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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ROUZBEH R. TAGHIZADEH[1]

Appeal 2019-003681
Application 15/241,585
Technology Center 1600

Before JEFFREY N. FREDMAN, DEBORAH KATZ, and JOHN G. NEW, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the Real Party in Interest as Auxocell Laboratories, Inc. App. Br. 2.

SUMMARY

Appellant files this appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claim 31 as unpatentable under 35 U.S.C. § 101 as being directed to nonstatutory subject matter.

Claim 31 also stands rejected as unpatentable under 35 U.S.C. §§ 102(b) and 103(a) over Fong, C.Y. et al., *Comparative Growth Behaviour and Characterization of Stem Cells from Human Wharton's Jelly*, 15 REPR. BIOMED. ONLINE 708–718 (2007) ("Fong").

We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM and enter a new ground of rejection.

NATURE OF THE CLAIMED INVENTION

Appellant's invention is directed to cell-depleted Wharton's Jelly that can be used as a medium for maintaining cells in culture. Spec. ¶¶ 21–23.

REPRESENTATIVE CLAIM

Claim 31 is the only claim on appeal and recites:

> 31. A cell culture medium comprising a cell-depleted Wharton's Jelly filtrate containing a buffer, wherein the cell-depleted Wharton's Jelly filtrate is prepared by a method comprising mincing umbilical cord tissue comprising Wharton's Jelly, subsequently diluting the umbilical cord tissue with the buffer, subsequently filtering the umbilical cord tissue to generate a filtrate, and sedimenting Wharton's Jelly stem cells from the filtrate to generate the cell-depleted Wharton's Jelly filtrate.

App. Br. 9.

ISSUES AND ANALYSIS

We agree with, and expressly adopt, the Examiner's findings, reasoning, and conclusion that the claims are directed to nonstatutory subject matter under 35 U.S.C. § 101. We further agree with, and expressly adopt, the Examiner's findings, reasoning, and conclusion that the claims would have been anticipated by, and obvious over, the prior art. We also enter a new ground of rejection. We address below the arguments raised by Appellant.

A. Rejection of claim 31 under 35 U.S.C. § 101

Issue

Appellant argues that the Examiner erred in concluding that the claim is directed to a product of nature, and therefore to a judicial exception under Section 101. App. Br. 2–5.

Analysis

The Examiner concludes that claim 31 is directed to a judicial exception without adding significantly more. Final Act. 3. The Examiner finds that claim 31 is directed to a product of nature because the chemical components comprised in the claimed culture medium are similar to those in naturally occurring Wharton's Jelly. *Id.* The Examiner finds that the additional element of "a buffer" does not weigh in favor of eligibility because the buffer is well understood, routine, and conventional, and is recited at a high level of generality. *Id.* at 4.

Appellant's claim 31 recites: "a cell culture medium comprising a cell-depleted Wharton's jelly filtrate containing a buffer …." App. Br. 9.

The claim further includes product-by-process limitations, i.e., the steps of mincing, diluting, filtering, and sedimenting. *Id.* However, "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself." *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985). Accordingly, we evaluate the patentability of the claim, including under Section 101, based on the product itself.

Appellant argues that the claimed product is not a cell-depleted jelly, but rather "a cell culture medium (filtrate)." Reply Br. 2. Claim 31 recites "a cell culture medium" in the preamble. However, "where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation." *Rowe v. Dror*, 112 F.3d 473, 478 (Fed. Cir. 1997). The body of claim 31 recites: "a cell-depleted Wharton's Jelly filtrate" and "a buffer." These elements constitute a structurally complete invention, and the preamble recites merely the intended use for the invention, i.e., a cell culture medium. Accordingly, we conclude that the preamble does not limit the claim.

In performing an analysis of patentability under Section 101, we follow the framework set forth by the Supreme Court in *Mayo Collaborative Servc's v. Prometheus Labs., Inc*., 566 U.S. 66 (2012). We are also mindful of, and guided by, the United States Patent and Trademark Office's 2019 Revised Patent Subject Matter Eligibility Guidance, 84(4) Fed. Reg. 50–57 (January 7, 2019) (the "Guidance").

Following the first step of the *Mayo* framework, we find that claim 31 recites a composition of matter and therefore falls into one of the broad

statutory categories of patent-eligible subject matter under 35 U.S.C. § 101. In the next step of the *Mayo* analysis, we determine whether the claim at issue is directed to a nonstatutory, patent-ineligible concept, i.e., a law of nature, a phenomenon of nature, or an abstract idea. *Mayo*, 566 U.S. at 70–71; Guidance 54 (step 2A, Prong 1). If we determine that the claim is directed to a judicial exception, we then determine whether the limitations of the claim reciting the judicial exception are integrated into a practical application. *Id.* (Step 2A, Prong 2). Finally, if we determine that the claim is directed to a judicially-created exception to Section 101, we evaluate the claims under the next step of the *Mayo* analysis, considering the elements of each claim both individually and "as an ordered combination" to determine whether additional elements "transform the nature of the claim" into a patent-eligible application. *Mayo*, 566 U.S. at 78–79; 2019 Guidance at 56 (Step 2B).

Claim 31 recites, in relevant part: "A cell culture medium comprising a cell-depleted Wharton's Jelly filtrate containing a buffer, wherein the cell-depleted Wharton's Jelly filtrate is prepared by a method comprising mincing umbilical cord tissue comprising Wharton's Jelly.[2]" Appellant's Specification discloses that the claimed composition comprises Wharton's Jelly that is extracted from umbilical cord tissue. *See* Spec. ¶ 21. "[W]hen the cells are separated from the digested tissue, the remaining, cell-depleted

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[2] Wharton's Jelly is the connective tissue of the umbilical cord. *See* J.E. Davies et al., *Concise Review: Wharton's Jelly: The Rich, but Enigmatic, Source of Mesenchymal Stromal Cells*, 6 STEM CELLS TRANSL. MED. 1620–30 (2017).

digested tissue is a rich, sterile solution that can be used for maintaining cells … some cells may be present, although in substantially reduced numbers, within this rich, sterile, cell-depleted solution derived from the digested tissue." *Id.* Therefore, the claim recites an isolated natural product, i.e., Wharton's Jelly that is substantially depleted of its cellular constituents.

Isolating a natural product and thereby creating a non-naturally occurring material does not necessarily result in patent-eligible subject matter. *See Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 593 (2013). In *Myriad*, the Supreme Court held claims directed to isolated DNA were not "saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a nonnaturally occurring molecule." 569 U.S. at 593. Rather, to be patent eligible, a "nonnaturally occurring manufacture or composition of matter" must possess "markedly different characteristics from any found in nature." *Id.* at 590–591 (citing *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980)).

Appellant argues that: "the cell-depleted Wharton's Jelly filtrate recited in claim 31 possesses markedly different characteristics from Wharton's Jelly in its natural state." App. Br. 3. Appellant argues that:

> [C]ompared to its naturally-occurring counterpart, Wharton's Jelly, the mixture of cell-depleted Wharton's Jelly filtrate and a buffer has markedly different characteristics (e.g., reduced viscosity, changed extracellular matrix structure, and lack of cells and unbroken tissues) which are relevant to the nature of the invention as a component of a cell culture medium and which are a result of the Appellant's efforts.

Id. at 4.

We are not persuaded by Appelant's argument. The Specification explains that cell-depleted Wharton's Jelly filtrate can be used as a medium for maintaining cells, e.g., culturing mesenchymal stem cells. *See* Spec. ¶¶ 21–23. However, naturally-occurring Wharton's Jelly *in situ* also provides an environment for maintaining stem cells. *See* Fong 708 ("Stem cells have been found in umbilical cord blood, the Wharton's jelly, and in the other perivascular mesenchymal areas within the cord"). Furthermore, the Wharton's Jelly recited in the claims is obtained by "mincing umbilical cord tissue comprising Wharton's Jelly, subsequently diluting the umbilical cord tissue with the buffer, subsequently filtering the umbilical cord tissue to generate a filtrate, and sedimenting Wharton's Jelly stem cells." Claim 31. In other words, Wharton's Jelly is extracted from the umbilical cord tissue, and then filtered to remove the cells present within the jelly, much as blood serum can be prepared by removing the cellular elements of blood. However, other than removal of the cells, the Wharton's Jelly remains structurally the same as it was prior to removal from the umbilical cord tissue, save for dilution with the buffer, which we address *infra*.

Appellant has not shown that the cell-depleted Wharton's Jelly filtrate is a transformation of the natural product, or that the claimed filtrate has properties not possessed by the naturally-occurring Wharton's Jelly *in situ*. Rather, the discovery that cell-depleted Wharton's Jelly filtrate functions as a culture medium is no more than the discovery of a property of the product of nature and is therefore not patent eligible. Consequently, we are not persuaded that the claimed cell-depleted Wharton's Jelly filtrate is markedly different from the natural product and we find that the claims recite a judicial exception, i.e., a product of nature.

We next determine whether the judicial exception is integrated into a practical application. *See* 2019 Guidance at 55 (Step 2A, Prong 2). For example, integration may include using the natural product in a particular treatment or prophylaxis for a medical condition or a particular manufacture that is integral to the claims. *Id.*

Appellant argues that the additional element, i.e., the buffer, allows the mixture to be used in a cell culture medium. App. Br. 5. Appellant argues that the buffer "provides resistance to pH changes that occur during the course of culturing cells, and the removal of cells that occur naturally within Wharton's Jelly allows the Wharton's Jelly cell-depleted filtrate to be used for culturing other cell types, avoiding contamination from cells normally present in Wharton's Jelly." *Id.* at 5.

We do not find this argument persuasive. Claim 31 recites an isolated natural product and its combination with a buffer. As we have explained *supra*, the preamble's recitation of "a cell culture medium" is not limiting upon the claim. Claim 31 thus recites a composition, *viz.*, Wharton's Jelly and a buffer, which has the natural property of being able to act as a cell culture medium, but the claims proper do *not* recite limitations requiring that the claimed composition be so used. As such, the limitations of the claim recite only the composition, a product of nature and a buffer, and do not recite the integration of that composition into any practical application.

Finally, we evaluate whether additional elements in the claims recite "an inventive concept —i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015). Particularly, we

evaluate whether the claims include specific limitations that are not "well-understood, routine, conventional activity previously engaged in by scientists who work in the field." *Mayo*, 566 U.S. at 79. Claim 31 combines an isolated natural product (cell-depleted Wharton's Jelly filtrate) with a buffer. It is universally acknowledged that buffering solutions are commonly combined with isolated natural products in the biological arts, and are known for washing, diluting, protecting, and storing biological tissue. *See* Spec. ¶¶ 18, 27; *see also Berkheimer v. HP Inc.*, 881 F.3d 1360, 1368 (Fed. Cir. 2018). There is no evidence of record that the claim includes other, unconventional elements, either alone or in combination. *See In re Marco Guldenaar Holding B.V.*, 911 F.3d 1157, 1161 (Fed. Cir. 2018). Accordingly, we find that the addition of a buffer to the Wharton's Jelly appends no more than routine and conventional material to the natural product.

We therefore conclude that the claims recite no additional elements that amount to significantly more than a patent on the ineligible concept itself. *See Ariosa*, 788 F.3d at 1378. Because the claim is directed to a judicial exception and the additional recited elements do not transform the judicial exception into a patent-eligible invention, we sustain the Examiner's rejection upon this ground.

B. Rejection of claim 31 under 35 U.S.C. §§ 102 and 103

Issue

Appellant argues that the Examiner erred in concluding that the claims are anticipated and obvious over the prior art. App. Br. 5–9.

Analysis

The Examiner finds Fong teaches a method of preparing a composition comprising cell-depleted Wharton's Jelly solution in a DMEM ("Dulbecco's modified Eagle's medium"). Final Act. 4 (citing Fong 709). The Examiner finds cell-depleted Wharton's Jelly solution is a supernatant produced by the steps of: 1) enzymatically digesting umbilical cord pieces in DMEM, 2) detaching Wharton's Jelly from the surrounding cord blood vessels into DMEM, 3) breaking up the gelatinous Wharton's Jelly mass by re-suspending with a pipette, and 4) centrifuging the suspension to remove cells. Ans. 9–10 (citing Fong 709). With respect to the buffer, the Examiner finds DMEM contains a sodium bicarbonate buffer system. *Id.* at 11. The Examiner finds the "supernatant of [] Fong et al., obtained through the steps similar to those recited in lines 3-6, is consequently [the] same as or equivalent to the 'cell-depleted Wharton's Jelly filtrate containing a buffer' recited in the instant claim." *Id.* at 10.

Appellant argues that Fong does not teach a cell culture medium comprising cell-depleted Wharton's Jelly. App. Br. 6. Appellant particularly argues that Fong discards "the supernatant comprising cell-depleted Wharton's Jelly and DMEM." *Id.* Appellant further argues that Fong does not teach the process steps of the claim, including mincing and filtering. Reply Br. 6–7.

With respect to the buffer, Appellant argues that DMEM does not include a buffer, citing a product description for modified DMEM that states: "DMEM uses a sodium bicarbonate buffer system (3.7 g/L) and therefore requires a 5–10% CO_2 environment to maintain a physiological pH." App. Br. 7. Appellant argues that "[m]ammalian cells are commonly cultured in DMEM or similar media at 5–10% CO_2, which form the bicarbonate buffer system for growing cells." *Id.* at 8.

We are not persuaded. As discussed *supra*, "cell culture medium" recited in the preamble is not a limitation of the claim if the body of the claim defines a structurally complete invention. *Supra* at 4. Moreover, although Fong does not disclose a filtrate, the Specification explains that both centrifugation and filtering provide cell-depleted Wharton's Jelly, and the patentability of the claim is determined by the product itself, and not by the product-by-process steps. Spec. ¶ 5. Accordingly, we address whether the prior art discloses a combination of cell-depleted Wharton's Jelly filtrate containing a buffer.

We begin with Appellant's argument with respect to the buffer. The product description of DMEM unambiguously states that DMEM uses a sodium bicarbonate buffer system in a concentration of 3.7 g/L. The reference to a 5–10% CO_2 environment merely instructs those of ordinary skill in the art on the correct incubator settings for culturing cells in DMEM. Accordingly, we do not agree with Appellant's argument with respect to the buffer.

We agree with Appellant that Fong teaches discarding the supernatant containing the cell-depleted Wharton's Jelly and DMEM. Nevertheless, patent law "establishes that a prior art reference which expressly or

inherently contains each and every limitation of the claimed subject matter anticipates." *Schering Corp. v. Geneva Pharm.*, 339 F.3d 1373, 1379 (Fed. Cir. 2003). "The extent of the inherent disclosure does not limit its anticipatory effect. In general, a limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." *Id.*

In *Schering*, our reviewing court found claims directed to a metabolite of loratadine ("DCL") were inherently anticipated by administering loratadine to patients, even if the existence of the DCL metabolite was fleeting and was not recognized in the art. *Id.* at 1377–1378. The court found that the prior art "need not describe how to make DCL in its isolated form. The [prior art] need only describe how to make DCL in any form encompassed by a compound claim covering DCL." *Id.* at 1381.

We agree with the Examiner that a composition of a cell-depleted Wharton's Jelly filtrate containing a buffer is the natural result flowing from the explicit disclosure of Fong. Although the cell-depleted Wharton's Jelly in Fong is not retained, it is nevertheless disclosed as existing for some period of time, and that is sufficient to establish inherent anticipation. *Schering*, 339 F.3d at 1379. Because Fong discloses the same composition as claim 31, we sustain the Examiner's rejection of the claim as anticipated and obvious. *In re McDaniel*, 293 F.3d 1379, 1385 (Fed. Cir. 2002) ("It is well settled that 'anticipation is the epitome of obviousness.'")

NEW GROUND OF REJECTION

We here enter a new ground of rejection. Independent claim 31 is unpatentable under 35 U.S.C. § 102(b) as being anticipated by Sobolewski,

K. et al., *Wharton's Jelly as a Reservoir of Peptide Growth Factors*, 26 PLACENTA 747–752 (2005) ("Sobolewski").[3]

Sobolewski discloses "that Wharton's jelly … contains several growth factors in amounts comparable to or higher than those in the umbilical cord arterial wall." Sobolewski 749. The growth factors include acidic FGF, basic FGF, EGF, IGF-I, PDGF and TGF-b. *Id.* at 747.

Sobolewski discloses the following method for isolating Wharton's Jelly:

> 20 cm sections of [ ] umbilical cords … were excised and submitted to isolation of Wharton's jelly and umbilical cord arteries using microsurgical technique. The tissue samples were washed with 0.9% NaCl and stored at -70°C until assay. Tissue homogenates (10% w/v) were prepared in 0.15 M Tris-HCl buffer, pH 7.6 or in 0.15 M acetic acid with the use of a knife homogeniser (20,000 rpm, 30 s, 0°C). The homogenates were submitted to ultrasonification (20 kHz, 3 × 15s, 0°C) and centrifugation at 10,000 × g for 30 min at 4°C. The supernatants (tissue extracts) were collected and subsequently assayed for growth factors using ELISA and Western blot analysis.

Id. at 748. Sobolewski's isolation method includes the steps of mincing umbilical tissue, diluting the tissue with a buffer, centrifuging the tissue, and collecting supernatant. As discussed *supra*, the natural result of this method is the same product of claim 31. Moreover, Sobolewski collects the cell-depleted Wharton's jelly containing a buffer and identifies numerous growth

[3] Appellant cited Sobolewski in an Information Disclosure Statement dated November 1, 2016.

factors that would be useful components in a cell culture medium. Accordingly, we find Sobolewski anticipates claim 31.

CONCLUSION

The rejection of claim 31 as unpatentable under 35 U.S.C. § 101, is affirmed.

The rejection of claim 31 as unpatentable under 35 U.S.C. §§ 102 and 103 is affirmed.

We have entered a new ground of rejection for independent claim 31 pursuant to 37 C.F.R. § 41.50(b). 37 C.F.R. § 41.50(b) provides that "[a] new ground of rejection . . . shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that Appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner . . . .
>
> (2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED

37 C.F.R. § 41.50(b)

Claim Rejected	35 U.S.C. §	Basis	Affirmed	Reversed	New Grounds
31	101	Eligibility	31		
31	102/103	Fong	31		
31	102	Sobolewski			31
Overall Outcome			31		31