

The opinion in support of the decision being entered today was *not* written for publication and is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte ALAN CUTHBERTSON, BARD INDREVOLL,
MAGNE SOLBAKKEN, TORGRIM ENGELL, MILL COLIN ARCHER,
and HARRY JOHN WADSWORTH

Appeal 2007-1140
Application 10/753,729
Technology Center 1600

ON BRIEF

Before MILLS, GREEN, and LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

Claims 1-11, 13-18, 20, and 22 are on appeal. We have jurisdiction under 35 U.S.C. § 6(b). We affirm the rejection under § 103, but because our reasoning differs from the Examiner, we designate it as a new ground of rejection. We vacate the obvious-type double-patenting rejection and remand to the Examiner for further consideration.

STATEMENT OF CASE

Claims 1-22 are pending (Substitute Br. 1). In the Answer, the Examiner withdrew certain rejections and, for reasons not clear from the record, stated that claims 12, 19, and 21 would be allowable if rewritten in independent form (Answer 3, 7).

The appealed claims are drawn to peptide-based compounds which comprise the tripeptide sequence arginine-glycine-aspartic acid (RGD) which is known to bind to integrin receptors (Specification 4: 19-32). Integrin receptors are located on cells involved in angiogenesis, the process of forming new blood vessels (*id.* at 4: 5-11). There are numerous diseases and indications associated with angiogenesis, including cancer and inflammatory diseases, such as atherosclerosis (*id.* at 3: 4-20). One approach in diagnosing diseases associated with angiogenesis is to target the integrin receptors located on the new or inflamed blood vessels. “The efficient targeting and imaging of integrin receptors associated with angiogenesis in vivo demands therefore a selective, high affinity RGD based vector that is chemically robust and stable.” (*Id.* at 6: 8-11). “[T]he invention provides new peptide-based compounds of Formula I as defined in the claims. These compounds have affinity for integrin receptors, e.g. affinity for the integrin [receptor] $\alpha v \beta 3$.” (*Id.* at 6: 18-21.)

The Examiner relies on the following evidence to establish the unpatentability of the claims:

Appeal No. 2007-1140
Application No. 10/753,729

X_6 represents a thiol-containing amino acid residue, and
 X_7 is absent or represents a biomodifier moiety
 Z_1 represents an antineoplastic agent, a chelating agent or a reporter moiety and
 W_1 is absent or represents a spacer moiety.

DISCUSSION

Rejection of claim 1-11, 13-18, 20, and 22 over Cuthbertson

To establish obviousness, the Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966) has required that the following factors be taken into consideration: (1) the scope and contents of the prior art; (2) the differences between the prior art and the claimed subject matter; (3) the level of skill in the pertinent art; and (4) evidence of secondary considerations.

Scope and contents of the prior art

Cuthbertson teaches peptide-based compounds for use as diagnostic imaging agents (1: 4-6). The compounds are defined by formula I (6: 34 to 9: 20). They comprise an RGD peptide component (“... X₃-G-D ...”) which is attached to X₁ and X₇-X₈ moieties. X₁ is defined to comprise a moiety “suitable for modifying the pharmacokinetics or blood clearance rate” and/or “a reporter (R) moiety suitable for in vivo imaging.” (7: 14-28.) X₇ is defined similarly (8: 24-25). X₈ “represents a reporter (R) moiety or is NH₂ or is absent.” (9: 10-15). The moiety for “for modifying the pharmacokinetics or blood clearance rate” is preferably polyethyleneglycol (7: 18-19). For convenience, we use the term “biomodifier” to describe this moiety because that is the term used for the same functional group in the instant application (Specification 8: 13-17). We also designate the end of the compound where X₁ is attached as the peptide’s N-terminus, and where the X₇-X₈ is attached as the peptide’s C-terminus, because these positions correspond to the amino- (N) and carboxy- (C) terminus of the RGD peptide component.

Differences between the prior art and the claimed subject matter

Appellants admit that the RGD peptide component is the same in instant claim 1 and Cuthbertson (Reply Br. 3). They assert, however, that “it is the different positions on the molecule where both the reporter and biomodifier components are attached that separates the present invention from Cuthbertson.” (Reply Br. 3).

We do not agree with Appellants’ characterization of the differences between the claimed invention and the prior art. Claim 1 lists a reporter moiety as being attached to X₁ at the peptide’s N-terminus. Cuthbertson teaches that a biomodifier or reporter can be present at the N-terminus (7: 24-28). At its C-terminus, claim 1 can have a biomodifier moiety. Cuthbertson also teaches that its peptide can have a biomodifier at its C-terminus, *e.g.*, where X₇ is a linker that comprises a functional side-chain “suitable for modifying the pharmacokinetics and blood clearance rates of the said agents” (8: 24 to 9: 15.) and where X₈ is NH₂ or absent. In sum, Cuthbertson teaches the reporter and biomodifier moieties may occupy the same positions which are claimed.

It is true that Cuthbertson discloses examples in which the reporter moiety is attached to the peptide’s C-terminal end, rather than on its N-terminus as required by claim 1. However, in evaluating the scope and content of the prior art, “[a]ll the disclosures in a reference must be evaluated . . . a reference is not limited to the disclosure of specific working examples.” *In re Mills*, 470 F.2d 649, 651, 176 USPQ 196, 198 (CCPA 1972). In this case, Cuthbertson clearly discloses a general formula I which teaches the reporter and biomodifier groups at the same positions described

by the formula recited in instant claim 1. Appellants admit this by characterizing the claimed subject matter as a “selection application.” (Substitute Br. 5; Dec. ¶ 2.) In other words, Cuthbertson’s formula I is broader than instant claim 1, permitting reporter (16, ll. 5-6) or biomodifier moieties at either end of the molecule.

Level of skill in the pertinent art

The prior art teaches that it was conventional at the time the invention was made to attach functional moieties to either end of an RGD peptide. In addition to Cuthbertson’s teaching of the interchangeability of reporter and biomodifier positions, we find the following disclosures pertinent to this issue:

1) Hart¹ describes cyclic RGD peptides as vectors for transporting DNA in cells (p. 3, l. 6 to p. 4, l. 1). The RGD peptide comprises a “polycationic component [which] may be linked at any position of” it. (Hart at p. 8, ll. 9-10.)

2) Dean² describes radiolabeled peptides (col. 4, l. 65 to col. 5, l. 5; col. 6, l. 59). Labeled RGD peptides are disclosed (col. 6, l. 59; Table spanning cols. 13-14). The radiolabel can be incorporated at any position of the peptide (col. 8, l. 24-36).

Based on this evidence, we consider it to have been commensurate with the level of ordinary skill in the art to chose and interchange positions of functional groups in an RGD peptide.

¹ Hart, PCT Pub. No. WO 98/54347, Dec. 3, 1998.

² Dean et al. (Dean), U.S. Pat. No. 5,965,107, Oct. 12, 1999.

Analysis

Cuthbertson teaches RGD peptide-based compounds for use as diagnostic imaging agents (1: 4-6). To accomplish the imaging function, the compounds contain a reporter at either end of the peptide (16: 5-6). In addition to the reporter, the peptide can also contain a moiety (“biomodifier”) for “modifying the pharmacokinetics or blood clearance rates” of the compound (7: 18-20; 8: 30-32), also at either end of the compound (*id.*). The examples show compounds with a biomodifier and reporter at the C-terminus (*e.g.*, at 38, compound 1d); and the biomodifier at the N-terminus and reporter at the C-terminus (*e.g.*, at 48, compound 4d). There are only a small number of possible configurations of a peptide-based compound with C- and/or N-terminal reporter and biomodifier moieties as generally described in Cuthbertson. The claimed compound, which represents one of these limited configurations, would be straightforwardly envisioned by the skilled worker in view of Cuthbertson’s general formula I, its specific examples (*e.g.*, compound 4d), and the teachings of Hart and Dean that functional groups can be located at any suitable position of an RGD peptide. A reference must be “considered in its entirety for what it fairly suggests to one skilled in the art.” *In re Hedges*, 783 F.2d 1038, 1039, 228 USPQ 685, 687 (Fed. Cir. 1986). In our view, Cuthbertson would have reasonably suggested to the skilled worker a RGD peptide having a reporter at its N-terminus and a biomodifier at its C-terminus as required by claim 1.

Obviousness also requires a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1443 (Fed. Cir. 1991). Cuthbertson’s teaching that reporter and biomodifier moieties can occupy

either the N- or C-termini of the peptide component provides evidence that the skilled worker would have reasonably expected that the claimed compound, with the reporter at the N-terminus and the biomodifier at the C-terminus, to have retained its activity as a diagnostic imaging agent. This is buttressed by Hart and Dean, both which teach that functional groups (*e.g.*, a polycation or radioactive reporter) can be incorporated at any position of the RGD peptide without affecting its binding or functional activity.

In view of the foregoing, we find sufficient evidence to establish a *prima facie* case of obviousness. Because our reasoning differs from the Examiner's, we designate this as a new ground of rejection under 37 C.F.R. § 41.50(b) to provide Appellants with an opportunity to respond.

Appellants argue:

¶Also, in Cuthbertson, the examples teach attachments of the reporter to the C-terminal end of the peptide X8 and biomodifier at the N-terminal end at X1. The present invention, however, specifies that the positioning of the biomodifier is at the C-terminal end X7, and X8 is absent.

(Reply Br. 4)

We do not find that this distinguishes the claimed invention from Cuthbertson. In Cuthbertson, the reporter moiety (X₈) is attached to the C-terminus by a spacer moiety (X₇) (7: 1-5; 8: 24-27; 9: 10-15). Cuthbertson's configuration is flipped in instant claim 1, where the reporter moiety is attached to the N-terminus by a spacer moiety (*i.e.*, the "linker" of Cuthbertson) W₁. In this case, the instant claim preserves the entire reporter structure by lifting the linker and reporter from the C-terminus of Cuthbertson, and attaching them to the N-terminus of the same peptide component.

Appellants also argue that “Cuthbertson teaches that a linker moiety is responsible for modifying the pharmacokinetics or blood clearance rates.” (Reply Br. 4.) But Cuthbertson also teaches that the linker moiety can be present without the reporter (“X8 . . . is NH₂ or absent”) (Cuthbertson 9: 10-15). Thus, we do not agree that this difference distinguishes the claimed invention from Cuthbertson.

Secondary considerations

“One way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of ‘unexpected results,’ i.e., to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected.” *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995).

An applicant cannot prove unexpected results with attorney argument and bare statements without objective evidentiary support. *See In re Lindner*, 59 C.C.P.A. 920, 457 F.2d 506, 508 (CCPA 1972); *In re Geisler*, 116 F.3d 1465 (Fed. Cir. 1997) (“attorney argument [is] not the kind of factual evidence that is required to rebut a prima facie case of obviousness”); *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) (“It is well settled that unexpected results must be established by factual evidence. Mere argument or conclusory statements ... [do] not suffice.”) (quoting *In re De Blauwe*, 736 F.2d 699, 705 (Fed.Cir.1984)).

CFMT Inc. v. Yieldup Inter’l Corp., 349 F.3d 1333, 1342, 68 USPQ 2d 1940, 1947 (Fed. Cir. 2003).

In this case, we find no evidentiary support for Appellants’ statement that the results obtained with “present invention” are “unexpectedly” better and “superior” when compared to Cuthbertson’s compounds (Substitute Br.

9). These are conclusory statements without a description or explanation of the test data upon which the conclusions are based. “[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art.” *In re Baxter Travenol Labs.*, 952 F.2d 388, 392, 21 USPQ2d 1281, 1285 (Fed. Cir. 1991). Appellants do not provide sufficient information to determine whether the comparison of the claimed compounds was with the closest prior art compounds of Cuthbertson. Moreover, the “unexpected results” must be “commensurate in scope with the degree of protection sought by the claimed subject matter.” *In re Harris*, 409 F.3d 1339, 1344, 74 USPQ2d 1951, 1955 (Fed. Cir. 2005). A showing that certain compounds within the scope of the claim have unexpected properties does not necessarily establish that all species within the scope of the claim possess the asserted unobvious property. In sum, we do not find Appellants’ evidence sufficient to rebut the prima facie case of obviousness.

Rejection of claim 1-11, 13-18, 20, and 22 over co-pending Application 10/269,575

An obvious-type double-patenting rejection over a co-pending application is appropriate when the claims of the co-pending application are not identical, “but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s).” M.P.E.P. § 804. It is not clear from the Examiner’s rejection what claims of co-pending U.S. Serial Application No. 10/269,575 were

considered to conflict with the instant claims. Appellants have taken it be the claims of U.S. Pat. Pub. 2003/0204049 which corresponds to the '575 Application (Substitute Br. 10). However, the published claims were amended in the co-pending application. In particular, the N-terminus of the peptide compound *claimed* in the co-pending '575 Application does not specify that it can be a reporter moiety (dated Sept. 18, 2006), a fact upon which the § 103 rejection over Cuthbertson is based. *See supra* on p. 7. Consequently, we vacate this rejection and remand to the Examiner to determine whether an obvious-type double-patenting rejection is appropriate in view of the currently pending claims of the co-pending application.

OTHER ISSUES

Upon return of the application to the technology center, the Examiner should reconsider the patentability of the subject matter of claims 12, 19, and 21, particularly in view of the new ground of rejection set forth in this decision.

With respect to claim 12, the Examiner should determine whether the chelating group disclosed in Cuthbertson at 11 is the same as the structure recited in the claim or an obvious variant of it.

Claim 19 recites that the antineoplastic agent of claim 18 is selected from a list of known antineoplastic agents. The Examiner should determine whether this subject is obvious over of Cuthbertson in view of the disclosure in WO 98/10795 cited on 5: 14-19 that doxorubicin attached to an RGD peptide has been used to target drugs.

For claim 21, the Examiner should consider whether any of the four compounds recited in the claim would have been obvious over Cuthbertson alone or combined with other prior art.

TIME PERIOD

This decision contains a new ground of rejection pursuant to 37 C.F.R. § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 C.F.R. § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that the appellant, **WITHIN TWO MONTHS FROM THE DATE OF THE DECISION**, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

- (1) Reopen prosecution. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
- (2) Request rehearing. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

If the new ground of rejection or remand results in further prosecution before the examiner and this does not result in allowance of the application, abandonment, or a second appeal, this case should be returned to the Board of Patent Appeals and Interferences for entry of a final decision.

Appeal No. 2007-1140
Application No. 10/753,729

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/41.50(b)/VACATE AND REMAND

Demetra J. Mills)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
Lora M. Green)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
)	
Richard M. Lebovitz)	
Administrative Patent Judge)	

RL

Appeal No. 2007-1140
Application No. 10/753,729

Amersham Health, Inc.
19 Department
101 Carnegie Center
Princeton, NJ 08540