

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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

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*Ex parte* BENITO O. DE LUMEN and ALFREDO F. GALVEZ

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Appeal 2007-1632  
Application 10/302,633  
Technology Center 1600

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Decided: December 27, 2007

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Before TONI R. SCHEINER, NANCY J. LINCK, and RICHARD M. LEBOVITZ,  
*Administrative Patent Judges.*

Opinion for the Board filed by *Administrative Patent Judge*  
NANCY J. LINCK.

Opinion Dissenting filed by *Administrative Patent Judge*  
RICHARD M. LEBOVITZ.

LINCK, *Administrative Patent Judge.*

**DECISION ON APPEAL**

This is a 35 U.S.C. § 134 appeal in the above-referenced case.<sup>1</sup>

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<sup>1</sup> The application was filed November 22, 2002 and is a continuation of U.S. Patent No. 6,544,956 (hereafter the “’956 Patent”). The ‘956 Patent, in turn, is a continuation of U.S. Patent No. 6,107,287. The real party in interest is The Regents of the University of California.

We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

### STATEMENT OF THE CASE

The field of the invention is modulation of mitotic activity in target cells (Specification (hereafter “Spec.”) 1-2.

The claimed subject matter is reflected in representative claim 1:<sup>2</sup>

1. A method of selectively killing a human neoplastic cell, said method comprising the step of:

administering directly at a target human neoplastic cell demonstrating undesirable mitotic function an effective amount of a nucleic acid encoding and expressing a peptide consisting essentially of 8 to 18 contiguous acidic amino acids independently selected from aspartic acid and glutamic acid residues, wherein the peptide is expressed in the target cell, and the target cell is thereby selectively killed.

The Examiner has rejected claims 1-22 under 35 U.S.C. § 112 ¶ 1, for lack of enablement.

### PATENTABILITY UNDER § 112, ¶ 1

#### *The Enablement Issue*

In the ‘956 Patent (the parent case), claim 1 reads:

1. A method of selectively killing a human neoplastic cell, said method comprising the step of:

administering directly at a target human neoplastic cell demonstrating undesirable mitotic function an effective amount of a nucleic acid encoding and expressing a peptide comprising at least 8 to 18 contiguous acidic amino acids independently selected from aspartic acid and glutamic acid residues, wherein at least 8 contiguous aspartic acid residues

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<sup>2</sup> Appellants do not separately argue the claims. Thus, our analysis is limited to representative claim 1.

are present in the peptide, and wherein the peptide is expressed in the target cell, and the target cell is thereby selectively killed.

Thus, the language “wherein at least 8 contiguous aspartic acid residues are present in the peptide” has been deleted from claim 1 in this case rendering a broader claim 1 than that issued.<sup>3</sup> The controversy in this case turns on this deletion (*see, e.g.*, Examiner’s Answer (hereafter “Ans.”) 12). According to the Examiner, without requiring at least 8 contiguous aspartic acid residues, experimentation to identify peptides with antimetabolic function would have been undue (Ans. 9-11).

Appellants agree as to the issue in this case but disagree with the Examiner’s finding that practicing the presently claimed invention would have required undue experimentation (Appeal Br. 2-5). Appellants support their argument by citing to the teachings in their Specification and relying on the level of skill in the art (*id.*).

In view of these conflicting positions, we frame the enablement issue as follows:

Would Appellants’ Specification have enabled the skilled artisan at the relevant time to “selectively kill[] a human neoplastic cell” by administering “a peptide consisting essentially of 8 to 18 contiguous acidic

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<sup>3</sup> Appellants argue the language “consisting essentially of” (not in claim 1 of the ‘956 Patent) limits the scope of claim 1, only permitting the inclusion of additional amino acid residues that “do not materially affect the basic and novel properties” of the claimed invention (Brief on Appeal (hereafter “Appeal Br.”) 4). We find it unnecessary to decide this issue. However, in the absence of any teaching as to what amino acid residues would materially affect these properties, we give this language its broadest reasonable interpretation, i.e., one substantially equivalent to “comprising” language.

amino acids independently selected from aspartic acid and glutamic acid residues,” in view of the Specification teachings (including those relating to “at least 8 contiguous aspartic acid residues”), and further in view of the level of skill in the art?

*Findings of Fact<sup>4</sup> Relating to § 112, ¶ 1*

*The Claims*

1. Appellants’ claims include embodiments disclosed and claimed in U.S. Patent No. 6,544,956 (see claim 1 (reproduced above)).

2. Appellants’ claims are limited in scope to peptides having 8 to 18 contiguous acidic amino acids independently selected from aspartic acid and glutamic acid residues.”

3. Appellants’ claims are further limited to proteins that selectively kill a human neoplastic cell.

4. Claims to methods using proteins having 8 contiguous aspartic acid residues are admittedly enabled (Ans. 12; see also issued claim 1 in parent case, i.e., U.S. Patent No. 6,544,956 (see claim 1)).

5. The claim limitation requiring 8 to 18 contiguous acidic amino acids (limited to aspartic and glutamic acids) and the teachings regarding peptides with at least 8 contiguous aspartic acids would have provided guidance to the skilled artisan as to what peptides have the potential to selectively kill a human neoplastic cell (FF 2-4).

6. As acknowledged by the Examiner, the level of skill of those in the art at the time the invention was made was “relatively high” (Ans. 9).

7. At the time the invention was made, it would have been “well within the purview of those skilled in this art to construct and use in the

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<sup>4</sup> Findings of Fact are abbreviated "FF".

claimed methods nucleic acids encoding any desired peptide comprising 8 to 18 contiguous Asp/Glu residues” (Declaration of Nancy K. Amy (hereafter “Amy Decl.”)).

8. “Furthermore, while there is no *a priori* guarantee that every such peptide will disrupt the targeted mitotic function, given the teachings of the application, only ordinary skill and routine experimentation” would have been “necessary to test the efficacy of any given such peptide against a target cell” (Amy Decl.).

9. “Finally, the specification teaches and exemplifies the use of the methods in bacterial, plant and mammalian cells, both *in vitro* and *in vivo*” (*id.*; *see also* Spec. 9-25 (disclosing working examples which would have taught the skilled artisan how to practice the claimed invention with numerous synthetic proteins)).

10. “While there is no *a priori* guarantee that the methods will disrupt mitotic function in every cell in every context, only ordinary skill and routine experimentation” would have been “necessary to test and confirm the efficacy of the methods with a given target cell and context” (Amy Decl.).

11. While experimentation to fully practice the claimed invention might have been extensive, it would have been routine for the skilled artisan and not undue (FF 1-10).

#### *Discussion of the Enablement Issue*

In making the above findings, we have considered the relevant *Wands* factors in light of the prior art teachings relied upon by the Examiner and Appellants, and the relevant caselaw. Based on our findings, we conclude

Appellants' Specification would have enabled the skilled artisan at the relevant time to practice their claimed method, in view of their teachings and the level of skill in the art (FF 1-11).

The primary flaw in the Examiner's reasoning is that "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." *Ex parte Jackson*, 217 USPQ 804, 807 (BPAI 1982), *quoted with approval in In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) and *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). *See also In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991) ("That *some* experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'"). In this case, we find the experimentation would have been routine and not undue (FF 11).

As the Examiner acknowledges, the claim 1 is enabled for the subgenus having "at least 8 contiguous aspartic acid residues" (FF 4). While claim 1 includes additional peptides, the claim itself provides additional guidance as to what those peptides must contain, i.e., "at least 8 to 18 contiguous acidic amino acids independently selected from aspartic acid and glutamic acid residues" (FF 5). Given the level of skill in the art, the Amy Declaration, and the teachings of the Specification (FF 6-10), the Examiner has not met her burden of establishing unpatentability by a preponderance of the evidence. *See, e.g., In re Kollar*, 286 F.3d 1326, 1329 (Fed. Cir. 2002) (noting the Office carries the initial burden of establishing unpatentability by a preponderance of the evidence).

With respect to her discussion of the *Wands* factors, the Examiner focuses primarily on lack of predictability, based on several references that teach or suggest the activity of peptides having 8 to 18 contiguous acidic amino acid fragments may vary (Ans. 8-10, 13). Because of these prior art teachings, the Examiner found the “unpredictability in the products, *e.g.*, proteins and/or polypeptides *comprising* a peptide domain composed of just 8-18 As[p] and/or Glu, other than at least 8 Asp residues, would result in a large amount of experimentation to demonstrate how an atypical *lunasin* peptide would retain its antimitotic function” (Ans. 10). Again, while the Examiner may be correct that a “large amount” of experimentation might have been necessary, the Examiner has failed to show how it would have been undue. Thus, we are unpersuaded by this line of reasoning, particularly when weighed against the other *Wands* factors (*see* FF 1-11).

The Examiner also faults Appellants for failing to “provide guidance as to how to identify a common mechanism or structural motif in common in all derivatives of the peptide as set forth in SEQ ID NO: 2 or, nucleic acid fragments of SEQ ID NO: 1, and which will serve as a basis for the assertion that all such derivatives are interchangeable in the instant invention” (Ans. 11). Again, we are unpersuaded. As the Examiner acknowledges (Ans. 5), the amount of guidance provided is only one of the *Wands* factors to be considered. *See Wands*, 858 F.2d at 737. Here, weighing all the *Wands* factors, including the level of skill in the relevant art, we find Appellants provided sufficient guidance such that the skilled artisan could have practiced the claimed invention without undue experimentation (FF 1-11). That is all the law requires. *See, e.g., In re Vaeck*, 947 F.2d at 495.

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CONCLUSION

We reverse the Examiner's lack of enablement rejection of claims 1-22 under 35 U.S.C. § 112 ¶ 1.

REVERSED

Dissenting Opinion by Lebovitz, *Administrative Patent Judge*.

Claim 1 in this appeal is directed to a “method of selectively killing a human neoplastic cell” comprising administering a nucleic acid encoding “a peptide consisting essentially of 8 to 18 contiguous acidic amino acids independently selected from aspartic acid and glutamic acid residues.” When expressed in the neoplastic cell, the peptide selectively kills it.

The Examiner contends that the Specification is enabled for methods which involve peptides comprising at least eight contiguous aspartic acid residues, but not for the full scope of the claim (Ans. 4-5). To support her position that the Specification lacks adequate guidance to enable the claimed invention, the Examiner cites four prior art patents, each which describes a peptide that satisfies the sequence limitation of claim 1 in having a contiguous stretch of both aspartic acid and glutamic acid residues (“D/E peptides”) (Ans. 9). The prior art peptides possess a distinct biological function different from the claimed activity of selectively killing neoplastic cells (*id.*). In contrast, there are no examples in the Specification of D/E peptides which perform in the claimed method. The Specification provides evidence of killing activity for only a limited group of peptides that comprise a contiguous stretch of aspartic acid residues (“D peptides”) (Ans. 7). Based on these findings, the Examiner concludes that it would be unpredictable that the D/E peptides would cause mitotic disruption and selectively kill neoplastic cells as required by claim 1 (Ans. 11).

Appellants do not challenge the Examiner’s findings about the activity of the prior art D/E peptides. Instead, they argue “that only ordinary skill and routine experimentation are necessary to test and confirm the efficacy of

the methods with a given target cell and context” (Appeal Br. 5). They also assert that to “the extent the Examiner is concerned that the claims might include inoperative embodiments” – apparently in reference to the Examiner’s evidence of the “inoperability” of the four D/E peptides – “it is not a function of the claims to specifically exclude possible inoperative substances” (Appeal Br. 4) (internal citations omitted).

In reversing the rejection, the majority agrees with Appellants that given the level of skill in the art and the teachings of the Specification, only routine experimentation would be necessary to carry out the full scope of the claims. The majority concludes that the Examiner focused on the lack of predictability, and failed to weigh it properly against the other *Wands* factors to be considered in determining whether a disclosure would require undue experimentation to enable the claimed invention. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Because I disagree with this conclusion, I respectfully dissent from the majority opinion.

“To 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.’” *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)). Undue experimentation “is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations.” *Wands*, 858 F.2d at 737. The *Wands* court summarized eight different factors<sup>5</sup> to be considered in making an

<sup>5</sup> “Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 1547 (BPAI 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4)

enablement determination, but the list was not inclusive nor was the test intended to be quantitative. *Forman*, 230 USPQ at 547. I agree with the majority that the Specification coupled with routine experimentation provides adequate guidance to make all species which are encompassed by the claim and to determine which would have the claimed activity of “selectively killing a human neoplastic cell.” But, this is only one factor to be considered in an enablement determination, and not the dispositive one under the facts presented in this appeal.

There are numerous cases in which a claim was found not to be enabled because there was no reliable evidence that its full scope could be achieved with the guidance of the application. *See Monsanto Co. v. Syngenta Seeds Inc.*, 503 F.3d 1352, 1361-62 (Fed. Cir. 2007); *In re Goodman*, 11 F.3d 1046, 1052 (Fed. Cir. 1993). The claims in *Goodman* and *Monsanto*, in particular, were of vaster scope than those at issue in this appeal, but the deficiency is of the same degree. In *Goodman*, the claims covered genetic transformation all plants, but the evidence showed that a large genus of plants – monocots – could not be reliably transformed. *Goodman*, 11 F.3d at 1052. The teachings in *Goodman*’s application did not cure the unpredictability. *Id.* I have the same concern here.

In this case, while there is evidence that peptides comprising a contiguous stretch of aspartic acids have the claimed activity, there is *none* for peptides comprising both aspartic acid and glutamic acid residues. In fact, there is evidence to the contrary. The Examiner cites four prior art D/E peptides that satisfy claim 1’s sequence limitations, but which exhibit

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the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.” *Wands*, 858 F.2d at 737.

biological functions distinct from the functional activity required by claim 1 (Ans. 9) and which do not perform as the Specification describes. Thus, like *Goodman*, there is unrebutted evidence that a significant portion of the scope of claim 1 will not work. Similarly, there is no guidance in the Specification that tells persons of ordinary skill in the art how to fix the problem to enable D/E peptides to selectively kill human neoplastic cells. Therefore, it is not a question of whether it is routine to make and test peptides within the scope of claim 1, but whether the D/E peptides encompassed by the claim can actually be made to work with the guidance provided by the Specification and in the context of the ordinary level of skill in the art.

Appellants have no explanation for why the only examples of record of D/E peptides do not perform as the Specification says they should. I do not view these failures as necessarily fatal to the full scope of claim 1. However, I believe these failures rebut the presumption that the Specification is enabled for the full scope of the claim, shifting the burden to Appellants to provide arguments or evidence to the contrary. They have not met this burden. While persons of skill in the art might have reasonably believed after reading the Specification that substituting one or more acidic glutamic acids in a peptide comprising a stretch of contiguous acidic aspartic acids would not affect the latter's ability to selectively kill cells, the countervailing evidence provided by the Examiner topples this belief. It raises reasonable doubt that the D/E peptides would work as claimed. For this reason, weighing the *Wands* or other factors is not the appropriate test for enablement in this case.

Of course, even in an unpredictable art, an applicant for a patent is not required to disclose every species encompassed by their claim which will

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work. *In re Angstadt*, 537 F.2d 498, 504 (CCPA 1976). “[I]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention. See *In re Angstadt*, 537 F.2d 498, 504 (CCPA 1976).” *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). The effect has not been “sufficiently demonstrated” when the only evidence of record is that the claimed invention is not generally operable for a substantial part of its scope. This fact outweighs, and takes precedence over the *Wands* factors. Thus, in my opinion, the claims are not enabled and the rejection should be affirmed.

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