

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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

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

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Ex parte ELLEN S. VITETTA, VICTOR F. GHETIE,  
JOAN SMALLSHAW and ROXANA G. BALUN

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Appeal No. 2006-1032  
Application No. 09/698,551

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HEARD: May 11, 2006

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Before SCHEINER, GRIMES and GREEN, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a method of eliciting an immune response to ricin A chain by immunizing an animal with a ricin A chain that has been altered so that its ability to cause vascular leak syndrome is reduced, and its native catalytic activity is reduced or absent. The examiner has rejected the claims as lacking enablement, and as lacking adequate written descriptive support. We have jurisdiction under 35 U.S.C. § 134. We reverse these rejections.

Background

Ricin is an enzymatic toxin consisting of two polypeptide chains, A and B. The ricin B chain contains galactose-binding sites that allow the complete toxin to be taken up

by a cell. The ricin A chain, once inside the cell, catalyzes a ribosome-inactivating reaction which shuts down protein synthesis. In addition to its ribosome-inactivating activity, the ricin A chain induces vascular leak syndrome (VLS), which may result in kidney damage, aphasia, and pulmonary edema. A single active molecule of the A chain is sufficient to kill a cell. Specification, pages 2-3.

“Various residues have been identified whose mutation produces catalytically inactive ricin A chain” (id., page 3). In addition, “[a]n amino acid motif (x)D(y) has been identified in [the ricin A chain] . . . that contributes to VLS” and “[m]utations in this sequence have been shown to reduce the ability of a peptide to produce the effects associated with VLS” (id., pages 2-3).

The present invention is directed to a method of eliciting an immune response to ricin A chain by immunizing an animal with a ricin toxoid – an immunogenic ricin A chain with reduced or absent catalytic activity, and a reduced ability to induce vascular leak syndrome. Id., page 4.

#### The Claims

Claims 1-6, 48-53, 56, 57, 59, 63, 65, 66, 68, 69, 71-77, 82 and 84-91 are the subject of appeal: claims 1-6, 48-53, 57, 59, 63, 66, 68, 69, 71-76 and 84-90 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement and adequate written descriptive support; in addition, claims 53, 56, 65, 77, 82 and 91 stand rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. Claims 54, 55, 58, 60-62, 64, 67, 70, 78-81 and 83 are also pending, but have been indicated to be allowable if rewritten in independent form. Claims 1 and 53 are representative of the subject matter on appeal and read as follows:

1. A method of eliciting an immune response to ricin A chain, comprising the steps of:

a) obtaining an altered ricin A chain having an amino acid sequence that has been altered relative to a ricin A chain toxin sequence of SEQ ID NO:1, to comprise:

i) a mutation in at least one of L74, D75, and V76, wherein said altered ricin A chain has reduced ability to cause vascular leak syndrome relative to ricin A chain toxin, and

ii) a mutation in at least one of Y80, Y123, E177, R180, N209, and W211, wherein said altered ricin A chain has reduced or absent catalytic activity; and

b) contacting said altered ricin A chain with an animal in an amount sufficient to elicit an immune response to ricin A chain toxin, wherein an immune response to ricin A chain toxin is elicited in said animal.

53. The method of claim 1, wherein said altered ricin A chain comprises:

- a) at least one of a L74A, D75A, D75E, D75N, V76M, or V76A mutation; and
- b) at least one of a Y80A or a E177D mutation.

### Discussion

#### Scope of Enablement

Claims 1-6, 48-53, 57, 59, 63, 66, 68, 69, 71-76 and 84-90 stand rejected under 35 U.S.C. § 112, first paragraph, because “the specification does not enable any person skilled in the art . . . to make and use the invention commensurate in scope with these claims.” Examiner’s Answer, page 4. The examiner notes that the altered ricin A chains used in the claimed method “encompass[ ] an extreme[ly] large combination of mutations” (id.), but “[t]he specification discloses only five specific amino acid substitutions in the vascular leak region . . . and only two specific amino acid substitutions in the catalytic site” (id.). According to the examiner, “predicting what changes can be made to the amino acid sequence of ricin A chain . . . [that] will [both]

retain [ ] structure and reduce vascular leak and enzyme activity in the toxin as a vaccine is unpredictable” (id., page 6), thus, “it would require undue experimentation of one skilled in the art to practice the claimed invention” (id., page 7) using “altered ricin A chain[s] other than the ones specifically exemplified” in the specification (id.).

“[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). “That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is ‘undue.’” In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (emphasis original). Whether the amount of experimentation required is undue is determined by reference to the well-known Wands factors. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In this case, we agree with appellants that the examiner has not established that practicing the full scope of the claims would have required undue experimentation. As appellants point out, “the specification identifies L74, D75, and V76 . . . of SEQ ID NO:1 as the VLS-inducing site of ricin A chain” (Brief, page 21), and “provides working examples demonstrating that mutations in the LDV sequence (specifically, L74A, D75N, D75A, D75E, and V76A) reduce the ability of ricin A chain to induce VLS” (id., pages 21-22). “The specification [also] identifies residues Y80, Y123, E177, R180, N209, and W211 of SEQ ID NO:1 as the enzymatic active site of ricin A chain” (id., page 21), and “provides working examples [demonstrating that] mutations in the enzymatic active site (specifically E177D and Y80A) . . . reduce catalytic activity” (id., page 22). In addition, “three methods . . . for assaying VLS-inducing ability [are] described in the specification”

(id., page 24), as are “[t]wo methods . . . for assaying ricin A chain catalytic activity” (id.). Finally, “the successful vaccination of an animal with a recombinant ricin A chain is described in the specification” (id., page 25). Thus, the specification teaches where to modify the amino acid sequence of the ricin A chain to reduce its catalytic activity and/or its ability to induce VLS, and demonstrates that a modified ricin A chain can retain its immunogenicity. See e.g., pages 6, 13, 15, 21 and 75-87 of the specification.

We accept, for the sake of argument, that it would be iterative and time consuming to produce and test multiple polypeptides with different combinations of modifications at the specified sites, and that many of the possible modifications would not produce an immunogenic A chain with reduced toxicity. Nevertheless, as explained in PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996), in determining whether experimentation would be undue, the quantity of experimentation required is less important than the quality of the guidance or direction provided:

[T]he question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement;” 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 . . . practice [of] a desired embodiment of the invention claimed.

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

Here, the examiner does not appear to question the ability of one skilled in the art to understand and follow the disclosed protocols for making and testing ricin toxoids. Nor, apparently, does the examiner question whether one skilled in the art, following those protocols, would have obtained immunogenic “ricin A chain[s] other than the ones specifically exemplified” (Answer, page 7), with impaired catalytic activity and a reduced ability to cause vascular leak syndrome. Given the explicit guidance and direction provided by the specification, we agree with appellants that “no more than routine screening would be required to practice the full scope of the claimed invention” (Brief, pages 22-23).

Finally, to the extent the examiner would require the specification to “teach how to make any and all altered ricin A chain[s] . . . having any combination of double mutation[s] in the vascular leak syndrome inducing site . . . and in the enzymatic site . . . [as well as] a method of eliciting any immune response” (Answer, page 5), we note that no authority has been cited in support of this requirement. On the contrary, “appellants are not required to disclose every species encompassed by their claims even in an unpredictable art.” In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 218 (CCPA 1976) (emphasis original).

On the facts of this case, we find that the examiner has not adequately explained why practicing the full scope of the claims would have required undue experimentation. Given the guidance and direction set forth in the specification, the process of making and testing ricin A chain variants with the properties required by the claims would appear to require nothing more than routine, iterative experimentation. The rejection of claims 1-6, 48-53, 57, 59, 63, 66, 68, 69, 71-76 and 84-90 for lack of enablement is reversed.

Written Description

The examiner also rejected claims 1-6, 48-53, 57, 59, 63, 66, 68, 69, 71-76 and 84-90 under 35 U.S.C. § 112, first paragraph, because “[t]he specification does not reasonably provide a written description of a method of eliciting any immune response to ricin A chain . . . wherein the amino acid at position L74, D75, and V76 is modified to any undisclosed amino acid, in combination with any mutation in at least one of Y80, Y123, E177, R180, N209 and W211 where the amino acid at said position is modified to any undisclosed amino acid” (Answer, pages 7-8). According to the examiner, “[t]he specification’s disclosure is inadequate to describe the claimed genus of ricin A chain toxin in” (id., page 8) because it does not provide “a representative number of altered [immunogenic] ricin A chains[s]” with “reduce[d] ability to cause vascular leak and/or reduced catalytic activity” (id.).

We disagree with the examiner’s rationale and conclusion. “The ‘written description’ requirement serves a teaching function, . . . in which the public is given ‘meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.’” University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 922, 69 USPQ2d 1886, 1891 (Fed. Cir. 2004) (citation omitted). Another “purpose of the ‘written description’ requirement is . . . [to] convey with reasonable clarity to those skilled in the art that, as of the filing date [ ], [the applicant] was in possession of the invention.” Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See also Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1329, 63 USPQ2d 1609, 1617 (Fed. Cir. 2002). The requirement is satisfied when the specification “set[s] forth enough detail to allow a person of ordinary skill in the art to

understand what is claimed and to recognize that the inventor invented what is claimed.” University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896. Whether or not a specification satisfies the requirement is a question of fact, which must be resolved on a case-by case basis (Vas-Cath, 935 F.2d at 1562-63, 19 USPQ2d at 1116), and it is the examiner’s “initial burden [to] present[ ] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims” (In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)).

“Applicants have some flexibility in the ‘mode selected for compliance’ with the written description requirement” (University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896), and it is well settled that actual reduction to practice is not necessary to satisfy the requirement (id. at 926, 69 USPQ2d at 1894). In University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), the court explained that “[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus” (id. at 1568, 43 USPQ2d at 1406). In addition, the court subsequently clarified that “the written description requirement would be met for [a claim] if [a] functional characteristic . . . were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed.” Enzo Biochem, 296 F.3d at 1324-25, 63 USPQ2d at 1613.

Finally, the court has made it clear that other factors, including the level of skill in the art, are relevant to whether a description satisfies § 112. See Capon v. Eshhar,

418 F.3d 1349, 1358-59, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005) (“[T]he determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.”).

Here, the specification sets forth the amino acid sequence of the native ricin A chain, identifies the sites responsible for its catalytic activity and its ability to induce VLS, and provides working examples describing specific amino acid substitutions that resulted in reduced or absent catalytic activity and/or reduced ability to induce VLS. See e.g., pages 6, 13, 15, 21 and 75-87 of the specification. In addition to the mutations described in the working examples, the specification clearly states that “[i]t is contemplated” that other amino acid insertions or substitutions “at the position (x) of . . . (x)D(y)” (Specification, page 18), “at the position (D) of . . . (x)D(y)” (id., page 18), or “at the position (y) of . . . (x)D(y)” (id., page 20) of the ricin A chain “would reduce its ability to promote VLS” (id., pages 18, 19 and 20). Similarly, the specification states that “[i]n addition to alterations in the (x)D(y) . . . sequence[ ] associated with VLS, . . . one or more residues important in maintaining the catalytic site’s structure . . . are specifically targeted for mutation” using the same techniques as “those used to mutate the (x)D(y) sequence” (id., page 21). Finally, the specification demonstrates that such limited modifications to the structure of the ricin A chain can be made without reducing the immunogenicity of the toxoid relative to the native toxin (id., page 87).

The examiner has not explained why these teachings would not have conveyed with reasonable clarity to one of skill in the art that appellants were in possession of a

genus of immunogenic ricin A chains with reduced or absent catalytic activity and reduced ability to induce VLS. The examiner's conclusory assertion that the working examples are not representative of a larger genus is insufficient to meet the examiner's "initial burden [to] present[ ] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims" (Wertheim, 541 F.2d at 263, 191 USPQ at 97).

Accordingly, the rejection of claims 1-6, 48-53, 57, 59, 63, 66, 68, 69, 71-76 and 84-90 as lacking adequate written descriptive support under 35 U.S.C. § 112, first paragraph, is reversed.

#### New Matter

Claims 53, 56, 65, 77, 82 and 91 stand rejected under 35 U.S.C. § 112, first paragraph, because V76M "and the combination of at least one of a Y80A or E177D" mutation "represents a departure from the specification and the claims as originally filed" (Examiner's Answer, page 3). We disagree.

To satisfy the written description requirement, the specification need not contain the identical words used in the claims. See Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("[T]he disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue."). The written description requirement is satisfied if the disclosure conveys with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. See id.

The specification teaches that the (x)D(y) vascular leak syndrome site on the ricin A chain consists of an L74-D75-V76 triplet (Specification, Table 3), and that "[i]t is

contemplated” that amino acid substitutions other than valine (V), leucine (L), or serine (S) “at the position (y) of . . . (x)D(y)” (id., pages 15 and 20) of the ricin A chain “would reduce its ability to promote VLS” (id., pages 18, 19 and 20). The substitution of methionine (M) for valine (V) at position 76 is specifically recited (id., page 20).

The specification also teaches that mutations in the VLS site are to be made in combination with mutations in residues of the catalytic site: “[i]n addition to alterations in the (x)D(y) . . . sequence[ ] associated with VLS, . . . one or more residues important in maintaining the catalytic site’s structure . . . are specifically targeted for mutation” (id., page 21), using the same techniques as “those used to mutate the (x)D(y) sequence” (id.). The tyrosine (Y) at position 80 is specifically identified as one of these residues. Moreover, the substitution of aspartic acid (D) for glutamic acid (E) at position 177 is disclosed in the working examples (id., page 80).

In our view, the specification conveys with reasonable clarity to those skilled in the art that the inventor was in possession of a modified ricin A chain with a methionine (M) at position 76, in combination with “at least one of a Y80A or E177D” as recited in the claims. The rejection of claims 53, 56, 65, 77, 82 and 91 under 35 U.S.C. § 112, first paragraph, is reversed.

Summary

The rejection of claims 1-6, 48-53, 57, 59, 63, 66, 68, 69, 71-76 and 84-90 under 35 U.S.C. § 112, first paragraph, as lacking enablement and adequate written descriptive support is reversed. In addition, the rejection of claims 53, 56, 65, 77, 82 and 91 under 35 U.S.C. § 112, first paragraph, as containing new matter is reversed.

REVERSED

Toni R. Scheiner	)	
Administrative Patent Judge	)	
	)	
	)	
	)	BOARD OF PATENT
Eric Grimes	)	
Administrative Patent Judge	)	APPEALS AND
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