

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 42

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte NASSIM USMAN,
ROBERT J. CEDERGREN,
JEAN-PIERRE PERREAULT,
JING-HUA YANG, and
ALEXANDER RICH

Appeal No. 2002-1251
Application No. 08/459,340

HEARD October 7, 2002

Before WINTERS, WILLIAM F. SMITH, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 74 and 80-82, all of the claims in the application. Claim 74 is representative and reads as follows:

74. A pharmaceutical composition, comprising:
at least one enzymatic nucleic acid molecule having a ribonucleotide at a catalytically critical site, at least one deoxyribonucleotide and at least one nucleic acid analog; and
a pharmaceutically acceptable carrier.

The examiner relies on the following references:

“Antisense ‘97: A roundtable on the state of the industry,” Nature Biotechnology, Vol. 15, pp. 519-524 (1997)

Branch, “A good antisense molecule is hard to find,” TIBS, Vol. 23, pp. 45-50 (1998)

Claims 74 and 80-82 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking both an adequate written description and an enabling disclosure in the specification.

We reverse.

Background

The specification discloses that a catalytic RNA, or ribozyme, can “act as a catalyst on another RNA or DNA molecule (substrate) by cleaving or ligating pieces of the substrate without changing itself in the process.” Page 1. “Although ribozymes are intriguing molecules, their use for in vivo applications is limited if not precluded. The all-RNA molecules are susceptible to degradation from enzymes (RNAses) present in vivo.” Id., page 2.

The specification (page 3) discloses

ribozyme like molecules . . . or “nucleozymes” [that] have ribonucleotides or nucleic acid analogues (hereinafter NAAs) at catalytically critical sites and NAAs or deoxyribonucleotides at non-catalytically critical sites. . . .

The nucleozymes . . . thus essentially are modified ribozymes having at least a portion, or all, of the ribonucleotides replaced with deoxyribonucleotides or NAAs. The nucleozymes are significantly more resistant to degradation than their all-RNA ribozyme counterparts because the chemicals or enzymes present in vivo do not recognize the nucleic acid internucleotide bonds.

The specification defines “catalytically critical sites” to “include sites which, if altered from a ribonucleotide or a NAA to a deoxyribonucleotide, substantially reduces or even eliminates catalytic activity.” Page 13. A “substantial” reduction in catalytic activity in turn is defined as a “reduction which limits the usefulness of the nucleozyme as a catalyst in vitro or in vivo.” Id. The specification describes how to identify catalytically critical sites in a given nucleozyme and discloses that, for example, “[t]he hammerhead nucleozyme has four catalytically critical sites which are the G9, G12, A13 and A29 positions” shown in the application’s Figure 1. Specification, page 14.

Finally, the specification discloses that nucleozymes also “may be used as therapeutic agents introduced in vivo due to their resistance to chemical and enzymatic degradation.” Page 6. Thus, “[a] nucleozyme may be provided in a pharmaceutical composition. The pharmaceutical composition would include at least one nucleozyme and a pharmaceutically acceptable carrier.” Id.

Discussion

1. Written description

The examiner rejected all of the claims on the basis that the specification did not adequately describe the claimed “pharmaceutical composition.” The examiner reasoned that

The specification as filed fails to teach any compositions which would provide for the *in vivo* (whole organism) delivery of ribozymes such that the ribozyme can find its target and cleave the target *in vivo*. The specification is wholly prophetic in this regard and fails to teach any compositions per se which would function as claimed.

Examiner's Answer, page 3. The examiner concluded that the claimed "subject matter . . . was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Id.

Appellants argue that

the claimed pharmaceutical compositions are fully described in the specification such that one skilled in the art would recognize that Appellants were in possession of the compositions at the time of filing the application. . . . [T]he specification describes sufficient relevant identifying characteristics of the compositions, including the functional characteristics of the composition. In addition, the specification provides a detailed drawing of the generic structural and chemical formulas[,] further evidencing Appellants' possession of the claimed enzymatic nucleic acids.

Reply Brief, page 6.

"In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue." Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000). Nonetheless, the disclosure must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. See id.

We agree with Appellants that the examiner has not shown the instant claims to lack an adequate written description in the specification. The claims are directed to a pharmaceutical composition comprising an "enzymatic nucleic acid molecule having a ribonucleotide at a catalytically critical site, at least one deoxyribonucleotide and at least one nucleic acid analog," together with a pharmaceutically acceptable carrier. See claim 74.

The specification, in turn, describes a pharmaceutical composition “includ[ing] at least one nucleozyme and a pharmaceutically acceptable carrier.” Page 6. The specification describes nucleozymes as “ribozyme like molecules . . . [that] have ribonucleotides or nucleic acid analogues (hereinafter NAAs) at catalytically critical sites and NAAs or deoxyribonucleotides at non-catalytically critical sites. The preferred nucleozymes have ribonucleotides at catalytically critical sites.” Page 3. Thus, the specification describes the claimed compositions, albeit not quite in ipso verbis.

The examiner does not seem to dispute that the specification describes, in words, the claimed composition. Rather, his position seems to be that the description is inadequate because it did not show that Appellants were “in possession” of a working, pharmaceutical composition. However, the “possession” test set out in the case law does not require actual, physical possession of the later-claimed product. See Lockwood v. American Airlines Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997): “One shows that one is ‘in possession’ of the invention by describing the invention, with all its claimed limitations. . . . One does that by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention.” (Citation and emphasis omitted.) “Put another way, one skilled in the art, reading the original disclosure, must immediately discern the limitation[s] at issue in the claims.” Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000).

As discussed above, the specification describes the claimed composition in the manner required by 35 U.S.C. § 112. The rejection for inadequate written description is therefore reversed.

2. Enablement

The examiner also rejected all of the claims on the basis of lack of enablement. The examiner asserts that

[o]ne skilled in the art would not accept on its face based on the limited guidance provided in the specification, the ability to deliver the claimed ribozymes via a composition in vivo such that target can be cleaved and further provide some effect within a whole organism. Note Branch who teach[es] that delivery of ribozymes in vivo is a highly unpredictable endeavor. The specification as filed fails to teach with particularity formulations of ribozymes which would necessarily be expected to deliver any ribozymes to a whole organism such that [the] target can be cleaved in the appropriate cells etc... and further where secondary effects might be provided such as for treatment as implied by the pharmaceutical language. Essentially no general guidelines to date are known for [the] successful delivery of ribozymes. Only limited examples are known. To date, undue trial and error experimentation depending on the target would have to be engaged [in] in order to practice the invention as claimed.

Examiner's Answer, pages 3-4.

Thus, the examiner does not seem to seriously dispute that the specification teaches those skilled in the art how to make compositions comprising a nucleozyme and a pharmaceutically acceptable carrier. We understand the examiner's position to be that the specification does not adequately teach how to use such compositions because it does not disclose how to administer the claimed composition so as to produce a therapeutically beneficial effect.

Appellants argue that the examiner

fails to provide any evidence whatsoever that the instant invention would not work for its intended purpose, other than alleging the unpredictability of in vivo efficacy based on the Antisense '97 article, or that ribozyme delivery is an unpredictable art based on the Branch article. Appellants, however, have provided ample data and guidance in the specification and indicated teachings in the art that demonstrate the efficacy of modified enzymatic nucleic acid molecules both in vitro and in vivo. . . . In the absence of any technical reasons and/or references to support its reasoning, the Office has failed to establish a prima facie case of lack of enablement.

Reply Brief, pages 12-13.

“When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. If the PTO meets this burden, the burden then shifts to the applicant to provide suitable proofs indicating that the specification is indeed enabling.” In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

We agree with Appellants that the examiner has not met the burden of providing evidence to support a prima facie case of nonenablement. The examiner provides no Wands-based analysis, based on the particular facts of the application and claims under consideration, supporting a conclusion that undue experimentation would have been required to use the claimed compositions

therapeutically. Instead of providing an analysis tailored to the specific facts of this case, the examiner seems to reason as follows:

- (1) Based on the state of the art, any method of using ribozymes therapeutically would have been considered nonenabled;
- (2) The ribozyme-containing compositions claimed here are intended to be used therapeutically;
- (3) Therefore, the specification cannot have enabled those skilled in the art to use the claimed compositions.

This approach to the enablement analysis is improper. “Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations.” In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are no per se rules of patentability. See In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995). Just as in the § 103 context, the use of per se rules, while undoubtedly less laborious than a searching analysis of the claimed invention, flouts § 112 and the case law applying it. The conclusion of enablement or nonenablement must rest on an individualized analysis of the invention as claimed, including all its limitations, in light of the guidance provided by the specification and the prior art. See Wands, 858 F.2d at 737, 8 USPQ2d at 1404.

In addition to the lack of individualized analysis, the examiner’s rejection also suffers from lack of evidentiary support. The only evidence the examiner cites in the statement of the rejection is an article by Branch. He characterizes Branch as teaching that “delivery of ribozymes in vivo is a highly unpredictable endeavor.” Examiner’s Answer, page 4. This characterization is not entirely

accurate. First, most of Branch is directed antisense therapy, not ribozymes. In addition, although the examiner focuses on problems relating to delivery of ribozymes in vivo, Branch's focus is on the difficulty involved in choosing an appropriate target site in a substrate RNA. To the extent that ribozyme target selection is relevant to the instant claims, it would seem to relate more to the scope of claims such as claim 74, which recites no structural limitations on the design of the recited nucleozyme, rather than, as the examiner would have it, to delivery of ribozymes in vivo. Branch does not state that delivery of ribozymes in vivo is problematic and therefore does not provide evidence to support the examiner's position.

Finally, "[i]t is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification." In re Sneed, 710 F.2d 1544, 1548, 218 USPQ 385, 388 (Fed. Cir. 1983). Terms appearing in the preamble of a claim do not necessarily limit the scope of the claim. See IMS Technology, Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, 54 USPQ2d 1129, 1137 (Fed. Cir. 2000) ("If the preamble adds no limitations to those in the body of the claim, the preamble is not itself a claim limitation and is irrelevant to proper construction of the claim.").

Here, the claims are directed to a "pharmaceutical composition" comprising a nucleozyme and a pharmaceutically acceptable carrier. See, e.g., claim 74. The preamble does not add any limitations to those appearing in the body of the claim and therefore does not further limit the claim. According to the broadest reasonable interpretation, therefore, the claims read on any

composition that comprises a nucleozyme and a pharmaceutically acceptable carrier such as water or saline. This interpretation is consistent with the specification, which discloses that nucleozymes can be used in applications other than therapy. See the specification, pages 5-6:

The present invention also pertains to methods of using the nucleozymes. . . . For example, a nucleozyme may be used as a ribonuclease, ligase, phosphotransferase, acid phosphatase, polymerase, or an RNA restriction endonuclease. . . .

The nucleozymes also may be used as therapeutic agents introduced in vivo due to their resistance to chemical and enzymatic degradation.

Under the examination procedures laid out in the Manual of Patent Examining Procedure (MPEP), an applicant need not enable every method of using a product in order to enable those skilled in the art to make and use the product itself; enabling a single method of using the product is sufficient. See MPEP § 2164.01(c) (“If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use.”).¹ The examiner has not addressed the alternative, non-therapeutic methods of using the claimed composition, nor provided any fact-based analysis of why these methods of using the claimed composition would have required undue experimentation.

¹ “While the MPEP does not have the force of law, it is entitled to judicial notice as an official interpretation of statutes or regulations as long as it is not in conflict therewith.” Molins PLC v. Textron, Inc., 48 F.3d 1172, 1180 n.10, 33 USPQ2d 1823, 1828 n.10 (Fed. Cir. 1995). See also Ethicon, Inc. v. Quigg, 849 F.2d 1422, 1425, 7 USPQ2d 1152, 1154 (Fed. Cir. 1988) (“The MPEP states that it is a reference work on patent practices and procedures and does not have the force of law, but it ‘has been held to describe procedures on which the public can rely.’”).

Summary

The examiner has not established that the claimed compositions are not adequately described or that they would have required undue experimentation to make or use. The rejections under 35 U.S.C. § 112, first paragraph, are reversed.

REVERSED

SHERMAN D. WINTERS)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
WILLIAM F. SMITH)	
Administrative Patent Judge)	APPEALS AND
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)	INTERFERENCES
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ERIC GRIMES)	
Administrative Patent Judge)	

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RIBOZYME PHARMACEUTICALS INC.
2950 WILDERNESS PLACE
BOULDER, CO 80301

EG/jlb