

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 44

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RALPH R. WEICHSELBAUM, DENNIS E. HALLAHAN,
VIKAS P. SUKHATME, and DONALD W. KUFE

Appeal No. 1999-1458
Application No. 07/943,812

ON BRIEF¹

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

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 3-21, 36, 38-41, 48-50 and 52-59, which are all the claims pending in the application.

¹ Pursuant to appellants request (Paper No. 39, received September 18, 1998) an oral hearing for this appeal was scheduled for Tuesday, October 9, 2001. Appellants, however, waived (Paper No. 43, received October 2, 2001) their request for oral hearing. Accordingly, we considered this appeal on Brief.

Claim 1 is illustrative of the subject matter on appeal and is reproduced

below:

1. An isolated and purified DNA molecule comprising a radiation responsive enhancer-promoter operatively linked to an encoding region that encodes at least one polypeptide, other than CAT, that one desires to have expressed in a radiation responsive manner, which encoding region is operatively linked to a transcription-terminating region, wherein said radiation responsive enhancer-promoter comprises a portion of the CArG domain from -550 to -50 of an Egr-1 promoter or a c-jun promoter.

The references relied upon by the examiner are:

Hung et al. (Hung)	4,370,417	Jan. 25, 1983
Mark et al. (Mark)	4,677,064	Jun. 30, 1987
Brent et al. (Brent)	4,833,080	May 23, 1989
Orr et al. (Orr)	4,835,098	May 30, 1989

Johnsson et al. (Johnsson), "The c-sis Gene Encodes a Precursor of the B Chain of Platelet-Derived Growth Factor," The EMBO Journal, Vol. 3, No. 5, pp. 921-928 (1984)

Angel et al. (Angel), "The Jun Proto-Oncogene is Positively Autoregulated by Its Product, Jun/AP-1," Cell, Vol. 55, pp.875-885 (1988)

Bonthron et al. (Bonthron), "Platelet-Derived Growth Factor A Chain: Gene Structure, Chromosomal Location, and Basis for Alternative mRNA Splicing," Proc. Natl. Acad., Vol. 85, pp. 1492-1496 (1988)

Christy et al. (Christy), "A Gene Activated in Mouse 3T3 Cells by Serum Growth Factors Encodes a Protein With 'Zinc Finger' sequences," Proc. Natl. Acad., Vol. 85, pp. 7857-7861 (1988)

Ghosh et al. (Ghosh), "Cloning of the p50 DNA Binding Subunit of NF- κ B: Homology to rel and dorsal," Cell, Vol. 62, pp. 1019-1029 (1990)

Moolten et al. (Moolten), "Curability of Tumors Bearing Herpes Thymidine Kinase Genes Transferred by Retroviral Vectors," Journal of the National Cancer Institute, Vol. 82, No. 4, pp. 297-300 (1990)

GROUND OF REJECTION

Claims 1, 3-21, 36, 48 and 52-55 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of nucleotide numbers because the frame of reference is not clearly defined.

Claims 1, 3-21, 36, 38-41, 48-50 and 52-59 stand rejected under 35 U.S.C. § 103 as being unpatentable over Christy or Angel in view of any one of Bonthron, Johnsson, Mark, Moolten, Hung, Orr, Ghosh or Brent.

We reverse and raise other issues for the examiner's consideration.

DISCUSSION

In reaching our decision in this appeal, we considered appellants' specification and claims, in addition to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer² for the examiner's reasoning in support of the rejections. We further reference appellants' Brief³, and appellants' Reply Brief⁴ for the appellants' arguments in favor of patentability. We note the examiner entered and considered the Reply Brief.⁵

² Paper No. 38, mailed July 14, 1998.

³ Paper No. 37, received May 11, 1998.

⁴ Paper No. 39, received September 18, 1998.

⁵ Paper No. 40, mailed October 1, 1998.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH:

As set forth in Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., 927 F.2d 1200, 1217, 18 USPQ2d 1016, 1030 (Fed. Cir. 1991):

The statute requires that “[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.” A decision as to whether a claim is invalid under this provision requires a determination whether those skilled in the art would understand what is claimed. See Shatterproof Glass Corp. v. Libbey-Owens Ford Co., 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir. 1985) (Claims must “reasonably apprise those skilled in the art” as to their scope and be “as precise as the subject matter permits.”).

Furthermore, claim language must be analyzed “not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary skill in the pertinent art.” In re Moore, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971).

According to the examiner (Answer, page 4) “[c]laims 1, 54 and 55 are indefinite in their recitation of nucleotide numbers because the frame of reference (i.e. which base is “0” or “1”) is not clearly defined.” In response, appellants argue (Brief, page 5) that:

[A]s a matter of scientific convenience, the base numbering of upstream regulatory regions typically relates to the start of transcription for the corresponding gene. Thus, even if there were no information in the literature on the numbering for these particular genes, and no guidance in the instant specification as to what regions are encompassed by the recitation of “-550 to -50,” the claims would, nonetheless, be clear. Those of skill in the art would understand the claims to include those residues that are 50 to 550 bases upstream of the translational start site, simply by convention.

With reference to page 14, "Scheme 1" of the specification, appellants argue (Brief, page 6) that this "convention is used in the instant specification." However, the examiner argues (Answer, page 7) that while "[a]ppellants argue that one skilled in the art would know that nucleotide '0' is the transcriptional start site ... the convention is that the transcriptional start site is nucleotide '1,' not '0'." In response, appellants argue (Reply Brief, page 4) "the 'conventional' numbering to which the examiner refers, where '+1' is the start, also used [sic] '-1' as one base before the start. Thus, '-550 to -50' is the same for both." We agree with appellants. We also note that in "SCHEME 1" of the specification (page 14) "+1" is defined as "0".

The examiner also finds (Answer, page 7) that "Angel et al. indicate that the jun gene has at least three transcriptional start sites. They state, '[t]he major start site of transcription was arbitrarily numbered +1' (Fig. 4) and later refer to 'two minor start sites' (p. 878, col. 1)." In response, appellants argue (Reply Brief, page 4), "Scheme 1 indicates the general position of the defined start site, if for no other reason, than the spacing of the six CArG domains." As we noted above, "SCHEME 1" of the specification (page 14) defines "+1" as "0." Therefore, regardless of the existence "minor start sites," Angel defined the "+1" site, this site to appellants specification is defined as "0" and is therefore the "frame of reference" from which -550 to -50 are determined.

Therefore, in our opinion, the claims reasonably apprise those skilled in the art as to their scope. Accordingly, we reverse the rejection of claims 1, 3-21, 36, 48 and 52-55 under 35 U.S.C. § 112, second paragraph.

THE REJECTION UNDER 35 U.S.C. § 103:

The examiner finds (Answer, bridging sentence, page 4) that Christy “disclose[s] DNA constructs comprising the Egr-1 ... promoter linked to the CAT reporter gene... [demonstrating] that a heterologous gene can be expressed under control of the Egr-1 promoter....” In addition, the examiner finds (Answer, page 5) that Angel “demonstrate[s] that a heterologous gene can be expressed under control of the c-jun promoter....” However, the examiner finds (id.) that “[n]either Christy et al. nor Angel et al. disclose DNA constructs in which the promoter is linked to a gene encoding a ‘therapeutic’ polypeptide.”

To make up for the deficiency of Christy and Angel, the examiner relies (Answer, page 5) on any one of Bonthron, Johnsson, Mark, Moolten, Hung, Orr, Ghosh or Brent, which teach the coding sequence of various proteins. With this the examiner concludes (Answer, page 6) that:

It would have been obvious to one of ordinary skill in the art at the time the invention was made to link either of the promoters taught by Christy et al. and Angel et al. to any of the coding sequences disclosed by Bonthron et al., Johnsson et al., Mark et al., Moolten et al., Hung et al., Orr et al., Ghosh et al. or Brent et al., in order to express the coding sequence.

According to the examiner (Answer, page 8) a person “of ordinary skill in the art knew that any coding sequence could be linked to any promoter for expression of the coding sequence. It is obvious to substitute known equivalents for the same purpose, even if there is not an express suggestion to substitute one equivalent component for another....” On the surface, the examiner appears to make out a reasonable prima facie case of obviousness. We note that when the prior art recognizes two components to be equivalent, an express suggestion to

substitute one for another need not be present in order to render such substitution obvious. In re Fout, 675 F.2d 297, 301, 213 USPQ 532, 536 (CCPA 1982).

According to appellants (Brief, page 9), the examiner ignored their unexpected results. Specifically, appellants argue (Brief, pages 9-10) that “[t]here is no teaching or suggestion in the prior art regarding the radiation inducibility of the claimed constructs ... [t]he examiner has not disputed these facts and even admits that the radiation inducibility of the claimed constructs was nonobvious.” To this the examiner argues (Answer, page 9), “[t]here is no evidence of unexpected results. Radiation inducibility is a previously unknown property of the jun and Egr-1 promoters, not an unexpected result of combining the promoters with any coding sequence other than CAT.” Once again, on the surface, there is some merit to the examiner’s argument. As set forth in In re Dillon, 919 F.2d 688, 693, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc):

There is no question that all evidence of the properties of the claimed compositions and the prior art must be considered in determining the ultimate question of patentability, but it is also clear that the discovery that a claimed composition possesses a property not disclosed for the prior art subject matter, does not by itself defeat a prima facie case. ... [In re Shetty, 566 F.2d 81, 86, 195 USPQ 753, 756 (CCPA 1977)]. Each situation must be considered on its own facts, but it is not necessary in order to establish a prima facie case of obviousness that both a structural similarity between a claimed and prior art compound (or a key component of a composition) be shown and that there be a suggestion in or expectation from the prior art that the claimed compound or composition will have the same or a similar utility as one newly discovered by applicant.

In In re Shetty, 566 F.2d 81, 86, 195 USPQ 753, 756 (CCPA 1977), the court found that:

Appellant merely shows that his novel compounds are appetite suppressants whereas the reference compounds are not so known. ... Presented with such an absence of comparative or other evidence with respect to the properties of the compounds and the claimed composition, we hold that [the] composition ... would have been obvious from and unpatentable over the prior art.

These cases appear to be consistent with the examiner's conclusion (Answer, page 11) that "[a]ppellants discovered that the promoters are ... induced by radiation. On the basis of this discovery, they wish to exclude others from using the promoters in combination with any coding sequence other than CAT, for any purpose. The [e]xaminer's interpretation of the law is that this is not permitted." But, if one looks under the surface, the facts of record in this case do not lead to the examiner's conclusion.

The claimed invention is drawn to "[a]n isolated and purified DNA molecule comprising a radiation responsive enhancer-promoter operatively linked to an encoding region that encodes at least one peptide, other than CAT..." According to the examiner (Answer, page 9), that the claimed promoter is radiation responsive is an inherent property of the promoter; it is not the "unexpected" result of combining this regulatory sequence (promoter) with a structural sequence other than CAT. We agree with this part of the examiner's analysis. However, the analysis does not end there.

In responding to appellants' arguments it appears that the examiner more fully develops his prima facie case of obviousness. According to the examiner (Answer, pages 8-9) "[t]hose of ordinary skill in the art knew that any coding sequence could be linked to any promoter for expression of the coding sequence. It is obvious to substitute known equivalents for the same purpose,

even if there is not an express suggestion to substitute one equivalent component for another.” It is this statement, however, that illustrates the deficiency in the examiner’s prima facie case. As we understand the examiner’s reasoning, as a general proposition, it would have been obvious to substitute known equivalent coding sequences, or known equivalent promoters.

It is, however, not entirely clear on this record what the examiner may mean by equivalent coding sequences. Furthermore, we find that the examiner has not established that the coding sequences are “equivalent.” Instead, the examiner finds (Answer, page 5) that each coding sequence encodes a different protein. Without a showing of equivalence the examiner has not established a prima facie case of obviousness.

That leaves the promoters. The examiner’s position appears to be, since the promoters of either Angel or Christy are “equivalent” to the promoters set forth in the secondary references it would be obvious to substitute one for the other. The examiner, however, failed to demonstrate that any of the promoters used by the secondary references are in fact radiation responsive, and therefore “equivalent” to the promoter of either Angel or Christy. Stated differently, there is no evidence on this record demonstrating that the promoters of the secondary references are radiation responsive. Therefore, there is no evidence on this record that the Angel or Christy promoters are equivalent to the promoters of the secondary references. Without a showing of equivalence the examiner has not established a prima facie case of obviousness.

In contrast to the facts in evidence on this record, in Dillon, 919 F.2d at 692, 16 USPQ2d at 1900-01 there was an art recognized equivalence between the tri-orthoesters of the primary reference and the tetra-orthoesters of the secondary reference. In Shetty, cited in Dillon, the structural similarity between the prior art compound and the claimed compound was such that one would have expected the two compounds to possess similar properties; evidence of unexpected properties was not of record. On this record, there is no evidence that the prior art structural genes are equivalent to each other. Furthermore, there is no evidence that appellants' promoter is equivalent to the prior art promoters. In addition, appellants demonstrate that their promoter has an unexpected advantage over other promoters (such as those found in the secondary references); specifically appellants' promoter is radiation responsive.

On reflection, in our opinion, there is no suggestion for combining the teachings of the references relied upon by the examiner in a manner that would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On this record, the examiner failed to provide the evidence necessary to support a prima facie case of obviousness. Accordingly, we reverse the rejection of claims 1, 3-21, 36, 48-50 and 52-59 under 35 U.S.C. § 103 as being unpatentable over Christy or Angel in view of any one of Bonthron, Johnsson, Mark, Moolten, Hung, Orr, Ghosh or Brent.

OTHER ISSUES:

We offer the following observations for the examiner's consideration.

I. Tsai-Morris:

Upon review of this administrative file, we note that Tsai-Morris⁶ appears to correspond to at least claim 1 of appellants' claimed invention. Specifically, Tsai-Morris teach "the isolation of a mouse Egr-1 genomic clone, its intron-exon structure and 935 bp of 5' flanking sequence. The gene spans about 3.8 kb and consists of 2 exons and one 700 bp intron." See abstract. In addition, Tsai-Morris teach (id.) that this clone contains "five elements whose sequence is nearly identical to the inner core 10 nucleotide region (CCATATTAGG) of the c-Fos serum response element..." We note that appellants specification defines the claimed CArG domain as a "serum response or CC(A/T)₆GG" domain. In addition, we note that this DNA molecule is expected to encode at Egr-1, which is a polypeptide other than CAT.

Upon return of this application, the examiner should take a step back and determine whether Tsai-Morris anticipates the claimed invention. In this regard, we note as set forth in In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990):

discovery of an unobvious property and use does not overcome the statutory restraint of section 102 when the claimed composition is known. While Spada's position is that his polymers are not anticipated by the polymers of Smith because their properties are different, Spada was reasonably required to show that his polymer compositions are different from those described by Smith. This burden was not met by simply including the assertedly different properties in the claims. When the claimed compositions are not

⁶Tsai-Morris et al. (Tsai-Morris), "5' flanking sequence and genomic structure of Egr-1, a murine mitogen inducible zinc finger encoding gene," Nucleic Acids Research, Vol. 16, No. 18, pp. 8835-8846 (1988).

novel they are not rendered patentable by recitation of properties, whether or not these properties are shown or suggested in the prior art.

II. Written Description:

As set forth in UC v. Eli Lilly and Co., 119 F. 3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997) “an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself.” Furthermore, Lilly 119 F.3d at 1568, 43 USPQ2d at 1406, indicates, “[a] definition by function ... does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.” In this regard, we note, for example, that unlike appellants’ claim 1, wherein the radiation responsive enhancer-promoter comprises a portion of the Egr-1 or c-jun promoter, claims 56-59 are broadly drawn to any “isolated and purified DNA molecule comprising a radiation responsive enhancer promoter.”

Upon return of this application, the examiner should take a step back and determine whether appellants’ specification provides an adequate written description of any “isolated and purified DNA molecule comprising a radiation responsive enhancer promoter” as set forth in claims 56-59.

REVERSED

Sherman D. Winters)
Administrative Patent Judge)
)

Appeal No. 1999-1458
Application No. 07/943,812

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

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Appeal No. 1999-1458
Application No. 07/943,812

Ronald B. Cooley
Arnold, White & Durkee
P.O. Box 4433
Houston, TX 77210