent. *Id.* 8. Wu also teaches that “to achieve maximum adsorptivity” of the protein on the activated carbon, “the pH of the solution should be around the IEP [isoelectric point] of the protein.” *Id.* 80. Wu then describes an experiment in which protein was removed from corn syrup (a “sugar solution”) using the activated carbon. *Id.* 138. Wu also describes another experiment, referred to as “binary protein adsorption,” in which bovine serum albumin (BSA) and lysozyme were mixed, adsorbed on activated carbon, and then the amount of adsorption of the two proteins was measured. *Id.* 96, 98. In neither experiment does Wu disclose using pH or the protein’s isoelectric point to achieve selective adsorption of the proteins. *Id.* 96. All the protein contaminants in the corn syrup were adsorbed onto the activated carbon; likewise, both the BSA and lysozyme were adsorbed at the same time by the activated carbon without using pH to selectively adsorb one over the other.

We agree with Appellant that the Examiner did not provide sufficient reason to selectively remove a proteinaceous impurity by “adjusting the solution pH of the sample, such that the pH is within 2.0 pH units of the isoelectric point of the proteinaceous impurity to be selectively removed” as recited in claim 1. As argued by Appellant, neither Kaersgaard nor Wu describe selective removal of a protein from a solution comprising other

proteins. Wu removes proteins from a mixture of proteins (BSA and lysozyme), but despite teaching that the maximal adsorption of a protein can be achieved using the pH of the protein's isoelectric point, does not apply this teaching to selectively adsorb one protein over another. The Examiner did not provide adequate reasoning to modify Wu to selectively remove protein impurities, but instead stated generally that "to imply that the teachings of Wu must be restricted to binding of pure proteins or removal of all proteins from a carbohydrate matrix [i.e., corn syrup] is very myopic."

Ans. 8. The Examiner also stated that Appellant's arguments "assume that a person of skill in the art cannot make the leap from the explicit experiments and motivations of the reference to other, closely related applications and goals," but the Examiner did not provide a reason for making the acknowledged "leap" from adsorbing all proteins from a solution to adsorbing only certain proteins based on their isoelectric point. *See KSR*, 550 U.S. at 418; *Belden*, 805 F.3d at 1073.

In sum, step (b) of adjusting the pH to within 2 pH units of the protein's isoelectric point and then (c) binding the protein impurity "to be selectively removed" is not described or suggested by the cited references. Lucas poses the problem, but does not provide a solution. Wu binds protein to activated carbon, but not in such a way that a protein impurity selectively binds to it in the presence of other proteins. Instead, as argued by Appellant, Wu attempts to remove all proteins in one step of adsorption to activated carbon. As our reviewing court has pointed out, ordinary creativity and/or common sense "cannot be used as a wholesale substitute for reasoned analysis and evidentiary support, especially when dealing with a limitation missing from the prior art references specified." *DSS Tech. Mgmt., Inc. v.*



*Apple Inc.*, 885 F.3d 1367, 1374 (Fed. Cir. 2018) *see also id.* at 1374–75 (“In cases in which common sense is used to supply a missing limitation, as distinct from a motivation to combine, . . . our search for a reasoned basis for resort to common sense must be searching.”) (internal quotations omitted).

“An examiner bears the initial burden of presenting a prima facie case of obviousness.” *In re Huai-Hung Kao*, 639 F.3d 1057, 1066 (Fed. Cir. 2011). Because that burden was met, the obviousness rejection of claim 1 is reversed. The Examiner cited additional references to reach limitations in certain dependent claims, but the Examiner did not find that these additionally cited references make up for the deficiency in the combination of Lucas, Kaersgaard, and Wu for claim 1. Consequently, the obviousness rejections of claims 3, 10, 12, and 26–35 are reversed.

#### CONCLUSION

The Examiner’s decision to reject claims 1, 3, 10, 12, and 26–35 is reversed.

DECISION SUMMARY

<b>Claims Rejected</b>	<b>35 U.S.C. §</b>	<b>Reference(s)/Basis</b>	<b>Affirmed</b>	<b>Reversed</b>
1, 3, 10, 12, 32, 33	103(a)	Lucas, Kaersgaard, Wu		1, 3, 10, 12, 32, 33
1, 3, 10, 12, 26–29, 32, 33	103(a)	Lucas, Kaersgaard, Wu, Loos		1, 3, 10, 12, 26–29, 32, 33
1, 3, 10, 12, 30–33	103(a)	Lucas, Kaersgaard, Wu, Abe		1, 3, 10, 12, 30–33
1, 3, 10, 12, 32–35	103(a)	Lucas, Kaersgaard, Wu, Lin		1, 3, 10, 12, 32–35
<b>Overall Outcome</b>				1, 3, 10, 12, 26–35

REVERSED