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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JAVIER PALOMAR-MORENO, MICHELLE HANNON, and PHILLIP BANNISTER

Appeal 2019-000653
Application 14/980,371
Technology Center 1600

Before SALLY GARDNER LANE, RAE LYNN P. GUEST, and DEBORAH KATZ, *Administrative Patent Judges*.

LANE, *Administrative Patent Judge*.

DECISION ON APPEAL

I. Statement of the Case

Appellant[1] seeks review under 35 U.S.C. § 134(a) of the final rejection of claims 10–12, 15–18, and 21–25[2] of application 14/930,371, filed December 28, 2018. (Appeal Brief filed May 07, 2018 (Appeal Br.) 6, 9, 10).

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[1] We use the term "Appellant" to refer to the "applicant" as defined in 37 C.F.R. § 1.42. The Appellant identifies the real party in interest as Boston Scientific Scimed, Inc. (Appeal Br. 3).

[2] Appellant cancelled claims 19 and 20 mooting the rejection of these claims. (*See* Appeal Br. 13; Amendment filed February 05, 2018).

We have jurisdiction under 35 U.S.C. § 6(b). We AFFRIM-IN-PART.

II. Claims on Appeal

The claims on appeal generally are directed to a drug delivery device having microparticles that are designed to release drugs into a feeder artery within the body of a subject. The microparticles are configured to release a first drug over a first time period of five days or less, and a second drug, that may be the same or different than the first drug, over a second time period also of five days or less. Between the first and second period there is a lag period of 2 to 6 weeks where substantially no drug release occurs. (Appeal Br. 14–15). According to Appellant, the claimed drug delivery system reduces the number of interventions required by allowing for a first chemotherapy treatment based on the first drug, followed by a lag period to allow a patient to rest between exposures to chemotherapy, followed by a second chemotherapy treatment. (Appeal Br. 7).

III. Evidence

The Examiner cited the following references in support of the rejections:

Blaskovich et al., US patent publication 2013/0323312 Al, published December 05, 2013. (Blaskovich).

Hahn, US patent publication 2007/0185569 Al, published August 09, 2007. (Hahn).

Doshi et al., US patent publication 2011/0264188 Al, published October 27, 2011. (Doshi).

Dinh et al., US patent publication 2005/0064005 Al, published March 24, 2005. (Dinh).

IV. Rejections

Claims 10–12, 15, 22, 24, and 25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Blaskovich. (Final Act. 3).[3]

Claim 23 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Blaskovich in view of Hahn. (Final Act. 16).

Claims 10–12, 16–18, 21, and 24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Doshi in view of Dinh. (Final Act. 17).

V. Discussion

A. Claims on Appeal

Claim 10 is representative of all the claims on appeal, claims 10–12, 15–18, and 21–25, and reads:

> 10. A delivery system comprising:
> a delivery device configured to release microparticles into a feeder artery within a body of a subject and
> microparticles that are configured to release a first drug over a first time period and to release a second drug over a second time period,
> wherein a lag period of substantially no drug release occurs between the first and second time periods, and
> wherein the first drug and the second drug may be the same or different,
> wherein the lag period ranges from 2 to 6 weeks, and
> wherein the first time period is a period of five days or less and wherein the second time is a period of five days or less.

[3] The Final Office Action was entered November 03, 2017.

(Appeal Br. 15, indentations added).

B. Rejection of claims 10–12, 15, 22, 24, and 25 over Blaskovich.

As the Examiner found, Blaskovich teaches a delivery system of multi-encapsulated microparticles for delivery of one or more drugs to a subject. The Examiner found that one embodiment of Blaskovich can be configured to contain multi-encapsulated microparticles that release two drugs as required by the Appellant's claims. (Examiner's Answer of August 31, 2018 (Ans.) 7, 10). That embodiment is illustrated at Figure 3:

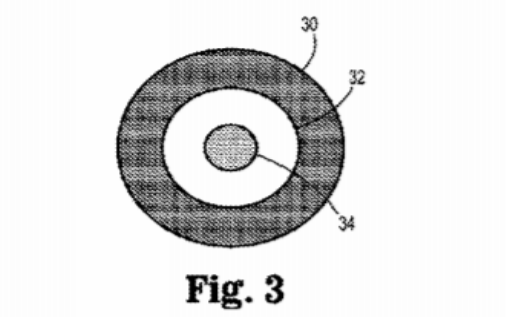

Fig. 3

Blaskovich Figure 3, shown above, "is a schematic diagram of a multi-encapsulated microsphere . . .." (Blaskovich ¶ 223).

The Examiner found that Blaskovich allows for a drug to be within layers 30, 32, and 34 of the microsphere shown at Figure 3. The Examiner points to statements in Blaskovich that the "release profiles of each of the bioactive agents may be discrete (e.g., not overlapping) based on desired use and therapy requirements" and that "an outer encapsulation may be free of any bioactive agents and may act as a buffer, preventing release of bioactive agents until the outer encapsulation has biodegraded." (Ans. 7). The Examiner also found that Blaskovich teaches that "some rounds of encapsulation may include no bioactive

agents based on the desired use" for the purpose of altering release rates such that one of the layers of the Figure 3 microparticles, such as layer 32, may be free of drug. (Ans. 7, 8, 14). The Examiner found that Blaskovich teaches that this drug free layer may be formed of a biodegradable material that is released into the body in a time period of one hour to several months or more depending on the chemical nature of the material. (Ans. 10, 11). As the Examiner found, among the biodegradable encapsulating material taught by Blaskovich, is polylactide-co-glycolide, also disclosed by Appellant as useful to allow lag time between drug releases. (Ans. 14; Specification filed December 28, 2015 (Spec.) 13). The Examiner also noted the teaching in Blaskovich that the timing of release of the bioactives within the microspheres may be modified by the manner and material of encapsulation. (Ans. 5).

The Examiner determined that Blaskovich does not teach specifically the limitation requiring a "lag period" of 2 to 6 weeks where substantially no drug release occurs between the first and second time periods. (Final Act. 5, 6). However, the Examiner concluded that one skilled in the art would have had sufficient reason, given the teaching of Blaskovich, to configure the Blaskovich delivery system to arrive at a delivery device having the claimed lag time such that the Appellant's claimed invention would have been obvious. (Final Act. 9–12).

The Examiner reasoned that one skilled in the art would have been motivated to optimize delivery through routine experimentation and in consideration of a patient's therapeutic needs as well as other factors such as the patient's weight, age, and tolerance. The Examiner found that the degradation period of the biodegradable encapsulating material "is clearly a result-effective

variable[.]" In support of the conclusion of obviousness, the Examiner cites, *inter alia*, the statement in *In re Aller* that "where 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). (Ans. 11).

The Appellant disagrees that the Examiner has articulated a sufficient reason to modify Blaskovich to arrive at its claimed invention and, in particular, the specific lag time of 2 to 6 weeks claimed. We have considered each of Appellant's arguments but do not find error in the Examiner's conclusion of obviousness.

The Appellant argues that one of ordinary skill in the art would not merely optimize for the sake of optimization and the Examiner has not provided a sufficient reason to do so from the teachings of Blaskovich. (Appeal Br. 7). However, the Examiner has pointed to a teaching in Blaskovich of a delivery system having a lag time with substantially no drug release between the first and second drug releases, i.e. having a discrete, not overlapping, release of drug. The Examiner also explained that one skilled in the art would have had reason to configure this delivery system to have, within the disclosed range of "about one hour to several months or more," a lag time appropriate to a patient's therapeutic needs as well as other factors such as the patient's weight, age, and tolerance. (Ans. 11, 12). The Examiner noted, in further support of the obviousness determination, that the range of "about one hour to several months or more" disclosed by Blaskovich encompasses the claimed range of 2 to 6 weeks. (Ans. 10); *see also In re Peterson*, 315 F.3d 1325, 1330 (Fed Cir. 2003) ("the existence

of overlapping or encompassing ranges shifts the burden to the applicant to show that his invention would not have been obvious.").

We also are not persuaded by the Appellant's argument that the Examiner relied upon improper hindsight in reaching the conclusion of obviousness. The basis of the Examiner's reasoning is provided within Blaskovich itself, which specifically provides for a "staggered release profile" (Blaskovich ¶¶ 326, 328; Figure 4) and tailoring release profiles by using biodegradable polymers depending on the desired use and therapy requirements. (Blaskovich ¶¶ 305, 326). Thus the Examiner did not engage in impermissible hindsight but instead relied upon knowledge found in Blaskovich without reliance on knowledge found only in Appellant's disclosure. *See In re McLaughlin*, 443 F.2d 1392, 1395, (CCPA 1971) ("Any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper."); *see also KSR* 550 U.S. at 421 (The fact finder should be cautious of *ex post* reasoning [but] "[r]igid preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it.").

The Appellant asserts that "[u]nlike a specific chemical structure, it is well known in the art that an array of factors would affect release of a therapeutic agent in a particle like that proposed by the Examiner based on Blaskovich including layer thickness, polymer molecular weight, polymer lactide/glycolide ratio and the presence or absence of other species." (Appeal Br. 8). The Appellant does not

point to a requirement within the claims for any of these factors or provide evidence of how these factors would affect drug release in a way not within the teaching of Blaskovich. Thus we are not convinced that these unclaimed factors distinguish the claims from what is obvious over Blaskovich.

The Appellant argues that the claimed delivery device and its release profile achieve improvements over the prior art. For example, the Appellant asserts that the microparticles described and claimed reduce the number of interventions required by allowing for a first chemotherapy treatment based on the first drug, followed by a lag period (to allow a patient to rest between exposures to chemotherapy), followed by a second chemotherapy treatment. (Appeal Br. 7). Had Appellant directed us to evidence of secondary considerations based on an improvement over the prior art we would have considered it in our review of the obviousness determination but the Appellant has not done so. *See E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018) ("A claimed range that demonstrates such unexpected results is referred to as a 'critical' range, and the patentee has the burden of proving criticality."); *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997) (Attorney argument is not evidence of unexpected results).

The Appellant argues the degradation time period found in Blaskovich of "about one hour to about several months or more, depending on the chemical nature of the material" relates to how long a material takes to be excreted or absorbed by the body and does not relate to allowing for a lag time where substantially no drug is released. (Appeal Br. 8, 9). We do not find this argument persuasive. Blaskovich states that this biodegradation time refers to how long it

takes for a material to lose structural integrity or break down under body conditions. (Blaskovich ¶ 305). Blaskovich also states that a buffer encapsulation composed of biodegradable material prevents the release of bioactive agent until the buffer layer is biodegraded. (Blaskovich ¶ 331). We agree with the Examiner that a drug-free layer of biodegradable material according to Blaskovich, e.g., a buffer layer, would result in a period of substantially no drug release, i.e., a lag time, which encompasses the lag time period recited in the claims of 2 to 6 weeks. (Ans. 14).

We also have considered the arguments in Appellant's Reply Brief, to the extent they differ from or add to the arguments addressed above, but do find any of the Reply Brief arguments persuasive. (*See* Reply Brief filed October 31, 2018 (Reply Br.).)

The Appellant argues that the Examiner improperly conflated the teachings of Figures 2 and 3 of Blaskovich in reaching the obviousness conclusion. (Reply Br. 9, 10). While the Examiner does discuss both Figures 2 and 3, the reasoning of the Examiner as it pertains to Figure 3 itself sufficiently supports the conclusion of obviousness. The Examiner's discussion of the biodegradable buffer layer shown in the Figure 2 embodiment is relevant to this reasoning because it informs the meaning of "biodegradable material" within the context of Blaskovich. (Ans. 8).

The Appellant argues that Blaskovich does not teach stents or any composition that would release the described microparticles. (Reply Br. 11, 12, 14). However, we agree with the Examiner who found that Blaskovich describes microparticles to be suitable for implanting into body lumens. We also agree with the Examiner's finding that the Blaskovich particles are taught to be useful to form

stents, medical devices that may release microparticles into a feeder artery within a body of a subject as the claims require. To the extent Blaskovich does not contain this express teaching, we agree with the Examiner that one would be motivated to incorporate the described "microparticles" into a medical device taught in Blaskovich, such as a stent, for purposes of delivery. (Ans. 10).

Thus the Examiner provided the required reasoning and rational underpinnings to support the conclusion of obviousness. *KSR International Co. v. Teleflex Inc.,* 550 US 398, 418 (2007) ("[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

The Appellant does not point to limitations in any of claims 11, 12, 15, 22, 24, or 25 that would distinguish those claims from Blaskovich on a basis not argued as to claim 10. Accordingly, we AFFIRM the rejection of claims 10–12, 15, 22, 24, and 25 as obvious over Blaskovich.

C. Rejection of claim 23 over Blaskovich in view of Hahn

Claim 23 depends from claim 10 and is rejected under 35 U.S.C. § 103 as being unpatentable over Blaskovich and Hahn. The Appellant argues that this rejection is deficient for the same reasons provided as to the rejection of claims 10–12, 15, 22, 24, and 25 over Blaskovich. The Appellant provides no argument regarding claim 23 other than an assertion that Hahn, which is cited for disclosure of doxorubicin, does not make up for deficiencies in Blaskovich. (Appeal Br. 9).

We do not find error in the Examiner's rejection of claims 10–12, 15, 22, 24, and 25 over Blaskovich. Since Appellant provides no additional reason why the rejection of claim 23 is in error, we AFFIRM this rejection.

D. Rejection of claims 10–12, 15–18, 21, and 24 over Doshi in view of Dinh

Claims 10–12, 15–18, 21, and 24 are rejected under 35 U.S.C. § 103 as being unpatentable over Doshi in view of Dinh.

The Examiner found that Doshi teaches a coated stent having a first drug on the outer surface and a second drug on an inner surface. The Examiner found that the second drug is released after the first drug on the outer surface is released. (Final Act. 17, 18). The Examiner found that Doshi does not expressly provide for a lag period where substantially no drug release occurs between the first and second drug releases. (Final Act. 18). However, the Examiner found that, because Doshi teaches that nano-carriers are released from the inner surface *after* the burst release of nano-carriers from the outer surface, there must be a lag period of some duration where substantially no drug is released. (Final Act. 19, 20).

Since Doshi does not expressly teach a lag period, it follows that Doshi also does not teach that there is a lag period of a particular duration. The Examiner therefore found that Doshi does not teach the limitation of the claims calling for a lag period of 2 to 6 weeks. (Final Act. 18).

The Examiner refers to Dinh, however, for a teaching of a three-layered drug delivery system having a middle barrier layer that can function to control the rate of release of the drugs by slowing the rate of permeation or increasing "lag time." (Final Act. 20, 21).

The Appellant disagrees that Doshi's teaching of release from an inner layer "after" drug release from an outer layer amounts to a teaching that there is a lag period between the releases, especially one of a two to six week duration. (Appeal Br. 10). The Examiner however asserts that one skilled in the art would have had reason to include in the Doshi delivery system a barrier layer as taught by Dinh to increase "lag time." (Final Act. 20, 21).

The Appellant argues, *inter alia*, that in Dinh, the "lag" time is not a lag period of substantially no release between two release periods as claimed but rather is the lag time associated with release through a barrier layer, a distinct concept. (Appeal Br. 11, 12).

Here, we agree with Appellant. While Dinh uses the term "lag time," Dinh does not indicate that this "lag time" is a period of substantially no drug release. Dinh specifically states that the barrier layer does not prevent permeation of the drug from the inner layer to the outer layer. (Ans. 19; Dinh ¶ 24). Dinh further states that as drugs permeate out of the system the barrier layer will include one or more drugs. (Dinh ¶44). Thus, we are not convinced that Dinh teaches a lag period as that term is used in the Appellant's claims, i.e., a time of substantially no drug release. It follows that Dinh also does not show a lag period of the claimed 2 to 6 weeks. Thus, the rejection of the claims over Doshi and Dinh is not supported by a preponderance of the evidence. *See In re Epstein*, 32 F.3d 1559, 1564 (Fed. Cir. 1994) (A preponderance of the evidence is the standard for rejecting claims at the USPTO).

Claims 11, 12, 15–18, 21, and 24 also include a requirement for a lag period of 2 to 6 weeks. The Examiner has not shown that a delivery system having this

requirement would have been obvious over Doshi and Dinh. We therefore REVERSE the rejection of claims 10–12, 15–18, 21, and 24 over Doshi in view of Dinh.

VI. Decision

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
10-12, 15, 22, 24, 25	103	Blaskovich	10–12, 15, 22, 24, 25	
23	103	Blaskovich, Hahn	23	
10–12, 15–18, 21, 24	§ 103	Doshi, Dinh		10–12, 15–18, 21, 24
Overall Outcome			10–12, 15, 22, 24, 25	16–18, 21

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

AFFIRMED-IN-PART.