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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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Ex parte HYUNG IL KIM[1]

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Appeal 2019-004018
Application 15/373,025
Technology Center 1600

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Before DEMETRA J. MILLS, ERIC B. GRIMES, and RYAN H. FLAX, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a medical device, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

STATEMENT OF THE CASE

"For polymers introduced into a living body it is desirable that they be non-toxic . . . as well as being biocompatible. . . . [P]olymers containing phosphorylcholine groups can enhance the biocompatibility of materials comprising the polymer." Spec. ¶ 2. The Specification states that

[1] Appellant identifies the Real Party in Interest as Dotter Intellectual Pte. Ltd. Appeal Br. 3.

"2-methacryloyloxyethyl phosphorylcholine (MPC) and hydrophobic monomers (e.g., monomers that interact with hydrophobic substances) can be randomly polymerized into a polymer chain to produce a water-soluble zwitterionic random copolymer containing phosphorylcholine groups." *Id*. ¶ 16.

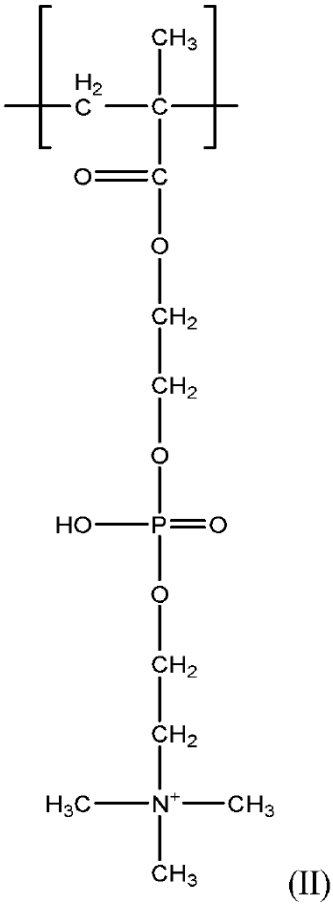
Formula (II) in the claims is a repeating unit derived from MPC. *Id*. ¶ 44. The claims also refer to the peak molecular weight and the polydispersity index of the recited copolymer. "Peak molecular weight (M_p) is the molecular weight at the highest peak (*e.g.*, the mode) of a molecular weight distribution for a polymer sample." *Id*. ¶ 66.

> The polydispersity index (PDI) . . . represents the breadth of the molecular weight distribution of a polymer in a sample. PDI, as used herein, refers to the ratio of the weight-average and number-average molecular weights (M_w/M_n). As polymer chains in a sample approach a uniform chain length, the PDI approaches 1. The larger the PDI the broader the range of molecular weights in a sample.

Id. ¶ 68.

Claims 40, 55–66, and 69 are on appeal. Claim 40 is representative and reads as follows:

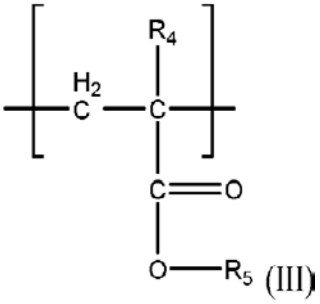
> 40. A medical device comprising a copolymer comprising a random distribution of a phosphorylcholine repeating unit and at least one hydrophobic repeating unit or a polymer blend comprising at least one biocompatible polymer and the copolymer, wherein the phosphorylcholine repeating unit has the formula (II)



(II)

and

wherein the at least one hydrophobic repeating unit has the formula (III)



(III)

wherein R^4 is a hydrogen atom or a methyl group, R^5 is an alkyl group having 3 to 8 carbon atoms and R^5 is not a hexyl group,

> wherein the copolymer has a polydispersity index (PDI) of less than 1.3 and a peak molecular weight (M_p) of less than 130,000;
>
> wherein the copolymer comprises about 30 mol% to about 50 mol% of the phosphorylcholine repeating unit; and
>
> wherein the copolymer is soluble in an aqueous solution.

DISCUSSION

The Examiner rejected claims 40, 55–59, 61–64, 66, and 69 under 35 U.S.C. § 103(a) as obvious based on Kim '920,[2] Kim 2009,[3] and Ishihara.[4] Final Action[5] 3. The Examiner finds that Kim '920 teaches a medical device comprising "PMB30W (Mw = 50 kDa), see Fig. 1 which is a random copolymer of MPC and BMA." *Id*. BMA is n-butyl methacrylate, a hydrophobic monomer. Spec. ¶ 38. The Examiner finds that Kim 2009 teaches that "PMB30W is a random copolymer of MPC and BMA and contains 30 mol% of" MPC monomer. Final Action 3.

The Examiner finds that neither of the Kim references teaches a copolymer with a PDI of less than 1.3. *Id*. The Examiner finds that Ishihara teaches "a method of making water-soluble phospholipid polymer having a small molecular weight distribution." *Id*. at 4. More specifically, Ishihara "teaches a method of making polymers of [MPC] . . . with 4,000–500,000 number average molecular weight and polydispersity index (PDI) of 1.01–1.50." *Id*.

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[2] WO 2010/035920 A1, published April 1, 2010.
[3] Hyung Il Kim et al., BIODEGRADABLE POLYMER FILMS FOR RELEASING NANOVEHICLES CONTAINING SIROLIMUS, 16 Drug Delivery 183–88 (2009).
[4] JP 2005239988, published September 8, 2005.
[5] Office Action mailed August 3, 2018.

The Examiner concludes that it would have been obvious "to optimize parameters such as peak molecular weight (Mp) of copolymers comprising MPC, BMA taught by Kim et al., and polydispersity index of copolymers" because "[o]ptimization of parameters such as the differences in molecular weights, and polydispersity index of copolymers, is routine to a person of ordinary skill in the art, and Ishihara et al. also teaches various copolymers with different molecular weights . . . , and PDI (M_w/M_n) can be obtained by using" Ishihara's method. *Id*.

We agree with the Examiner that the device of claim 40 would have been obvious to a person of ordinary skill in the art based on the cited references. Kim '920 discloses "a . . . blend of poly(L-lactide) (PLLA) and a phosphorylcholine group-containing copolymer (PPCP) . . . and cardiovascular devices using the blend." Kim '920 1:6–9. Kim '920 exemplifies blends of PLLA and PMB30W. *Id*. at 9:24. "Water-soluble amphiphilic PMB30W (Mw = 50 kDa) was synthesized from an MPC unit and a BMA unit at a ratio of 3 to 7"; i.e., 30% MPC and 70% BMA. *Id*. at 9:27 to 10:1. Kim 2009 describes PMB30W as "a biocompatible and water-soluble amphiphilic polymer; poly (2-methacryloyloxyethyl phosphorylcholine (MPC)-*random*-*n*-butyl methacrylate (BMA)." Kim 2009 184, left col. (emphasis in original).

Ishihara states that polymers having MPC as a subunit have attracted attention because they have high biocompatibility, among other properties. Ishihara ¶ 2. However, since previously studied polymers were "obtainable by conventional free radical polymerization . . . [i]t was difficult to control the structure." *Id*.

Ishihara discloses that "[b]y applying the reversible addition fragmentation chain transfer [RAFT] polymerization method, it is possible to obtain a polymer having a narrow molecular weight distribution"; i.e., "a number average molecular weight of 4,000 to 500,000 and a polydispersity index (Mw/Mn) of 1.01 to 1.50." *Id*. ¶ 10. Ishihara exemplifies synthesis of an MPC/BMA random copolymer with Mn = 41,000; polydispersity (Mw/Mn) = 1.40, and 65 mol% MPC. *Id*. ¶ 27.

In view of the above disclosures, it would have been obvious to modify the PMB30W polymer of the Kim references to have a polydispersity index (PDI) of less than 1.3, because Ishihara discloses a method of making MPC/BMA copolymers with a PDI between 1.01 and 1.50. Ishihara also discloses that a narrow molecular weight distribution is desirable, since it describes the "Problem to be Solved by [its] Invention" as "to provide an acrylic acid derivative polymer having *a narrow molecular weight distribution* and a phospholipid polar group having a reactive functional group at the end of the polymer chain." *Id*. ¶ 9 (emphasis added). The closer a polymer sample's PDI is to 1.0, the narrower its molecular weight distribution. Spec. ¶ 68. Thus, a narrow molecular weight distribution, as desired by Ishihara, would result in a PDI close to 1.00.

At a minimum, Ishihara shows that the PDI of an MPC/BMA random copolymer is a result-effective variable, and therefore one that is obvious to optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (CCPA 1955). "[D]iscovery of an optimum value of a result effective variable in a known

process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276 (CCPA 1980). Thus, the device of claim 40 would have been obvious based on the cited references.

Appellant argues that Ishihara's RAFT method

> cannot produce a copolymer of 30 mol% MPC (or about 30 mol% to about 50 mol%). Ishihara teaches the use of water as the solvent. As water does not solubilize the hydrophobic monomers (e.g., the BMA), the resultant copolymers prepared with water as the solvent invariably contain a higher percentage of MPC.

Appeal Br. 14. Appellant argues that "the copolymers claimed herein are produced with alcohol as the solvent. *See, e.g.*, claim 69. . . . Thus, the resultant copolymers prepared with alcohol may contain a lower amount of MPC (e.g., about 30 mol% to about 50 mol %) than is taught by the aqueous RAFT method of Ishihara." *Id*.

This argument is unpersuasive. First, Ishihara does not limit its method to using only water as a solvent. As the Examiner pointed out (Ans. 5), Ishihara teaches that its solvent can include up to 49% of another solvent such as alcohol. *See* Ishihara ¶ 15 ("[W]ater is . . . preferably used as a component of a mixed solvent in which a water-soluble organic solvent such as alcohol is added within a range not exceeding 49%."). Appellant has pointed to no evidence showing that Ishihara's RAFT method is incapable of producing a copolymer of 30–50 mol% MPC units.

In addition, the Specification's examples appear to support the Examiner's position that "[b]y varying the feed ratios of the MPC monomer, and BMA monomers using the RAFT polymerization taught by Ishihara, one can make polymers with different mole percent of MPC content." Ans. 6.

The Specification describes "RAFT random copolymerization of the MPC monomer and a hydrophobic methacrylate monomer." Spec. ¶ 112. Samples 2 and 9 were synthesized under identical conditions except for the starting concentrations of BMA and MPC: Sample 2 was made from a mixture that included 30% MPC (1.69/(1.69 + 3.95) = 0.30) and resulted in a copolymer having 29 mol% MPC, while Sample 9 was made from a mixture that included 50% MPC and resulted in a copolymer having 52 mol% MPC. Spec. ¶ 117 (Table 1-2).

The data in the Specification, therefore, do not support Appellant's position that the solvent used in the RAFT polymerization reaction determines the mol% of MPC in the resulting copolymer.

Appellant also argues that "the Examiner cites no teaching or suggestion in the art that supports this conclusion that arriving at a low PDI, low M_p copolymer that remains soluble in aqueous solution would have been feasible with a reasonable expectation of success." Appeal Br. 15. Appellant argues that

> it is only in the present application that one finds the teaching that the RAFT method can be used to produce copolymers wherein the phosphorylcholine repeating unit comprises about 30 mol% to about 50 mol%, in addition to having a PDI less than 1.3 and M_p less than 130,000, *and* remain soluble in an aqueous solution.

Id.

This argument is unpersuasive. Kim 2009 states that PMB30W, with 30 mol% MPC units, is a "water-soluble amphiphilic polymer." Kim 2009 184, left col. Ishihara states that the problem to be solved by its invention was "[t]o provide a water-soluble phospholipid polymer having a small

molecular weight distribution." Ishihara 1, boxed paragraph. Appellant has provided no evidence or technical reasoning to suggest that modifying the water-soluble PMB30W of the Kim references to have a narrow molecular weight distribution (i.e., a low PDI), as taught by Ishihara, would result in a polymer that was not water-soluble.

Appellant argues that "[t]he present application, moreover, exemplifies the benefits of the claimed copolymers as being capable of excretion in urine, as compared to copolymers, such as those disclosed in Ishihara, comprising a higher phosphorylcholine repeating unit content." Appeal Br. 15. Appellant points to the Specification's Comparative Samples 2.12 to 2.18 as evidence that copolymers with a mol% MPC that is higher than the 30–50 mol% range of the claims could not be excreted in urine. *Id*.

This argument is unpersuasive, because it is not supported by the evidence in Appellant's Specification. The Specification states that "when the MPC monomer mole fraction of phosphorylcholine group-containing copolymer is 80% or less it can be excreted in the urine." Spec. ¶ 146. Thus, a copolymer with an MPC content of up to 80 mol% can be excreted in urine. In any event, the Kim references disclose PMB30W, which has an MPC content of 30 mol%, which is within the range recited in the claims.

For the reasons discussed above, we affirm the rejection of claim 40 under 35 U.S.C. § 103(a) based on Kim '920, Kim 2009, and Ishihara. Claims 55–59, 61–64, and 66 were not argued separately and therefore fall with claim 40. 37 C.F.R. § 41.37(c)(1)(iv).

Appellant argues that Ishihara "fails to teach or suggest the specific steps recited in claim 69." Appeal Br. 18. Appellant argues that "[a]s the

synthesis methodology differs substantially," "the Examiner has failed to establish that one of ordinary skill in the art would have any reasonable expectation of successfully arriving at the claimed copolymer . . . by following the (also different) methodology set forth in Ishihara." *Id*. at 19.

This argument is unpersuasive. The Specification provides working examples of the RAFT copolymerization of samples 1–21. Spec. ¶ 112. The Specification states that a chain transfer agent "was dissolved in alcohol," and after purging with nitrogen, an initiator "was added to the stirred solution." *Id*. ¶ 113. "The MPC monomer and a hydrophobic methacrylate monomer, for example, n-butyl methacrylate (BMA) . . . were added to the reaction mixture." *Id*.

The Specification's description of the synthesis of samples 1–21 does not say that the hydrophobic monomer was combined with a solvent to produce a microemulsion before the reaction mixture was prepared, as recited in claim 69. The Specification does not support the position that the process recited in claim 69 produces a structurally distinct product.

"The patentability of a product does not depend on its method of production. If the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985) (citation omitted). "Where a product-by-process claim is rejected over a prior art product that appears to be identical, although produced by a different process, the burden is upon the applicants to come forward with evidence establishing an unobvious difference

between the claimed product and the prior art product." *In re Marosi*, 710 F.2d 799, 803 (Fed. Cir. 1983).

Appellant has pointed to no evidence showing that the reaction steps recited in claim 69 result in a copolymer that is structurally different from the copolymer synthesized according to the method made obvious by Kim '920, Kim 2009, and Ishihara. We therefore affirm the rejection of claim 69 under 35 U.S.C. § 103(a) based on Kim '920, Kim 2009, and Ishihara.

The Examiner rejected claims 60 and 65 under 35 U.S.C. § 103(a) as obvious based on Kim '920, Kim 2009, Ishihara, and Glauser.[6] Final Action 10. With respect to this rejection, Appellant argues that "Glauser fails to remedy the deficiencies of Kim I, Kim II, and Ishihara." Appeal Br. 16.

Because we do not find any deficiencies in the combination of Kim '920, Kim 2009, and Ishihara, and because Appellant has waived arguments directed to Glauser, we affirm the rejection of claims 60 and 65 under 35 U.S.C. § 103(a). *See* 37 C.F.R. § 41.37(c)(1)(iv) (The Appeal Brief must contain "[t]he arguments of appellant with respect to each ground of rejection."); *Hyatt v. Dudas*, 551 F.3d 1307, 1314 (Fed. Cir. 2008) ("In the event of such a waiver, the PTO may affirm the rejection of the group of claims that the examiner rejected on that ground without considering the merits of those rejections.").

[6] US 2005/0208093 A1, published September 22, 2005.

CONCLUSION

In summary:

Claims Rejected	Basis	Affirmed	Reversed
40, 55–59, 61–64, 66, 69	§ 103(a) Kim ’920, Kim 2009, Ishihara	40, 55–59, 61–64, 66, 69	
60, 65	§ 103(a) Kim ’920, Kim 2009, Ishihara, Glauser	60, 65	
Overall Outcome		40, 55–66, 69	

TIME PERIOD FOR RESPONSE

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

AFFIRMED