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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte BAOMING JIANG, ROGER I. GLASS and JEAN-FRANCOIS SALUZZO

Appeal 2017-000915
Application 13/718,648[1]
Technology Center 1600

Before ERIC B. GRIMES, ROBERT A. POLLOCK, and DAVID COTTA, *Administrative Patent Judges*.

COTTA, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a vaccine composition. The Examiner rejected the claims on appeal under 35 U.S.C. § 101 as directed to patent ineligible subject matter, under 35 U.S.C. § 102(a) as anticipated, under 35 U.S.C. § 103(a) as obvious, and on the ground of obviousness-type non-statutory double patenting.

We affirm.

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[1] According to Appellants, the real party in interest is the Government of the United States of America. App. Br. 1.

STATEMENT OF THE CASE

The Specification discloses that "[o]f the various enteric pathogenic viruses causing severe diarrhea in children, rotavirus is the most common causing an average of 611,000 deaths per year." Spec. 1. The Specification suggests that "[v]accination against rotavirus-mediated disease is one strategy for addressing this significant health problem." *Id.* However, "[t]here is a dearth of effective methods for inactivating rotavirus and vaccine compositions including inactivated rotavirus. A particular difficulty is treatment of live rotavirus to inactivate the virus while maintaining antigenicity associated with substantially intact double-layer and triple-layer rotavirus particles." *Id.* Accordingly, "[t]here is a continuing need for methods of inactivating rotavirus and compositions including inactivated rotavirus." *Id.*

The Specification states: "the present invention relates to methods of thermally inactivating rotavirus and inactivated rotavirus vaccine compositions." *Id.*

Claims 29, 31–34 and 36–45 are on appeal. Claims 29 and 45 are representative and read as follows:

> 29. A vaccine composition comprising: antigenic thermally-inactivated animal or human rotavirus characterized by a substantially intact rotavirus particle structure, wherein the substantially intact rotavirus particle structure is selected from the group consisting of: triple-layer rotavirus particles, double-layer rotavirus particles, and a combination of triple-layer rotavirus particles and double-layer rotavirus particles; and a sterile, pyrogen free pharmaceutically acceptable carrier.
>
> 45. A vaccine composition comprising: antigenic thermally-inactivated animal or human rotavirus characterized by a

> substantially intact rotavirus particle structure, wherein the substantially intact rotavirus particle structure is selected from the group consisting of: triple-layer rotavirus particles, double-layer rotavirus particles, and a combination of triple-layer rotavirus particles and double-layer rotavirus particles; and an adjuvant.

App. Br. 11–12.

The claims stand rejected as follows:

Claims 29, 31–34 and 36–45 were rejected under 35 U.S.C. § 101 as directed to patent ineligible subject matter.

Claim 45 was rejected under pre-AIA 35 U.S.C. 102(a) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Knape[2] as evidenced by Crawford.[3]

Claims 29, 31–34, 36, 37, 43, and 44 were rejected under pre-AIA 35 U.S.C. 103(a) as obvious over the combination of Knape and Thomas[4] as evidenced by Crawford.

Claims 38–42 were rejected under pre-AIA 35 U.S.C. 103(a) as obvious over the combination of Knape, Thomas and Hoshino[5] as evidenced by Crawford.

Claim 45 was rejected on the ground of obviousness-type non-statutory double patenting over claims 1–11 of US Patent No. 8,357,525 B2.

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[2] Knape et al., US Patent Publication No. 2002/0155128 A1, published Oct. 24, 2002 ("Knape").
[3] Crawford et al., *Characterization of Virus-Like Particles Produced by the Expression of Rotavirus Capsid Proteins in Insect Cells,* 68(9) JOURNAL OF VIROLOGY 5945–5952 (1994) ("Crawford").
[4] Thomas et al., US Patent No. 5,605,692, issued Feb. 25, 1997 ("Thomas").
[5] Hoshino et al., US Patent Publication No. 2002/0058043 A1, published May 16, 2002 ("Hoshino").

Claims 29, 31–34 and 36–44 were rejected on the ground of obviousness-type non-statutory double patenting over claims 1–11 of US Patent No. 8,357,525 B2 in view of Thomas.

Claim 45 was rejected on the ground of obviousness-type non-statutory double patenting over claims 1–14 of US Patent No. 8,822,192 B2.

Claims 29, 31, 34, 36, 43, and 44 were rejected on the ground of obviousness-type non-statutory double patenting over claims 1–14 of US Patent No. 8,822,192 B2 in view of Thomas.

Claim 45 was provisionally rejected on the ground of obviousness-type non-statutory double patenting over claims 19–29 of copending US Patent Application No. 14/461,663 (now issued as US Patent No. 9,498,526 B2).

Claims 29, 31, 34, 36, 43, and 44 were provisionally rejected on the ground of obviousness-type non-statutory double patenting over claims 19–29 of copending US Patent Application No. 14/461,663 (now issued as US Patent No. 9,498,526 B2).

FINDINGS OF FACT

1. Crawford discloses: "Rotaviruses are triple-layered particles." Crawford Abstract.

2. The Specification discloses: "A particular difficulty is treatment of live rotavirus to inactivate the virus while maintaining antigenicity associated with substantially intact double-layer and triple-layer rotavirus particles." Spec. ¶ 4.

3. Table 1 of Moe[6] is reproduced below.

Table 1. *The decrease in titre of human rotavirus in faeces under different RH's at 20° C*

Mean decrease in titre (log_{10} FCFU/ml) ±S.D.[a]	RH				
	13%	33%	55%	75%	92%
1 day	0.25±0.17	0.52±0.08	0.52±0.09	0.22±0.11	0.17±0.06
2 days	0.50±0.11	0.78±0.10	0.90±0.09	0.40±0.06	0.17±0.07
3 days	0.74±0.16	1.06±0.19	1.38±0.14	0.68±0.18	0.29±0.06
4 days	1.20±0.20	1.47±0.16	1.92±0.18	0.88±0.04	0.53±0.11
5 days	1.24±0.16	1.59±0.22	2.35±0.19	0.90±0.23	0.59±0.09
7 days	1.42±0.23	2.21±0.37	3.23±0.26	1.34±0.52	0.74±0.20
9 days	1.93±0.25	3.14±0.18	4.09±0.28	1.78±0.33	1.00±0.24
11 days	2.23±0.16	4.31±0.35	—	1.88±0.22	1.20±0.17
13 days	2.76±0.30	—	—	2.85±0.68	1.92±0.49

[a] Standard deviation based on three samples

Table 1 discloses "[t]he mean decrease in log_{10} titre (FCFU/ml) and standard deviation based on three replicates of human rotavirus in faeces exposed to five RH's [relative humidities] and 20° C." Moe 181.

4. Table 2 of Moe is reproduced below.

Table 2. *Virus inactivation rates (K values) of human rotavirus in faeces at five RH's and three temperatures*

Temperature	Virus inactivation rate (K-value in log_{10} FCFU/day) RH				
	12—14%	33—34%	51—59%	75—76%	92—94%
4° C	0.061	0.081	0.116	0.060	0.034
20° C	0.196	0.363	0.452	0.197	0.132
37° C	0.678	1.456	1.917	0.806	0.363

Table 2 discloses "[t]he differences in virus survival at different RH's and temperatures." *Id.* at 182.

5. The Specification discloses: "Examples of suitable aqueous and nonaqueous carriers include water, ethanol, polyols such as propylene glycol, polyethylene glycol, glycerol, and the like, suitable mixtures thereof; vegetable oils such as olive oil; and injectable organic esters such as ethyloleate." Spec. ¶ 73.

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[6] Moe et al., *The Effects of Relative Humidity and Temperature on the Survival of Human Rotavirus in Feces,* 72 ARCHIVES OF VIROLOGY 179–186 (1982) ("Moe"). Moe was cited by the Examiner as evidence that inactivated rotaviruses exist "under various humidity and temperature conditions that fall within those that occur naturally." Ans. 9.

6. The Specification discloses: "Adjuvants are known in the art and illustratively include Freund's adjuvant, aluminum hydroxide, aluminum phosphate, aluminum oxide, iron oxide, saponin, dextrans such as DEAE dextran, vegetable oils such as peanut oil, olive oil, and/or vitamin E acetate, mineral oil, bacterial lipopolysaccharides, peptidoglycans, and proteoglycans." Spec. ¶ 80.

7. Knape discloses: "Bovine rotavirus is cultured on monolayer cell cultures that are prepared by known methods and inoculated with the viral agent." Knape ¶ 37.

8. Knape discloses:

> An effective inactivated vaccine is prepared after inactivating the virus. In general, this preparation is accomplished by propagating the virus on, e.g., fetal bovine kidney cells, until an adequate titer is obtained. The virus is then inactivated by treating it at approximately 20–40° C. with an inactivating agent known in the art, e.g., formalin, ethyleneimine derivatives, ultraviolet radiation or **heat**, and preferably β-propiolactone, for such a length of time and/or concentration of inactivating agent as to effectively inactivate the virus. **These procedures and their details are well known in the art**. An adjuvant may be added to enhance the antigenicity. That adjuvant may be any of those known in the art, e.g., Freund's incomplete, alginate, aluminum hydroxide gel, or potassium alum, preferably an oil based adjuvant.

Id. ¶ 38 (emphasis added).

9. Knape discloses: "The rotavirus strains identified as Cody 81-4 and B641 were isolated from a calf with diarrhea." *Id.* ¶ 40.

SUBJECT MATTER ELIGIBILITY

Determination of subject matter eligibility involves a two-step test. First one must determine if the claimed subject matter is directed to a judicially recognized exception such as a product of nature. *Mayo Collaborative Serves. v. Prometheus Lab., Inc.* 132 S. Ct. 1289, 1297 (2012). If the claims address a judicially recognized exception, the next step is to determine if the claims recite additional elements that transform the nature of the claim. *Id.*

In rejecting the pending claims as directed to patent ineligible subject matter, the Examiner found that rotaviruses were products of nature. Final Act.[7] 3. The Examiner cited Crawford and the Specification as evidence that triple-layer rotaviruses occur in nature. *Id.* The Examiner also found that inactivated rotaviruses exist in nature, as reflected in Lytle's[8] teaching that solar radiation inactivates viruses and Moe's teaching that rotaviruses may be inactivated under various naturally occurring humidity and temperature conditions. *Id.* The Examiner then concluded that the structural characteristics of the claimed heat-inactivated rotaviruses were "not expected to be markedly different" from the characteristics of naturally-inactivated rotavirus particles. *Id.*

Having determined that the claims were directed to a nature-based product, the Examiner next considered whether the claims included additional elements that amounted to significantly more than the judicial exception. *Id.* at 3–4. The Examiner found that the recitation of a "sterile,

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[7] Office Action mailed November 30, 2015 ("Final Act.").
[8] Lytle et al., *Predicted Inactivation of Viruses of Relevance to Biodefense by Solar Radiation,* 79(22) J. VIROL. 14244–14252 (2005).

pyrogen free pharmaceutically acceptable carrier" in claims 29, 31–34 and 36–44 did "not alter the structure of the viral particles, enhance its functions, or establish meaningful limitations on viral particles" and the recitation of an "adjuvant" in claims 31–33 and 45 did "not structurally change the rotavirus particles." *Id.* at 4. Based on these findings, the Examiner concluded that the additional recited elements did not add enough to confer patent eligibility on the claimed product of nature. *Id.*

We agree with the Examiner that the claims are directed to patent-ineligible subject matter. With respect to the first step of the subject matter eligibility determination, Moe discloses that rotaviruses are inactivated under temperature and humidity conditions present in nature. FF3 & FF4. Crawford discloses that rotaviruses have the claimed triple-layered structure. FF1; *see also* FF2. Accordingly, we find that the claims are directed to products of nature.

Appellants argue that the Examiner has not met the burden of establishing that thermally inactivated rotaviruses exist in nature. Appellants contend that the Examiner cannot rely upon Lytle for this teaching because Lytle relates to "the effects of solar UV radiation on viruses, not heat" and that the UV radiation studied in Lytle was at a wavelength "not found in the sunlight that reaches the earth's surface." App. Br. 3–4. We are not persuaded because Appellants do not address Moe, which establishes that inactivated rotaviruses exist under temperature and humidity conditions present in nature.

Appellants argue that the claimed compositions are distinct from naturally occurring rotavirus because they have a "substantially intact rotavirus particle structure." App. Br. 4. As support, Appellants cite the testimony of Dr. Baoming Jiang that "it is not trivial to heat inactivate a

rotavirus while preserving a substantially intact rotavirus particle structure" and that it is "well-known [that] a virus can be destroyed (i.e. not structurally intact), and therefore inactivated, by heat." *Id.* (citing Jiang Decl.[9] ¶ 5). We are not persuaded. While we do not doubt Dr. Jiang's testimony that heat *can* destroy viral structure, Appellants have not persuaded us that the heat and humidity conditions described in Moe destroy viral structure.

Appellants argue that the claims are narrowly tailored to the claimed composition such that the claims are "clearly not all encompassing so as to 'tie up' the broad concept of 'inactivated rotavirus.'" App. Br. 3. But even assuming that one can find other meaningful uses of the claimed inactivated rotavirus, "the absence of complete preemption does not demonstrate patent eligibility." *Ariosa Diagnostics, Inc.* v. *Sequenom, Inc.,* 788 F.3d 1371, 1379 (Fed. Cir. 2015).

With respect to the second step of the subject matter eligibility determination, Appellants argue that the claimed compositions are distinguished from naturally inactivated rotavirus by the presence of a "sterile, pyrogen free pharmaceutically acceptable carrier" (claim 29 and claims depending therefrom) or an "adjuvant" (claims 31–33 and 45). App. Br. 5. We are not persuaded. The addition of a pharmaceutical carrier, which may simply be water (*see* FF5), or of an adjuvant, which the Specification teaches are known in the art (*see* FF6, FF8), to a naturally occurring inactivated rotavirus is not sufficient to transform the claimed natural product into patent-eligible subject matter. *Mayo,* 132 S.Ct. at 1300 ("[S]imply appending conventional steps, specified at a high level of

[9] Declaration of Dr. Baoming Jiang Under 37 C.F.R. § 1.132, dated Jan. 21, 2015 ("Baoming Decl.").

generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable.").

Accordingly, we affirm the Examiner's rejection of claims 29, 31–34 and 36–45 as directed to patent ineligible subject matter.

ANTICIPATION AND OBVIOUSNESS

The Examiner rejected claim 45 as anticipated by or alternatively obvious in view of Knape and claims 29, 31–34, 36, 37, 43 and 44 as obvious over the combination of Knape and Thomas. Appellants argue both rejections together based on arguments specific to Knape. App. Br. 6. Appellants argue the rejection of claims 38–42 as obvious over the combination of Knape, Thomas, and Hoshino under a separate heading, but rely solely on arguments made with respect to independent claim 29. *Id.* at 9. Accordingly, we address all three rejections together. We designate claim 45 as representative.

The Examiner found that Knape disclosed a vaccine composition comprising heat inactivated bovine rotavirus. Final Act. 5. The Examiner acknowledged that Knape "does not indicate that the inactivated rotaviruses are double or triple layer," but found that they were "expected to be triple layer since that is the natural state of rotaviruses that are isolated from a natural source" as evidenced by Crawford and the Specification. *Id.* at 6.

We agree with the Examiner that the claim 45 is anticipated by Knape and that claims 31–34 and 36–45 would have been obvious over the cited art. We address Appellants' arguments below.

Appellants argue that "[n]o reference to particle structure of an inactivated particle is apparent in Knape." App Br. 7. Appellants assert "there are no previously known vaccine compositions including 'antigenic thermally-inactivated rotavirus characterized by an intact rotavirus particle

structure' or methods of producing such compositions" and there is "no basis" for the Examiner's assertion that Knape describes heat inactivated rotaviruses that have the claimed particle structure. App. Br. 6–7. We are not persuaded.

Knape discloses that rotaviruses may be isolated from natural sources (FF9) and inactivated by heat using procedures "well known in the art." FF7 & FF8. Crawford provides evidence that naturally occurring rotaviruses have a triple layered structure, as recited in claim 45. FF1. Accordingly, we agree with the Examiner that Knape's heat inactivated rotaviruses would be "expected to be triple-layer since that is the natural state of rotaviruses that are isolated from a natural source." Ans. 12.

Appellants argue that the Knape reference is non-enabling "since the mere mention of 'heat' in Knape without any description of methods of heat inactivation and without details of any procedure to produce antigenic thermally-inactivated rotavirus characterized by an intact rotavirus particle structure would not allow one of skill in the art to make the claimed invention." App. Br. 8.

Prior art cited by an Examiner is presumed to be enabled. *In re Sasse,* 629 F.2d 675, 681 (CCPA 1980); *see also In re Antor Media Corp.*, 689 F.3d 1282, 1288 (Fed. Cir. 2012). Once such a reference is found, the burden is on the Appellants to provide evidence rebutting the presumption. *Id.* Here, Appellants offer the testimony Dr. Jiang that "it is not trivial to heat inactivate a rotavirus while preserving a substantially intact rotavirus particle structure" and that "a virus can be destroyed (i.e. not structurally intact), and therefore inactivated, by heat." Jiang Decl. ¶ 5. We find, however, that Dr. Jiang's testimony is not sufficient to rebut the presumption that Knape is enabled, particularly in view of Knape's disclosure that the

"procedures and their details" for inactivating rotaviruses are "well known in the art." FF8. *In re Sasse,* 629 F.2d at 681.

Dr. Jiang's testimony that viruses "can be" destroyed by heat also fails to persuade us that the claimed heat inactivated rotaviruses have a different structure than those disclosed in Knape. The fact that viral structure "can be" destroyed by heat does not mean that Knape's rotaviruses were destroyed by heat, or even that it is likely that they were destroyed. Appellants do not provide persuasive evidence that using heat activation methods known in the art to inactivate rotaviruses, as disclosed in Knape, would result in a virus with a different structure than that in the claims.

Appellants argue that the recognition of "a scientific article reporting results described in the present specification" in Sanders,[10] a publication on vaccines, shows their work to be "novel and worthy of mention" and provides "evidence of both novelty and nonobviousness of the present claims." App. Br. 7–8. We are not persuaded. To the extent the mention of Appellants' work in a review article and characterization of it as "novel" constitutes industry praise, it is insufficient to overcome the strong showing of obviousness presented here.[11] *See Leapfrog Enterprises, Inc.* v. *Fisher-Price, Inc.,* 485 F.3d 1157, 1162 (Fed. Cir. 2007) ("given the strength of the prima facie obviousness showing, the evidence on secondary considerations was inadequate to overcome a final conclusion" of obviousness).

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[10] Sanders et al., *Chapter 2, Inactivated Viral Vaccines, in* VACCINE ANALYSIS: STRATEGIES, PRINCIPLES, AND CONTROL (Nunnally et al., eds.) (2015).

[11] For the reasons set forth above, we have addressed the anticipation rejection together with the obviousness rejections. We note that industry praise as an objective indicia of non-obviousness would not apply to the Examiner's rejection of claim 45 as anticipated by Knape.

Accordingly, we affirm the Examiner's rejection of claim 45 as anticipated and of claims 29, 31–34 and 36–45 as obvious.

DOUBLE PATENTING

Appellants do not address the Examiner's multiple obviousness-type double patenting rejections. We therefore summarily affirm these rejections. *See* Manual of Patent Examining Procedure § 1205.02 ("If a ground of rejection stated by the examiner is not addressed in the appellant's brief, that ground of rejection will be summarily sustained by the Board.").

SUMMARY

For these reasons and those set forth in the Examiner's Answer and Final Office Action, we affirm the Examiner's rejection of: claims 29, 31–34 and 36–45 under 35 U.S.C. § 101 as directed to patent ineligible subject matter; claim 45 under pre-AIA 35 U.S.C. 102(a) as anticipated by or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Knape as evidenced by Crawford; claims 29, 31–34, 36, 37, 43, and 44 under pre-AIA 35 U.S.C. 103(a) as obvious over the combination of Knape and Thomas as evidenced by Crawford; claims 38–42 under pre-AIA 35 U.S.C. 103(a) as obvious over the combination of Knape, Thomas and Hoshino as evidenced by Crawford; claim 45 on the ground of obviousness-type non-statutory double patenting over claims 1–11 of US Patent No. 8,357,525 B2; claims 29, 31–34 and 36–44 on the ground of obviousness-type non-statutory double patenting over claims 1–11 of US Patent No. 8,357,525 B2 in view of Thomas; claim 45 on the ground of obviousness-type non-statutory double patenting over claims 1–14 of US Patent No. 8,822,192 B2; claims 29, 31, 34, 36, 43, and 44 on the ground of obviousness-type non-statutory double patenting over claims 1–14 of US Patent No. 8,822,192 B2 in view of Thomas; claim 45 on the ground of obviousness-type non-statutory

double patenting over claims 19–29 of copending US Patent Application No. 14/461,663 (now issued as US Patent No. 9,498,526 B2); and claims 29, 31, 34, 36, 43, and 44 on the ground of obviousness-type non-statutory double patenting over claims 19–29 of copending US Patent Application No. 14/461,663 (now issued as US Patent No. 9,498,526 B2).

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).

AFFIRMED