

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte ELLIS L. REINHERZ, JIRI NOVOTNY, STEPHEN T. SMILEY,  
PING LI and RAMESH GANJU

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Appeal No. 94-1483  
Application No. 07/695,141<sup>1</sup>

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ON BRIEF

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Before WINTERS and WILLIAM F. SMITH, Administrative Patent Judges, and MCKELVEY, Senior Administrative Patent Judge.

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 2 through 16, 18, 20 through 22, 24 through

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<sup>1</sup> Application for patent filed May 8, 1991. According to appellants, this application is a continuation-in-part of Application No. 07/523,632, filed May 15, 1990, now abandoned.



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Chaudhary et al. publication in view of the Becker et al. and Mariuzza et al. publications" (Examiner's Answer, page 3, last paragraph).

On consideration of the record, including the Appeal Brief (Paper No. 22) and the Examiner's Answer (Paper No. 23), we reverse the examiner's rejection under 35 U.S.C. § 103. We enter new grounds of rejection based on the description and enablement requirements of 35 U.S.C. § 112, first paragraph.

#### THE EXAMINER'S REJECTION

On reflection, we find that when all the prior art is considered together, one of ordinary skill in the art would not have a sufficient basis for the requisite, reasonable expectation of success to sustain a rejection under 35 U.S.C. § 103. Nor do the cited references provide an enabling disclosure necessary to sustain this rejection. The examiner's rejection is reversed.

#### NEW GROUNDS OF REJECTION

Under the provisions of 37 CFR § 1.196(b), we enter the following new grounds of rejection.

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Description Requirement, 35 U.S.C. § 112, First Paragraph

Claims 14 through 16, 18, 20 through 22, 24 through 28, and 32 through 34 are rejected under 35 U.S.C. § 112, first paragraph, as based on an inadequate written description of the claimed invention.

These claims are drawn to (1) genetic material, including DNA; (2) an expression vector containing DNA; (3) a prokaryotic or eukaryotic host cell containing the expression vector; and

(4) a method of culturing the host cell. They all fall short of complying with the written description requirement of the statute because appellants' specification does not provide the kind of specificity necessary to support them.

As stated in Univ. of Cal. v. Eli Lilly and Co., 119 F.3d 1559, 1566-69, 43 USPQ2d 1398, 1404-07 (Fed. Cir. 1997), an adequate written description of genetic material, such as DNA or cDNA, requires a precise definition, e.g., by structure, formula, chemical name, or physical properties. A mere wish or plan for obtaining the claimed chemical invention, or a general method for obtaining the genetic material involved, will not do. What is required is a description of the DNA

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itself. Speaking in terms of human insulin-encoding cDNA, the court stated that "[d]escribing a method of preparing a cDNA or even describing the protein that the cDNA encodes . . . does not necessarily describe the cDNA itself." Univ. of Cal., 119 F.3d at 1567, 43 USPQ2d at 1405. The court emphasized that a high degree of specificity is required in describing and supporting claims to genetic material. This is not accomplished by setting forth the name of the protein that cDNA encodes. In this context, the court stated that "[a] definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is." Univ. of Cal., 119 F.3d at 1568, 43 USPQ at 1406. The best way of complying with the written description requirement, perhaps the only way, is to set forth the precise sequence of nucleotides that make up the claimed genetic material.

Here, appellants set forth the nucleotide sequence for a fluorescein-specific single chain T-cell receptor. See Figure 2 of the specification. Claims 14 through 16, 18, 20 through 22, 24 through 28, and 32 through 34, however, are not limited to that subject matter. Rather, the claims recite genetic

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material coding for soluble, single chain T-cell receptors for a wide variety of different antigens. With respect to all antigens except fluorescein, the specification does not set forth a precise definition of the genetic material involved, e.g., by the description of a representative number of nucleotide sequences. Therefore, consistent with the principles enunciated in Univ. of Cal., 119 F.3d at 1566-69, 43 USPQ2d at 1404-07, we find that claims 14 through 16, 18, 20 through 22, 24 through 28, and 32 through 34 fall short of complying with the written description requirement of the statute because appellants' specification does not provide the kind of specificity necessary to support them.

Enablement Requirement, 35 U.S.C. § 112, First Paragraph

Claims 2 through 16, 18, 20 through 22, 24 through 28 and 31 through 34 are rejected under 35 U.S.C. § 112, first paragraph, as based on a non-enabling disclosure.

The claimed invention is directed to a soluble, single chain polypeptide comprising a Ti \$ subunit fragment joined to a Ti " subunit fragment by an amino acid linker (claim 3) and a similar soluble, single chain polypeptide comprising a Ti ( subunit fragment joined to a Ti \* subunit fragment, also by an

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amino acid linker (claim 4). Further, appellants claim nucleic acids having a sequence coding for a soluble, single chain polypeptide recited in claim 3 (claim 14).

As explained in the paragraph bridging pages 1 and 2 of the specification (citations omitted):

The T cell receptor (TCR) is a molecular complex consisting of multiple subunits that mediate the recognition of antigen in the context of a particular major histocompatibility complex (MHC) product. . . . The antigen/MHC binding moiety, termed Ti, is a disulfide-linked heterodimer of 90 kD consisting of one " and one \$ subunit on the majority of peripheral T lymphocytes. Both subunits are immunoglobulin-like, being composed of variable and constant domains, the former encoding the unique specificity of a given T cell clone. Ti, in turn, is non-covalently associated with a set of four invariant monomorphic subunits ((, \*, , and .), collectively termed CD3. All six receptor subunits are trans-membrane proteins and all but the , and . subunits possess N-linked glycan moieties. The Ti " and \$ subunits likely form a binding site for antigen and major histocompatibility complex (MHC) through interaction of their variable domains whereas the CD3 subunits are thought to subserve signal transduction functions. In addition, it is known that a subpopulation of T cells (# 5% of peripheral T lymphocytes) exist that contain T cell receptors which contain Ti ( and Ti \* subunits that form heterodimers which form a binding site for antigen and MHC through interaction of their variable domains. Furthermore, there is now direct evidence to show that at least in the case of one nominal antigen which is a hapten, there is a subsite on the Ti molecule which directly binds hapten in the absence of MHC with an affinity constant of  $10^{-5}$ .

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TCRs are further explained at page 2, lines 19 through 31 of the specification as follows:

Each  $T_i$  " and  $S$  subunit contains two extracellular domains, created by intrachain disulfide bonding of cysteine residues and a carboxy terminal hydrophobic transmembrane region followed by 5-6 amino acid cytoplasmic tails. The genes encoding the T cell receptor are assembled from separate gene segments, one of which encodes an invariant carboxy terminal constant region, while two or three other segments (V, D and J) encode the variable region of the molecule which recognizes antigen and MHC. Within the variable region are three regions of hypervariability that form the antigen binding pocket.

An indication of the scope of the claims on appeal appears at page 6, lines 7 through 21 of the specification as follows:

[T]he biologically active, soluble, single chain T cell receptor of the present invention binds at least one antigen which is bound by a T cell receptor present on the surface of a T lymphocyte of mammalian origin. Typically, the biologically active, soluble, single chain T cell receptor is capable of binding the antigen or antigens it would bind as a component of a complete T cell receptor, either alone or in the context of a particular major histocompatibility molecule. However, biologically inactive single chain T cell receptors also have value, for example, as immunogens to initiate in a mammalian host an immune response against a particular T cell subtype.

A further indication of the scope of the present claims appears at page 8, lines 14 through 26 of the specification:

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The present invention includes soluble, single chain T cell receptors in which the portions of the subunit fragments used are unmodified (i.e., the sequence used is the same as is present in the corresponding naturally occurring T cell receptor subunit), modified (i.e., the sequence of the naturally occurring T cell receptor subunit has been changed by the deletion, addition or substitution of at least one amino acid residue, for example, by replacing one or more hydrophobic amino acid residues with hydrophilic amino acid residues), or a combination of modified and unmodified subunit fragments.

Polypeptide claims 3, 4, and nucleic acid claim 14, are each directed to a genus of compounds seemingly unlimited in scope because, for every antigen-MHC complex which can be formed, there is a corresponding T cell receptor which would comprise either Ti \$ and " subunits or Ti ( and \* subunits. Each combination of Ti " and \$ subunits or Ti ( and \* subunits would uniquely recognize each unique antigen.

As stated in In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971):

[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason

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for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling.

As recognized in Marzocchi, 439 F.2d at 223, 169 USPQ at 370, the unpredictability of a technical field may "alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim."

The information relied on to establish enablement in this application includes a single success said to have been achieved by appellants in obtaining the nucleotide sequence coding for a fluorescein-specific single chain T-cell receptor. The following, relatively broad statement is set forth at page 11, lines 5 through 20 of the specification:

The soluble, single chain T cell receptors of the present invention may be produced using various methods. For example, they may be obtained by synthetic means, i.e., chemical synthesis of the polypeptide from its component amino acids, by methods known to those of ordinary skill in the art. For example, the solid phase procedure described by Houghton et al., Proc. Natl. Acad. Sci. 82:5135 (1985) may be employed. It is preferred that the soluble, single chain T cell receptors be obtained by production in prokaryotic or eukaryotic host cells expressing a DNA sequence coding for the single chain T cell receptors as described herein, or by in vitro translation of the mRNA encoded by

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the DNA sequence coding for the single chain T cell receptors.

In addition, the specification indicates at page 12, lines 22 through 31 that:

It should be understood that the methodology described herein can be used to prepare soluble, single chain T cell receptors derived from animal species other than humans, and soluble, single chain T cell receptors for a wide variety of different antigens, for example, fluorescein, foreign major histocompatibility molecules (MHC) and peptide antigens in the context of MHC molecules. These variations are included within the scope of the present invention.

In sum, appellants have described a single specific nucleic acid coding for unique Ti " and \$ subunits. In order to make and use other soluble, single chain polypeptides or corresponding nucleic acids according to the present invention, appellants refer one skilled in the art to conventional "methodology."

As explained in PPG Indus. Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996):

In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. See, e.g., In re Goodman, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993); Amgen, Inc. v. Chugai

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Pharmaceutical Co., 927 F.2d 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991); In re Vaeck, 947 F.2d at 496, 20 USPQ2d at 1445. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." Atlas Powder Co., v. E.I. DuPont de Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of Appeals summarized the point well when it stated:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (1982).

On these facts, we believe that a hypothetical person skilled in the art could not make and use the claimed invention<sup>2</sup>

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<sup>2</sup> Though we have discussed only claims 3, 4 and 14 in setting forth our reasons in support of this rejection, nevertheless, the rejection extends to all claims pending. We have reviewed each claim and find that no claim further limits the independent claims in a substantive manner regarding the scope of the Ti " and \$ subunit or the Ti ( and \* subunit polypeptides or corresponding nucleic acids. Rather, the dependent claims are directed to other peripheral aspects of the invention beyond the polypeptides and nucleic acid sequences required to make and use the claimed invention throughout its scope.

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throughout its scope without undue experimentation. The specification does not provide sufficient guidance explaining how such hypothetical person could make and use other polypeptides or nucleic acid sequences within the scope of the claims on appeal. As set forth in Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997):

Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

The facts in this case are similar to those reported in Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d at 1213-14, 18 USPQ2d at 1027 where the court determined that the disclosure under review did not provide adequate support for "Amgen's desire to claim all EPO gene analogs." The court observed that "Amgen has claimed every possible analog of a gene containing about 4,000 nucleotides, with a disclosure only of how to make EPO and a very few analogs." Here, appellants teach how to make only one soluble, single chain polypeptide comprising a Ti \$ subunit fragment joined to a Ti

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" subunit fragment by an amino acid linker, and a corresponding nucleic acid sequence coding therefore, while claiming a vast array of hypothetical soluble, single chain polypeptides and corresponding nucleic acid sequences of the general type discussed in the specification.

For these reasons, we newly reject claims 2 through 16, 18, 20 through 22, 24 through 28 and 31 through 34 under 35 U.S.C.

§ 112, first paragraph, as based on a non-enabling disclosure.

This decision contains new grounds of rejection pursuant to 37 CFR § 1.196(b) (amended effective Dec. 1, 1997, by final rule notice, 62 Fed. Reg. 53,131, 53,197 (Oct. 10, 1997), 1203 Off. Gaz. Pat. & Trademark Office 63, 122 (Oct. 21, 1997)). 37 CFR § 1.196(b) provides, "[a] new ground of rejection shall not be considered final for purposes of judicial review."

37 CFR § 1.196(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 proceedings (37 CFR § 1.197(c) as to the rejected claims:

(1) Submit an appropriate amendment of the claims so rejected or a showing of facts relating to

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the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner . . . .

(2) Request that the application be reheard under § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record . . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED - 37 CFR § 1.196(b)

	SHERMAN D. WINTERS	)	
	Administrative Patent Judge	)	
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	WILLIAM F. SMITH	)	BOARD OF
PATENT	Administrative Patent Judge	)	APPEALS AND
		)	INTERFERENCES
		)	
		)	
	FRED E. McKELVEY	)	
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