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FASKEN MARTINEAU DUMOULIN LLP
333 Bay Street, Suite 2400
Bay Adelalde Centre, Box 20
TORONTO, ONTARIO M5H 2T6
CANADA

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JIANG LIU,
MICHAEL RICHARD JOHNSTON, and XIAO YU WU

Appeal 2019-005662
Application 12/063,614
Technology Center 1600

Before FRANCISCO C. PRATS, TAWEN CHANG, and
RACHEL H. TOWNSEND, *Administrative Patent Judges.*

CHANG, *Administrative Patent Judge.*

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from the Examiner's decision to reject claims 1, 7–23, 25–33, 35, 43, 84–89, and 93. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM IN PART.

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[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant did not identify the real party in interest in the Appeal Brief.

STATEMENT OF THE CASE

The Specification states that the lymphatic system is "an anatomical location which is frequently affected by cancer and other diseases." Spec. 1:5–6. The Specification further states that

> [c]ontrol of lymphatic metastasis improves the outcome of many cancers. Presently, local-regional therapies, such as surgery and radiation, are the most effective means of treating regional lymphatics, but often do not completely eradicate all lymphatic metastatic disease. Systemic chemotherapy is limited by systemic side effects and often cannot effectively penetrate the lymphatic system, presumably because of a 'blood-lymph barrier'. Lymphatic drug delivery becomes even more compromised after extensive cancer surgery due to the disruption of blood and lymphatic vessels. Currently, there is a lack of effective treatment options for specifically targeting lymphatic metastasis. Therefore, effective therapeutic modalities based on a better understanding of the pathophysiology of lymphatic system are clearly needed to improve the treatment of tumor within the lymphatic system.

Id. at 3:8–20.

According to the Specification, "[t]he distinct physiological function of the lymphatic system in the clearance of foreign particulate matters has generated interest in the use of microparticulate systems for the targeting of therapeutic agents to regional lymph nodes." Spec. 3:21–24. Further according to the Specification, "th[e] invention relates to the targeted delivery of therapeutic agents formulated in conjunction with micro- and/or nanoparticulate carriers to the lymphatics and lymph nodes and implantable devices containing the particulate carriers." *Id.* at 1:7–10.

CLAIMED SUBJECT MATTER

The claims are directed to an implantable biocompatible and biodegradable matrix. Claim 1 is illustrative:

> 1. An implantable biocompatible and biodegradable matrix comprising a plurality of bioactive complexes disposed throughout the matrix, the matrix selected to release the bioactive complexes over a predetermined first time interval when the matrix degrades,
>
> each bioactive complex having a range of sizes sufficient to selectively target and enter the lymphatic system upon release from the matrix, the bioactive complex comprising at least one particle forming material and at least one bioactive agent disposed throughout the particle forming material,
>
> the bioactive complex adapted to release an effective amount of the at least one bioactive agent within the lymphatic system over a second time interval.

Appeal Br. 12 (Claims App.).

REJECTION(S)

A. Claims 1, 7–14, 18–23, 25–33, 35, 43, 84–89, and 93[2] are rejected under 35 U.S.C. § 112(b) or 35 U.S.C. § 112 (pre-AIA), second paragraph, as being indefinite. Ans. 3.

B. Claims 1, 7, 8, 14, 18–22, 25–31,[3] 35, 43, 84–89, and 93[4] are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Haynes,[5] Kennedy,[6] and optionally Illum.[7] Ans. 4.

C. Claims 9–14, 23, and 32 are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Haynes, Kennedy, Illum, and Guire.[8] Ans. 10.

D. Claim 33 is rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Haynes, Kennedy, Illum, and Hennink.[9] Ans. 11.

E. Claims 84, 85, and 87–89 are rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Haynes, Kennedy, Lee,[10] Berkland,[11] and optionally Illum. Ans. 12.

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[2] The Examiner states in the Answer that claims 1, 7–14, 18–23, 25–33, 35, 43, and 84–93 are rejected as indefinite. However, claims 90–92 have been cancelled. Appeal Br. 19 (Claims App.).

[3] The Examiner did not include claim 31, which depends from claim 1 and additionally recites that "the bioactive complex and/or matrix contain additives," in the list of the claims rejected as obvious over Haynes, Kennedy, and optionally Illum. Appeal Br. 16 (Claims App.); Final Act. 5; Ans. 4. However, in the body of the rejection the Examiner discusses the prior art as teaching that additives can be added. Ans. 5, 7. Accordingly, we understand that the obviousness rejection over Haynes, Kennedy, and optionally Illum also applies to claim 31.

[4] The Examiner states in the Answer that claims 1, 7, 8, 14, 18–22, 25–31, 35, 43, and 84–93 are rejected as obvious over Haynes, Kennedy, and

OPINION

A. Indefiniteness rejection (claims 1, 7–14, 18–23, 25–33, 35, 43, 84–89, and 93)

1. Issue

The Examiner concludes that the claims are indefinite because "the functional limitations in [the] claim[s] are not clearly linked to the structure(s) that provide that function." Ans. 3. In particular, the Examiner finds that the Specification provides only "a single exemplary formulation with a 'gelatin sponge' and microparticles comprised of the drug paclitaxel with PLGA," and "it is not clear if this construct releases an 'effective' amount of paclitaxel within the lymphatic system." *Id.* at 4.

Appellant contends that "the exemplary formulation must release an effective dose as the results of intraoperative implantation of gelatin sponges

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optionally Illum. However, claims 90–92 have been cancelled. Appeal Br. 19 (Claims App.).

[5] Haynes et al., US 5,972,366, issued Oct. 26, 1999.

[6] Kennedy et al., US 6,488,952 B1, issued Dec. 3, 2002.

[7] L. Illum et al., *Development of Systems for Targeting the Regional Lymph Nodes for Diagnostic Imaging: In Vivo Behaviour of Colloidal PEG-Coated Magnetite Nanospheres in the Rat Following Interstitial Administration*, 18 PHARMACEUTICAL RES. 640 (2001).

[8] Guire et al., WO 03/030879 A1, published Apr. 17, 2003.

[9] Hennink et al., US 2002/0131952 A1, published Sept. 19, 2002.

[10] Woo-kyoung Lee et al., *Investigation of the Factors Influencing the Release Rates of Cyclosporin A-loaded Micro- and Nanoparticles Prepared by High-Pressure Homogenizer*, 84 J. CONTROLLED RELEASE 115 (2002).

[11] Cory Berkland et al., *PLG Microsphere Size Controls Drug Release Rate through Several Competing Factors*, 20 PHARMACEUTICAL RES. 1055 (2003).

containing PLGA-PTX and PLM-Dox significantly reduced lymphatic tumor metastases in experimental animal tumor models." Appeal Br. 4.

In response, the Examiner asserts that the rejection is not one of lack of written description; rather, the claims are indefinite because "[it] is not clear if the cited structure possesses the required function and one of ordinary skill in the art cannot [determine] the metes and bounds of the claims." Ans. 15.

The issue with respect to this rejection is whether a preponderance of the evidence of record supports the Examiner's conclusion that claims 1, 7–14, 18–23, 25–33, 35, 43, 84–89, and 93 are indefinite.

2. *Analysis*

On the record before us, we find Appellant to have the better position.

The claims recite functional limitations, namely that "[the] bioactive complex[es] ha[ve] a range of sizes sufficient to *selectively target and enter the lymphatic system upon release from the matrix*" and are "*adapted to release an effective amount of the at least one bioactive agent within the lymphatic system over a second time interval*."

Functional language in a claim does not, in and of itself, render a claim indefinite. *See, e.g.*, *In re Swinehart*, 439 F.2d 210, 213 (CCPA 1971). Nevertheless, the Examiner appears to argue that, in order to be definite, the claim must recite the structures necessary to achieve the functional limitation. *See, e.g.*, Final Act. 4 (stating that "[t]he amendments to claim 1 have not added sufficient structure to indicate how the claim[s] are adapted to provide the claimed function").

We are not persuaded. "[A]n inventor need not explain every detail because a patent is read by those of skill in the art." *BASF Corp. v. Johnson*

Matthey Inc., 875 F.3d 1360, 1366 (Fed. Cir. 2017) (explaining that "[t]he mere observation of information not 'recited' [in the claims] does not answer the question whether a person of ordinary skill in the art would *need* to be given the . . . information to understand . . . whether a composition is 'effective to catalyze' the . . . reactions"). Neither is it the function of the claims to specifically exclude possible inoperative embodiments. *In re Dinh-Nguyen*, 492 F.2d 856, 858–59 (CCPA 1974). Finally, although functional language may render the scope of the claim broad, "breadth is not to be equated with indefiniteness." *In re Miller*, 441 F.2d 689, 693 (CCPA 1971).

To the extent the Examiner's rejection is based on the finding that the disclosure in the Specification does not support and/or enable the skilled artisan to practice the full scope of the claims without undue experimentation, the appropriate rejections are lack of written description and/or enablement.

Accordingly, we reverse the Examiner's rejection of claims 1, 7–14, 18–23, 25–33, 35, 43, 84–89, and 93 as indefinite.

B. Obviousness rejection over Haynes, Kennedy, and optionally Illum (claims 1, 7, 8, 14, 18–22, 25–31, 35, 43, 84–89, and 93)

1. Issue

The Examiner finds that Haynes discloses a majority of the limitations in claim 1, except it does not explicitly teach that a "bioactive complex comprising at least one particle forming material and at least one bioactive agent disposed throughout the particle forming material." Ans. 6. However, the Examiner finds that Kennedy discloses this limitation because it teaches "a semisolid delivery system . . . comprised of a hydrogel . . . with a

multiparticulate therapeutic delivery system," including a preferred embodiment wherein the multiparticulate component is comprised of the biodegradable copolymer poly(lactic-co-glycolide) (PLGA)[12] and the therapeutic agent is dispersed in the particles. *Id.*

The Examiner concludes that it would have been obvious to a skilled person to incorporate Kennedy's therapeutic particles into a matrix taught by Haynes, because Kennedy teaches that "porous matrixes can contain particulates of therapeutic agent dispersed in a particle forming material such as PLGA." Ans. 7. The Examiner notes that the prior art teaches that "[a] wide variety of drugs such as antibiotics or anti-inflammatories can be delivered" and further notes that the prior art particle size of 20 nm–30 μm overlap with, and thus renders prima facie obvious, the size ranges claimed and described in the Specification as selectively targeting and entering the lymphatic system. *Id.*

The Examiner finds that Haynes also does not discuss "particles entering the lymphatic system." Ans. 8. The Examiner finds, however, that Illum discloses that "interstitially administered colloids with a size less than 100 nm will drain through the interstitium to initial lymphatic vessels and should drain effectively from the site of injection th[r]ough the lymphatic vessels to lymph nodes," that "[t]he lymph nodes can be the site of spread of metastatic disease and are a pathway for growth of malignancies," that "[u]ptake of administered colloids into the lymph system has been

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[12] The Specification states that "[s]uitable embodiments of the invention include particles made from degradable polymers such as polylactides (PLA), polyglycolides (PGA)[,] and their copolymers (PLGA)." Spec. 14:11–13.

demonstrated for biodegradable nanospheres of PLGA surface modified with poloxamine block co-polymers and copolymers of poly(lactide)-PEG," that uptake was also being demonstrated for "PEG coated magnetite particles for use in imaging lymph nodes," and that "[b]oth the size (<100 nm) and surface properties are necessary for satisfactory uptake in regional lymph nodes." *Id.*

The Examiner concludes that it would have been obvious to a skilled artisan to combine Illum with the drug-containing matrix suggested by Haynes in view of Kennedy to arrive at the claimed invention, because Haynes teaches a general system of controlled release of drug particles from a matrix and Illum teaches both that "metastasis can occur through the lymph system" and that "particles can be targeted for uptake of the lymph system by their size and surface characteristics to provide controlled release of drug targeted to the lymphatic system." Ans. 9.

Appellant contends that the Examiner's suggested combination of Haynes, Kennedy, and Illum would render Haynes unsatisfactory for its intended purpose and/or change its principle of operation. Appeal Br. 5–6. Appellant contends that the cited prior art does not suggest the limitation of "the matrix selected to release the bioactive complexes over a predetermined first time interval when the matrix degrades." *Id.* at 6. Appellant contends that the particle size to be used for the claimed invention would not have been obvious to a skilled artisan. *Id.* at 7–8. Finally, Appellant contends that secondary considerations of non-obviousness, specifically praise by others, supports the non-obviousness of the claims. *Id.* at 9.

Appellant does not separately argue the claims. We therefore focus our analysis on claim 1 as representative. The issue with respect to this

rejection is (1) whether a preponderance of evidence supports the Examiner's conclusion that the combination of Haynes, Kennedy, and optionally Illum renders claim 1 obvious, and, if so, (2) whether Appellant has provided evidence of secondary considerations of non-obviousness that, when considered together with the evidence of obviousness, shows claim 1 to be nonobvious.

2. Analysis

We agree with the Examiner that the combination of Haynes, Kennedy, and Illum renders claim 1 obvious. We address Appellant's arguments below. Only those arguments timely made by Appellant in the briefs have been considered; arguments not so presented are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2015); *see also Ex parte Borden*, 93 USPQ2d 1473, 1474 (BPAI 2010) (informative) ("Any bases for asserting error, whether factual or legal, that are not raised in the principal brief are waived.").

Appellant contends that a skilled artisan would not have had reason to combine Haynes with Kennedy and Illum to arrive at the claimed invention, because the combination "would render the implantable absorbable sponges in Haynes unsatisfactory for their intended purpose of providing local therapeutic benefits." Appeal Br. 5.

We are not persuaded. As the Examiner points out, Haynes' invention is not limited to providing local therapeutic benefits. Haynes states, for example, that

> [f]urther aspects of our invention include the ability to control the rate and mode of release of the drug by choice of concentration and type of adjuvant used, as well as the ability to incorporate the drug at high payload (up to 4 gm Drug/gm

> Carrier Material). Thus, drugs can be delivered at high concentrations to the adjoining tissue for long durations to prevent the growth of bacteria, to facilitate wound healing and *to even give systemic drug delivery*, when needed.

Haynes 21:51–58 (emphasis added).

Appellant next contends the prior art does not suggest the claim limitation of "the matrix selected to release the bioactive complexes over a predetermined first time interval when the matrix degrades." Appeal Br. 6. In particular, Appellant contends that, "even if the particles described in Haynes dissociate from the matrix, such dissociation is not the result of the degradation of the matrix nor is the matrix in Haynes selected to degrade over a predetermined time interval as recited in Claim 1." *Id.* Appellant contends that "the mere fact that a matrix biodegrades and that particles may be released therefrom does not suggest that the two are causally linked." *Id.*

We are not persuaded. The Specification states:

> [T]wo different types of biodegradation may generally be identified. . . . [O]ne type of biodegradation may involve cleavage of bonds (whether covalent or otherwise) in the polymer backbone. . . . In contrast, another type of biodegradation may involve cleavage of a bond (whether covalent or otherwise) internal to a side chain or that connects a side chain to the polymer backbone. For example, an antineoplastic taxane or other chemical moiety attached as a side chain to the polymer backbone may be released by biodegradation. . . . As used herein, the term "biodegradation" encompasses both general types of biodegradation.

Spec. 25:8–21. Thus, under the broadest reasonable interpretation in light of the Specification, "matrix selected to release the bioactive complexes over a predetermined first time interval when the matrix degrades," as recited in claim 1, encompasses the release of bioactive complexes resulting from

cleavage of a bond, including a non-covalent bond, between the matrix and the bioactive complex.

Haynes teaches that its drug microparticles may be bound to the carrier matrix by "naturally occurring chemical affinity . . . between the . . . microparticles and . . . the carrier," including "hydrophobic interaction, hydrogen bonding and ionic interactions," as well as via "binding . . . to the carrier . . . by means of [an] adjuvant which has chemical affinity for both." Haynes 7:19–37. Haynes teaches that drugs can be released from the carrier via diffusion or flow of either the drug monomers or the drug microparticles from the carrier matrix. *Id.* at 9:12–15. Haynes further teaches that the rate of release of the drug monomers and microparticles may be adjusted by various mechanisms including, e.g., selection of adjuvant materials. *Id.* at 9:11–10:15. Thus, Haynes teaches "matrix selected to release the bioactive complexes over a predetermined first time interval when the matrix degrades" under the broadest reasonable interpretation of that phrase, because it suggests release of either drug monomers or microparticles through cleavage of the bonds between the drug monomer/microparticle and the carrier matrix.

Appellant contends that "the dual purpose in Haynes of the delivery of . . . pharmaceuticals (or drugs) to targeted tissue at a controlled rate, *while maintaining its hemostatic function* . . . requires independent degradation and delivery mechanisms." Appeal Br. 6. Appellant contends that "a degradation based delivery mechanism as described in . . . instant claim 1 would change [Haynes'] principle of operation" because "Haynes contemplates the release of drug microparticles being dependent upon the firmness of attachment to (or entrapment within) the carrier material, which

can be controlled by selection of primary adjuvant materials" and is "dependent on the amount of tidal flow resulting from squeezing and releasing of the preparation in the medium in which it is placed." *Id.* Thus, Appellant contends that "a degradation based delivery mechanism . . . would change [Haynes'] principle of operation. *Id.*

As an initial matter, and as discussed above, the broadest reasonable interpretation of the phrase "the matrix selected to release the bioactive complexes over a predetermined first time interval when the matrix degrades" encompasses the release of bioactive complexes bound to the matrix through the cleavage of the bonds between drug particles or adjuvant and the matrix, which is disclosed in Haynes. Thus, we are not persuaded that Haynes's dual purpose of maintaining hemostasis and delivery of drugs "requires independent degradation and delivery mechanisms" or that the claimed "degradation based delivery mechanism" would change Haynes' principle of operation. As for Appellant's argument that Haynes teaches that the rate of release of drug particles may be "dependent on the amount of tidal flow resulting from squeezing and releasing of the preparation in the medium in which it is placed," we note that, as the Examiner points out, claim 1 does not preclude factors other than matrix degradation from affecting release rate. Ans. 18.

Appellant also contends that a skilled artisan would not have had a reasonable expectation of success in administering Illum's particles subcutaneously, because Illum teaches that "both the size (i.e., less than 100 nm) and surface properties of the particles are necessary for satisfactory uptake in the regional lymph nodes for subcutaneously administered nanoparticles" and, thus, a skilled artisan "would not be able to distinguish

the qualities that would make a particle suitable for lymphatic uptake." Appeal Br. 7.

We are not persuaded. The relevant question for obviousness is whether a skilled artisan would have had a reasonable expectation of success in making or carrying out the *claimed* composition or process. *See, e.g.*, *PAR Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1196 (Fed. Cir. 2014). Claim 1 is a composition claim and does not require subcutaneous administration. Thus, an obviousness finding does not require a showing that a skilled artisan would have reasonably expected to successfully administer Illum's particles subcutaneously.

Appellant contends that Illum teaches away from the claimed invention because a skilled artisan in view of Illum "would not use particles larger than 100 nm to achieve particle uptake in the regional lymph nodes and as such Illum discourages the solution claimed." Appeal Br. 8.

We are not persuaded. "[A] reference will teach away when it suggests that the developments flowing from its disclosures are unlikely to produce the objective of the applicant's invention." *Syntex (U.S.A.) LLC v. Apotex, Inc.*, 407 F.3d 1371, 1380 (Fed. Cir. 2005). In this case, claim 1 does not recite specific particle size ranges or require uptake in the regional lymph node. Thus, Illum does not teach away from the *claimed* invention. Indeed, claim 1 clearly contemplates use of particles that are 100 nm or smaller. For example, claim 87, which depends from claim 1, recites bioactive complex size "from about 10 nm to about 100 nm." Appeal Br. 19 (Claims App.).

Appellant contends that Haynes' disclosure of an overlapping range of particle size would not render the claimed bioactive complex obvious

because the claimed particles are "selected for a wholly different purpose (e.g., anticancer treatment using cytotoxic agents) and are of a wholly different structure (with particle forming material)." Appeal Br. 8.

We are not persuaded. As an initial matter, and as discussed above, claim 1 does not recite specific ranges as to the size of the bioactive complex. To the extent Appellant's argument is that the limitation "bioactive complex having a range of sizes sufficient to selectively target and enter the lymphatic system upon release from the matrix" imposes specific restrictions on the size of the bioactive complex, we remain unpersuaded. Claim 84 depends from claim 1 and recites bioactive complex "from about 10 nm to about 11.2 μm." Appeal Br. 19 (Claims App.). Haynes teaches that the dimension of its drug microparticle is most preferably between 2 μm and 100 nm, which is encompassed by the range recited in claim 84. Haynes 6:51–55. Thus, absent persuasive evidence to the contrary, which Appellant has not provided, Haynes teaches particles having "a range of sizes sufficient to selectively target and enter the lymphatic system upon release from the matrix." *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) ("Where . . . the claimed and prior art products are identical or substantially identical . . . the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.").[13]

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[13] We note in addition that Illum teaches particle size of less than 100 nm, which also overlaps the particle size range disclosed in the Specification and recited in claim 84, and further teaches that particle size is a result-effective variable for targeting the lymphatic system. Illum 640 (stating that "[i]nterstitially administered colloids with a size less than 100 nm, will drain through the interstitium to the initial lymphatic vessels" until they are

As to Appellant's argument that the claimed particles are "selected for a wholly different purpose (e.g., anticancer treatment using cytotoxic agents)" than those disclosed in Haynes, we note that "[i]n determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls," so long as there is a reason to combine the prior art elements in the claimed manner. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 419–20 (2007). Thus, the fact that the claimed particles are "selected for a wholly different purpose" does not render the claims non-obvious.

Similarly, with respect to Appellant's argument that Haynes' disclosures of particle size do not render the claimed particle size obvious because the claimed bioactive complex are "of a wholly different structure (with particle forming material)," we note that Appellant has not disputed that Kennedy discloses bioactive complexes comprising particle forming materials. "Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. . . . [The reference] must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole." *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). Appellant has provided no persuasive argument why a skilled artisan would not consider the particle size range disclosed by Haynes, which Haynes

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captured within the lymph nodes); Spec. 12:3–19 (describing embodiments where in particles range in size from 50 nm to 11.2 μm); Appeal Br. 19 (Claims App.) (claim 84 reciting bioactive complex "from about 10 nm to about 11.2 μm).

teaches as pertinent to the rates of release (Haynes 6:55–56), to be similarly relevant to the particles disclosed in Kennedy.

Finally, Appellant cites to the Wu Declaration[14] to argue that secondary considerations of non-obviousness, specifically praise by others, supports the non-obviousness of the claims. Appeal Br. 9.

We are not persuaded. The Wu Declaration states that "[t]he invention has been praised as an important and innovative step by numerous independent members of the scientific community." Wu Decl. ¶ 7. While we agree that industry praise is evidence of secondary considerations of non-obviousness, "to be accorded substantial weight . . . the evidence of secondary considerations must have a 'nexus' to the claims, *i.e.*, there must be 'a legally and factually sufficient connection' between the evidence and the patented invention." *Henny Penny Corp. v. Frymaster LLC*, 938 F.3d 1324, 1323 (Fed. Cir. 2019). In particular, "[t]he evidence presented to rebut a prima facie case of obviousness must be commensurate in scope with the claims to which it pertains." *In re Dill*, 604 F.2d 1356, 1361 (CCPA 1979).

In this case, Appellant presents documents to show that "[a] new drug-delivery system" developed by Dr. Jiang Liu, an inventor of the patent application at issue, won the second-place prize in the 2008 Innovation Challenge Award sponsored by the Natural Sciences and Engineering Research Council of Canada (NSERC). Wu Decl., Ex. B. 1, 2, 4.[15] The

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[14] Declaration of Xiao Yu Wu, Ph.D. (May 9, 2013). Dr. Wu is an inventor of the patent application at issue.

[15] Exhibit B to the Wu Declaration is not paginated. Thus, all references to page numbers in Exhibit B of the Wu Declaration refer to page numbers as if

documents describe the Microparticulate Lymphatic Targeting System (MLTS) that won the award as "a system that successfully targets lymph nodes in delivering chemotherapy drugs" by embedding "bioabsorbable particles that contain anti-cancer drugs" in "a special gelfoam that is meant to be implanted near lymph nodes." *Id.* at 1. The documents note that, "[i]n laboratory tests, [Dr. Liu] has been able to increase the drug exposure in the desired areas to 400 times what can be achieved by regular injections, with fewer side effects." *Id.*

As an initial matter, Appellant has not provided persuasive evidence that the bioabsorbable particles of MLTS comprises "at least one particle forming material and at least one bioactive agent disposed throughout the particle forming material," as recited in claim 1. Moreover, claim 1 is significantly broader than the system described above, and Appellant has not persuasively argued that there is a reasonable basis for concluding the untested embodiments encompassed by claim 1 would behave in the same manner as MLTS. *Cf. In re Lindner*, 457 F.2d 506, 508 (CCPA 1972) (finding evidence of alleged unexpected results to be insufficient to overcome prima facie case of obviousness where claims are much broader in scope than the tested composition and there is "no 'adequate basis for reasonably concluding that . . . compositions included by the claims would behave in the same manner as the [single] tested composition'").

Appellant also presents documents to show that Dr. Liu's "Trans-lymphatic Chemotherapy Technology" was the first place winner of the Ever

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Exhibit B was numbered consecutively beginning with the first page after the cover page.

Green World Chinese Venture Creation Competition and that the American Association for Cancer Research presented the AACR-Aflac Award to Dr. Liu for developing "a [n]ovel [a]nti-cancer [t]echnology." Wu Decl., Ex. B 3, 5. These documents, however, do not describe the technology being praised and thus do not provide evidence of the nexus to the claims that is necessary for secondary considerations to be accorded substantial weight.

Finally, Appellant presents a summary of the committee discussion of a grant application by Dr. Wu entitled "[b]iodegradable nanoparticles for targeted drug delivery to lymphatic metastatic cancer cells." Wu Decl., Ex. B. 6–7. While the summary states that "[t]he proposed research addresses an important clinical problem with immediate relevance to the field," that "[t]he proposal was well-written with a good rationale and clearly-defined hypotheses," and that "[t]he approach is novel and is supported by the accompanying preliminary data," the summary does not describe the proposed research in any detail or provide evidence of its success. *Id.* at 6. Thus, we accord the summary little weight for purposes of our obviousness analysis.

Accordingly, for the reasons discussed above, we affirm the Examiner's rejection of claim 1 as obvious over Haynes, Kennedy, and Illum. Claims 7, 8, 14, 18–22, 25–31, 35, 43, 84–89, and 93, which are not separately argued, fall with claim 1.

C. Obviousness rejection over Haynes, Kennedy, Illum, and Guire (claims 9–14, 23, and 32)

With respect to the obviousness rejection over Haynes, Kennedy, Illum, and Guire, Appellant contends that the combination "would result in the bioactive complexes, as presently claimed, and the bioactive agents (e.g.,

paclitaxel) contained therein being released locally and/or in view of Illum not targeted for lymphatic delivery in the event the bioactive complexes are released." Appeal Br. 10.

Appellant does not separately argue the claims, we therefore focus our analysis on claim 9 as representative. We are not persuaded for the same reasons discussed above with respect to claim 1. The Examiner has established a prima facie case that the combination of Haynes, Kennedy, Illum, and Guire would result in a matrix comprising bioactive complexes having structures that are "identical or substantially identical" to the matrix and bioactive complexes recited in claim 9. Thus, the burden is shifted to Appellant to show that the matrix and bioactive complexes suggested by the prior art "do not necessarily or inherently possess the characteristics of [the] claimed product," i.e., bioactive complex that "selectively target and enter the lymphatic system upon release from the matrix" or "release an effective amount of the at least one bioactive agent within the lymphatic system." *In re Best*, 562 F.2d at 1255. Appellant's conclusory attorney arguments do not meet this burden. Accordingly, we affirm the Examiner's rejection of claim 9 as obvious over Haynes, Kennedy, Illum, and Guire. Claims 10–14, 23, and 32, which are not separately argued, fall with claim 9.

D. *Obviousness rejection over Haynes, Kennedy, Illum, and Hennink (claim 33)*

With respect to the obviousness rejection over Haynes, Kennedy, Illum, and Hennink, Appellant contends that

> Applicants have previously noted in remarks dated April 4, 2018 that the encapsulation of free drug disclosed in Hennick [sic], in association with the particles and matrix taught by

> Kennedy, Haynes and Illum, will result only in additional local delivery of free (or non-encapsulated) drug.

Appeal Br. 10.[16] Appellant thus appears to rely only on the same arguments as those made with respect to the rejection of claim 1 over Haynes, Kennedy, and optionally Illum. We are not persuaded for the reasons already discussed above with respect to the rejection of claim 1.

E. Obviousness rejection over Haynes, Kennedy, Lee, Berkland, and optionally Illum (claims 84, 85, and 87–89)

Appellant does not separately argue the claims. We therefore focus our analysis on claim 84, which depends from claim 1 and further recites that "bioactive complex is from about 10 nm to about 11.2 μm." Appeal Br. 19 (Claims App.).

The Examiner cites Lee and Berkland as disclosing particle sizes "above 100 nm such as a couple hundred nanometers or in the micron range." Ans. 12. The Examiner concludes that it would have been obvious to a skilled artisan "to use drug containing particles as in Kennedy with varying sizes in the hundreds of nanometers or micron size range to provide the desired drug release," because Lee and Berkland teach that "particle size influences the release rate of the drug and[,] by varying particle size, delivery rates such as zero order or pulsatile can be achieved." *Id.* at 14. The Examiner further finds that the limitations relating to the size of the bioactive complex are obvious because such size is "clearly a result effective

[16] We are unable to locate in the record Appellant's remarks dated April 4, 2018. We assume that Appellant is referring instead to the April 30, 2018 Response to Office Action.

parameter that a person of ordinary skill in the art would routinely optimize." *Id.*

Appellant contends that "the larger particles disclosed in Lee (Table 1) and Berkland could not have reasonably been expected to reach the lymphatic system considering the size limitations taught for lymphatic delivery in Illum which specifically teaches away from the invention." Appeal Br. 10. Appellant further argues that Berkland on its own or in view of Illum "teaches away from the invention," because "Berkland teaches particles which provide localized drug delivery and high local drug concentrations." *Id.*

We are not persuaded for the reasons similar to those discussed above. As to Appellant's argument that a skilled artisan would not have reasonably expected the larger particles disclosed in Lee and Berkland to reach the lymphatic system, we note that claim 84 is a composition claim and thus does not require its bioactive complexes to reach the lymphatic system, merely that they have a size such that they would selectively target and enter the lymphatic system if administered. Claim 84 recites a size range that will achieve such a result. The obviousness issue with respect to the composition only requires a skilled artisan to have reason to, and reasonable expectation of success in, making bioactive complexes having the recited size, not the knowledge that in making bioactive complexes of that size that they will reach the lymphatic system when administered.

Furthermore, claim 84 is not limited to bioactive complex having a "larger" particle size. Instead, claim 84 recites "bioactive complex . . . from about 10 nm to about 11.2 μm." Appeal Br. 19 (Claims App.) Thus, even if obviousness requires a reasonable expectation that the prior art particle will

be taken up by the lymphatic system, the particle size limitation in claim 84 is obvious because Illum teaches that interstitially administered colloids with a size less than 100 nm, which overlaps the range recited by the claim, will drain through the interstitium to the initial lymphatic vessel. Illum 640, left column.

As for Appellant's arguments regarding teaching away, we have already discussed why Illum does not teach away from the claimed invention. Berkland teaches that "biodegradable polymer microspheres that can deliver a therapeutic at a constant rate over a prolonged time following a single administration can . . . provide localized drug delivery and high local drug concentrations." Berkland 1055, left column. This, however, does not suggest that such microspheres may not also be used to selectively target and enter the lymphatic system. Thus, Berkland does not teach away from the invention, either on its own or in view of Illum. *See, e.g.*, *Baxter Int'l, Inc. v. McGaw, Inc.*, 149 F.3d 1321, 1328 (Fed. Cir. 1998) (explaining that "reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant").

Accordingly, we affirm the Examiner's rejection of claim 84 as obvious over Haynes, Kennedy, Lee, Berkland, and Illum. Claims 85 and 87–89, which are not separately argued, fall with claim 84.

F. Claims 15–17

The Examiner states in the Final Action that all pending claims are rejected. Final Act. 1. As Appellant points out, however, the Examiner did not provide a specific basis of rejection for pending claims 15–17. Appeal Br. 4. Accordingly, the Examiner has not established a prima facie case of

invalidity as to claims 15–17, and we reverse the Examiner's rejection of these claims.

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/ Basis	Affirmed	Reversed
1, 7–14, 18–23, 25–33, 35, 43, 84–89, 93	112(b) or 112 (pre-AIA), second paragraph	Indefiniteness		1, 7–14, 18–23, 25–33, 35, 43, 84–89, 93
1, 7, 8, 14, 18–22, 25–31, 35, 43, 84–89, 93	103(a)	Haynes, Kennedy, Illum	1, 7, 8, 14, 18–22, 25–31, 35, 43, 84–89, 93	
9–14, 23, 32	103(a)	Haynes, Kennedy, Illum, Guire	9–14, 23, 32	
33	103(a)	Haynes, Kennedy, Illum, Hennink	33	
84, 85, 87–89	103(a)	Haynes, Kennedy, Lee, Berkland, Illum	84, 85, 87–89	
15–17				15–17
Overall Outcome			1, 7–14, 18–23, 25–33, 35, 43, 84–89, 93	15–17

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). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED IN PART