

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today
(1) was not written for publication in a law journal and
(2) is not binding precedent of the Board.

Paper No. 34

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GREGORY J. RUSSELL-JONES
and STEVEN W. WESTWOOD

Appeal No. 1996-1273
Application 07/956,003¹

HEARD: October 5, 1999

Before PAK, WARREN and LIEBERMAN, *Administrative Patent Judges*.

WARREN, *Administrative Patent Judge*.

Decision on Appeal and Opinion

This is an appeal under 35 U.S.C. § 134 from the decision of the examiner refusing to allow claims 3, 4, 14 through 21 and 25 through 29 as amended subsequent to the final rejection.²

We have carefully considered the record before us, and based thereon, find that we cannot

¹ Application for patent filed November 30, 1992.

² See specification pages 29-30, the amendment of August 17, 1994 (Paper No. 12) and the amendment of June 12, 1995 (Paper No. 20). The latter amendment further canceled claims 8 through 10, 30 and 31 which were finally rejected on October 19, 1994 (Paper No. 13).

sustain either of the grounds of rejection advanced by the examiner on appeal.³

The examiner has based the rejection of all of the appealed claims under 35 U.S.C. § 112, second paragraph, on the premise that these claims are indefinite and fail to particularly point out and distinctly claim the subject matter which appellants regard as their invention because the term “analogue” is indefinite since this “term is similar to ‘derivatives’ which is held to be indefinite,” relying on the authority of *Petrolite Corp. v. Watson*, 149 F.Supp 1, 113 USPQ 248 (D.D.C. 1957) (answer, page 4).⁴ We are unaware of any authority, including that cited by the examiner, which holds that the term “derivative” or the term “analogue” is *per se* indefinite under the second paragraph of § 112. Thus, where the term “analogue” appears in a claim, as in any ground of rejection advanced on the record, the initial burden of establishing a *prima facie* case that the appealed claims are indefinite under the second paragraph of § 112 because of the presence of this term rests with the Examiner. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ 2d 1443, 1444 (Fed. Cir. 1992), citing *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984) (“As discussed in *In re Piasecki*, the examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability.”). It is well settled that a determination of whether a claim complies with the second paragraph of § 112 involves an analysis of whether the language of the claim as a whole sets out and circumscribes “a particular area with a reasonable degree of precision and particularity,” *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971), wherein “[t]he operative standard for determining whether this requirement has been met is ‘whether those skilled in the art would understand what is claimed when the claim is read in light of the specification.’” *The Beachcombers, Int’l. v. WildeWood Creative Prods.*, 31 F.3d 1154, 1158, 31 USPQ2d 1653, 1656 (Fed. Cir. 1994), citing *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565,

³ The final rejection (Paper No. 13; page 2) included a ground of rejection of claims 8 through 10 under 35 U.S.C. § 112, first paragraph, which appealed claims have been canceled (*see supra* note 2).

⁴ This is the sole basis for rejecting the appealed claims under the second paragraph of § 112 advanced by the examiner on appeal. The other grounds under the second paragraph of § 112 set forth in the final rejection (Paper No. 13; pages 2-3) are assumed to have been withdrawn. *Ex parte Emm*, 118 USPQ 180 (Bd. App. 1957).

1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986).

The record on appeal does not contain any analysis by the examiner establishing that one of ordinary skill in this art would not understand what is claimed by the claim language “a Vitamin B₁₂-analogue that binds Castle’s intrinsic factor,” found in each of independent claims 25 through 28, when read in light of the specification. Thus, in giving this claim language the broadest reasonable interpretation consistent with appellants’ specification as it would be interpreted by one of ordinary skill in this art, *In re Morris*, 127 F.3d 1048, 1053-56, 44 USPQ2d 1023, 1027-30 (Fed. Cir. 1997); *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989), the appealed claims encompasses *any and all* Vitamin B₁₂-analogues that bind Castle’s intrinsic factor even though extended cogitation may be necessary for one skilled in this art to comprehend the entire scope of the class of Vitamin B₁₂-analogues. *See, e.g., In re Gardner*, 427 F.2d 786, 788, 166 USPQ 138, 140 (CCPA 1970) (“Breadth is not indefiniteness.”). *See* appellants’ reply brief (pages 2-3). Accordingly, we reverse this ground of rejection.⁵

Turning now to the ground of rejection of the appealed claims under 35 U.S.C. § 103 over Ranney or Papahadjopoulos or Geho or Guo in view of Russell-Jones⁶ or vice versa (answer, pages 4-8), it is well settled that in order to establish a *prima facie* case of obviousness, “[b]oth the suggestion and the reasonable expectation of success must be found in the prior art and not in applicant’s disclosure.” *In re Vaeck*, 947 F.2d 488, 493, 493-95, 20 USPQ2d 1438, 1442, 1443-44 (Fed. Cir. 1991). Thus, the examiner must establish a *prima facie* case of obviousness by showing that some objective teaching or suggestion in the applied prior art taken as a whole and/or knowledge generally available to one of ordinary skill in the art would have led that person to the claimed invention, including each and every limitation of the claims, without recourse to the teachings in appellants’ disclosure. *See*

⁵ Because we find that the examiner has not established a *prima facie* case of indefiniteness under the second paragraph of § 112, we have not considered either the Schneider or Hogenkamp references cited by appellants at page 7 of their principal brief or the U.S. patents cited by appellants at page 3 of their reply brief.

⁶ The references relied on by the examiner with respect to this ground of rejection are listed at page 3 of the answer.

generally, In re Oetiker, 977 F.2d 1443, 1447-48, 24 USPQ2d 1443, 1446-47 (Fed. Cir. 1992)
(Nies, J., concurring).

The appealed claims, as represented by claim 25,⁷ are drawn to a complex, for oral delivery of a substance to the circulation or lymphatic drainage system of a host, that comprises at least a microparticle coupled by covalent bond, hydrophobic interaction or both to a carrier which is Vitamin B₁₂ or a Vitamin B₁₂-analogue that binds Castle's intrinsic factor. The microparticle is specified to be a microsphere or microcapsule that entraps or encapsulates the substance, maintains the substance deleteriously unaffected by intestinal digestive substances and releases the substance into the circulation or lymph. The carrier Vitamin B₁₂ or a Vitamin B₁₂-analogue that binds Castle's intrinsic factor is specified to be effective to transport the complex into the circulation or lymphatic drainage system of a host via the intestinal mucosal epithelium. Upon comparing the claimed invention with the prior art, the examiner applied essentially two different sets of prior art in rejecting the appealed claims. The first set consists of Ranney, Papahadjopoulos, Geho and Guo which the examiner characterizes as teaching the "concept of attaching various target molecules specific for tissues where the drug delivery is desired to microspheres" but not "vitamin B₁₂ as the targeting molecule" (answer, pages 5-6). The second set consists of Russell-Jones which is characterized by the examiner as teaching the "instant concept of delivering a drug by complexing it with the carrier, B₁₂" that is "administered orally and the purpose is to deliver the drug in the intestines where B₁₂ binds to the intrinsic factor" but not the "use of microspheres" (answer, page 6).

Thus, the examiner submits two alternative positions in the rejection (answer, page 6) which are essentially the same, that is, it would have been obvious to one of ordinary skill in this art to modify the drug delivery system of Russell-Jones by coupling the "microspheres containing the drug to B₁₂" rather than the "drug itself . . . since encapsulation of drugs in microspheres results in their sustained release in the intestines" as shown by Ranney, Papahadjopoulos, Geho and Guo. In this respect, the examiner

⁷ We decide this appeal on claim 25 because, as noted by the examiner (answer, page 2), appellants have not stated that the appealed claims do not stand or fall together. 37 CFR § 1.192(c)(7) (1995).

cites appellants' argument that Russell-Jones "teaches the covalent coupling of [the] B₁₂ molecule to a drug and not a microsphere encapsulating a drug" and in response thereto takes the "position that B₁₂ is a targeting molecule recognizing intrinsic factor just as the targeting molecules recognizing specific targets taught by the cited prior art and thus, it would be obvious to an artisan to use B₁₂ as a targeting molecule with the expectation of obtaining similar results" (answer, page 8). Indeed, appellants point out, *inter alia*, that Russell-Jones "uses a vitamin B₁₂ molecule to transport only one active substance molecule per oral administration" and further contend, *inter alia*, that "nowhere is it taught or suggested that a vitamin B₁₂-microparticle/active ingredient complex would be effective" in submitting that the only suggestion to combine the cited prior art is taken from their own disclosure (principal brief, page 13, see also principal brief, pages 11-12 and 13-14). We agree with appellants.

There is agreement that Russell-Jones is the sole reference of record which teaches the use of Vitamin B₁₂ as a carrier to which a single drug is covalently bonded to form a drug delivery system. This reference contains the following disclosure in discussing the invention taught therein in the context of the prior art:

Recent work by us utilizing a number of molecules with the ability to bind to the intestinal mucosa has demonstrated effective oral immunization using low doses of these binding proteins or by coupling various antigens or haptens to these carriers. Uptake and delivery to the circulation of these molecules from the intestine seemed to be due to receptor mediated endocytosis.

It has been known for some time that a number of specific uptake mechanisms exist in the gut for uptake of dietary molecules. Thus there are specific uptake mechanisms for monosaccharides, disaccharides, amino acids and vitamins. Most of these uptake mechanisms depend upon the presence of a specific protein or enzyme such as monosaccharidase or diaccharidase situated in the mucosal lamina propria which binds to the molecule and transports it into the cells lining and [sic] lamina propria.

Two *notable exceptions* to these uptake mechanisms are found with iron transport and *VB12 uptake*. In both these cases a specific binding protein is released into the intestine, which binds to its ligand in the lumen of the gut.

. . . .

Similarly, the absorption of physiological amounts of VB12 by the gut requires that it be complexed with a naturally occurring transport protein known as intrinsic factor (IF) This protein is released into the lumen of the stomach by parietal cells in the fundus. *Once bound*

*to intrinsic factor, the VB12-IF complex interacts with a membrane bound receptor for IF located on the terminal ileum of the small intestine. The receptor-IF-VB12 complex is then internalized by a process of receptor mediated endocytosis . . . Allen and Majerus . . . demonstrated that it is possible to chemically modify VB12, couple it to a resin and use the VB12-resin to affinity purify IF. This finding suggested to us that *it may be possible to couple large macromolecules (such as the resin used by Allen and Majerus) to VB12 and to still preserve it's ability to interact specifically with intrinsic factor.* By coupling molecules to VB12 in such a way as to preserve the ability of VB12 to interact with intrinsic factor it was hoped that we could use the natural uptake mechanism for VB12 [to] deliver VB12 and various molecules coupled to it, to deliver various proteins, drugs or other pharmaceutically active molecules to the circulation. [Pages 1-2; emphasis supplied.]*

Based on this disclosure of Russell-Jones, the principal issue raised on the record before us is similar to the question initially posed by Russell-Jones (page 2): would one of ordinary skill in this art have found in the combined teachings of the applied prior art the suggestion to couple a microsphere to Vitamin B₁₂ with the reasonable expectation of preserving the ability of Vitamin B₁₂ to interact specifically with intrinsic factor to form a complex capable of further interacting with a membrane bound receptor for intrinsic factor located on the terminal ileum of the small intestine and thus effective to transport the complex into the circulation or lymphatic drainage system of a host via the intestinal mucosal epithelium wherein the substance contained in the microsphere is released, as required by the appealed claims? We find that the examiner has not supplied the evidence and/or scientific explanation which answers this question in the affirmative.

We find that Russell-Jones discloses that the uptake mechanism for Vitamin B₁₂ is an exception to the uptake mechanisms for dietary molecules and receptor mediated endocytosis for intestinal mucosa binding proteins and antigens or haptens coupled thereto. Indeed, Vitamin B₁₂, that is, cobalamin, a complex compound containing cobalt, must bind to intrinsic factor released into the intestine in such manner as to form a complex capable of further interacting with a membrane bound receptor for intrinsic factor located on the terminal ileum of the small intestine. We further find that based on the discussion in Russell-Jones, one of ordinary skill in this art would have reasonably expected that the epithelial uptake across bowel mucosa of the heparin microspheres of Ranney Examples 1 and 2, the heparin surface coated dextran microsphere of Ranney Example 3 and heparin nanosphere of Ranney Example 14 as disclosed in Ranney Example 15, would be obtained via a different uptake mechanism

than that known for Vitamin B₁₂. The same difference in uptake mechanism is also seen between Vitamin B₁₂ as taught by Russell-Jones and the “intraduodenal injection (oral)” of an hepatocyte directed vesicle microparticle disclosed in Geho (pages 16-17 and 22 and Supplemental Experiment 3; see also, e.g., pages 3 and 7-11 and page 23, second full paragraph). A different mechanism would also appear to be the case with the use suggested for the protein-coupled activated liposomes in Papahadjopoulos (e.g., page 19).⁸ Thus, on this record, one of ordinary skill in this art would not have been led to combine Russell-Jones with any and all of Ranney, Papahadjopoulos and Geho in view of the differences in the uptake mechanism for the drug delivery system.

Thus, on the record before us, we find that the mere fact that it was known in the art to couple microspheres to much different target compounds to form drug delivery systems that will provide epithelial uptake across bowel mucosa as shown by Ranney, Papahadjopoulos and Geho, as relied on by the examiner, would have been insufficient to suggest to one of ordinary skill in this art that the coupling of a microparticle in place of a single drug compound to Vitamin B₁₂ in the drug delivery system of Russell-Jones would reasonably be expected to successfully permit the Vitamin B₁₂ to effectively transport the complex into the circulation or lymphatic drainage system of a host via the intestinal mucosal epithelium. Accordingly, because the examiner has not provided evidence and/or scientific reasoning in the record why one of ordinary skill in this art would have found in the combined teachings of Russell-Jones, Ranney and Geho the suggestion and the reasonable expectation of success in modifying the single drug coupled to Vitamin B₁₂ of Russell-Jones in order to arrive at the claimed invention, it is manifest that the only direction to appellants’ claimed invention as a whole encompassed by the appealed claims on the record before us is supplied by appellants’ own specification. *Compare Vaeck*, 947 F.2d at 493-95, 20 USPQ2d at 1443-44.

⁸ The mechanism taught by Guo (see, e.g., col. 3, lines 1-2, and col. 14, lines 30-59, and Example XII) is simply dissimilar in that this reference discloses that the liposome *per se* binds to mucosal tissue, *inter alia*, ocular tissue and gastrointestinal mucosa, where the drug is released.

The examiner's decision is reversed.

Reversed

CHUNG K. PAK)	
Administrative Patent Judge)	
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CHARLES F. WARREN)	BOARD OF PATENT
Administrative Patent Judge)	APPEALS AND
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