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Recent Development

RECENT DEVELOPMENTS IN PATENT LAW: SELECTED BIOTECHNOLOGY CASES INTERPRETING § 112 AND § 101

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Table of Contents

I.	Introduction	281
II.	Enablement	282
	A. Ex parte Tanksley	282
	B. Ex parte Humphreys	282
	C. Fiers v. Revel	283
	D. In re Wright	284
	E. Ex parte Maizel	285
	F. Ex parte DeCastro	285
	G. In re Goodman	286
III.	Utility	287
	A. Ex parte Aggarwal	287
	B. Ex parte Balzarini	287
	C. Ex parte Deuel	288
IV.	Conclusion	289

I. Introduction

The present paper summarizes several recent decisions by the Patent and Trademark Office and the courts that interpret the statutory requirements of utility and enablement as applied to biotechnology. These decisions reflect the continued application of a relatively higher standard of disclosure to establish enablement and utility for the invention relating to the "unpredictable" art of biotechnology, as compared to a mechanical or electrical case.

*282 II. Enablement

A. Ex parte Tanksley[1]

Ex parte Tanksley relates to the enablement of claims to cDNA clones by reference to alphanumeric designation. The claims were directed to a cDNA clone selected from a Markush grouping of clones designated by alphanumeric designation.[2] The specification provided a chromosome map identifying the relative positions of the alphanumerically designated clones in the collection. A few of the clones were indicated to be highly analogous to known chlorophyll binding protein (CAB) genes and ribulose biphosphate carboxylase (RuBPC) genes.[3] The specification did not include any partial or complete sequence information of any of the clones or any information on the function of proteins encoded or partially encoded by the cDNAs claimed.[4]

The Board rejected the claims under 35 U.S.C. § 112, second paragraph, as failing to "sufficiently point out and distinctly claim the invention"[5] because the description in the specification was insufficient to distinguish the claimed subject matter from the prior art and inadequate to apprise the public of the boundaries of protection of the claims.[6]

Complete sequence information of the clones recited in the claims was not required to satisfy § 112. The Board stated that providing at least a partial base sequence and/or function of the proteins encoded in the cDNAs may have provided a sufficiently "art recognized manner" of defining the clones such as to satisfy § 112.[7] The Board also noted that the absence of working examples in a specification in itself is not fatal to enablement. However, the absence of examples "taken together with other considerations, such as the complexity and unpredictability [of the particular art] and lack of guidance in the specification,"[8] could lead to a conclusion that "undue experimentation would be required [by] one of ordinary skill in the art [to use] the claimed invention."[9]

B. Ex parte Humphreys[10]

Ex parte Humphreys relates to the deposit of biological materials and the enablement of method claims that use biological materials. The claims were directed to methods for isolating a gene involved in the biosynthesis of a first polyketide antibiotic. The methods employed a number of biological materials, including nucleic acid probes with at least *a part* of *a* gene involved in the biosynthesis of a second polyketide antibiotic.[11]

The Board found that the written description in the specification of the plasmids used as probes to identify *a part* of the gene recited in the claims would not enable one skilled in the art to reproduce the invention,[12] and declared that a deposit of the plasmid was required to satisfy the how to "make and ***283** use" requirement of 35 U.S.C. § 112, first paragraph.[13] Access to the plasmid from a private source was deemed unpersuasive on the issue of enablement to make and use the invention, as there existed no evidence to establish an unlimited public access to the biological material over the life of an issued patent to the invention.[14]

The application also included method claims for producing a first polyketide antibiotic. The Board affirmed the rejection of these claims under § 112, first paragraph, concluding that access to the plasmid and to the gene fragment would not enable one skilled in the art to practice this particular invention to the scope claimed.[15]

C. Fiers v. Revel[16]

Fiers v. Revel relates to the conception and enablement of claims to a DNA molecule claimed *per se.* The issue of conception of a DNA molecule was discussed relative to satisfaction of the written description requirement of § 112.[17]

The case involved a three-way interference declared among three foreign parties -- Fiers, Sugano, and Revel.[18] The patents included claims to DNA that codes for human fibroblast beta-interferon (BETA-IF).[19] The count of the interference was: "A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide."[20]

Fiers' earliest patent application disclosed a method for isolating DNA coding BETA-IF, and, with a later filed application, disclosed the complete DNA nucleotide sequence coding for BETA-IF.[21] Sugano's earliest patent application disclosed the complete DNA nucleotide sequence coding for BETA-IF and a method for isolating that DNA.[22] Revel's earliest patent application disclosed a method for isolating a fragment of DNA for BETA-IF and a method for isolating the messenger RNA (mRNA) coding for BETA-IF, but did not disclose the DNA sequence coding for BETA-IF.[23]

To determine which party was the first to conceive of the invention of the count, the court declared that conception of a substance claimed *per se* without reference to a process requires conception of the structure, name, formula, or definitive chemical or physical properties of the substance.[24] In the case of a claim to a DNA molecule, the court stated that conception does not occur solely with definition of a method of preparation.[25] The court further stated:

> ***284** The difficulty that would arise if we were to hold that a conception occurs when one has only the idea of a compound, defining it by its hoped-for function, is that would-be inventors would file patent applications before they had made their inventions and before they could describe them. That is not consistent with the statute or the policy behind the statute, which is to promote disclosure of inventions,

> not of research plans. While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity.[26]

Sugano was found to have been the first to conceive the invention because the disclosure of the nucleotide sequence of the gene conveyed with reasonable clarity to those skilled in the art that as of the filing date, Sugano was in possession of the DNA coding for ?-IF. Sugano's disclosure of the complete and correct nucleotide sequence of the DNA molecule coding for ?-IF was also found to satisfy the written description requirement of § 112.[27]

The court held that failure to disclose the actual DNA sequence, or other sufficient "definition" of the DNA molecule, constituted a failure to demonstrate conception. The court further held that failure to establish conception also constituted failure to establish enablement, stating that logically, one cannot enable an invention that has not been conceived.[28]

The rule from *Fiers* is that conception of a DNA molecule claimed *per se* is not established until an adequate written description, either in the form of a structure, name, formula or definitive chemical or physical properties sufficient to distinguish it from other molecules, is disclosed. *Fiers* also teaches that disclosure of the nucleotide sequence of a DNA molecule is sufficient to satisfy the written description requirement of § 112, and is one way that conception of a DNA molecule can be established.[29]

***D. In re Wright*[30]**

In re Wright relates to the scope of enablement provided by a single working example for generic claims to RNA vaccines.[31] The claims were directed to processes for producing live, nonpathogenic vaccines against pathogenic RNA viruses, vaccines, and methods of using the vaccines[32]. The specification provided only a single working example of a specific RNA vaccine.[33] The issue before the court was whether the scope of enablement provided by the specification was commensurate with the scope of the claims.[34] The court characterized the claims as encompassing "*any and all,* non-pathogenic vaccines, and processes for making such vaccines, which elicit immunoprotective activity in *any* animal toward *any* RNA virus."[35]

The court upheld the rejection of the claims under § 112 on the grounds that Wright had failed to establish, by evidence or argument, that a skilled artisan "would believe reasonably"[36] that Wright's ***285** success with a particular RNA virus could be extrapolated with a reasonable expectation of success to the scope of RNA viruses, or even the scope of all avian RNA viruses, encompassed by the claims as of the date the application was filed.[37] Neither the limited success of others in developing vaccines to other RNA viruses or the submitted affidavit evidence was considered persuasive on the issue of "undue experimentation" to rebut the § 112 rejection.[38]

Wright stands for the proposition that an applicant with broadly defined claims to a biotechnology related invention and only a limited disclosure should be prepared to establish, by evidence and/or arguments, that as of the effective filing date, one of ordinary skill in the art would reasonably believe that the disclosure could be extrapolated to the full scope of the claims.

***E. Ex parte Maizel*[39]**

Ex parte Maizel relates to the enablement of claims that include the phrase "biologically functional equivalents thereof."[40] The claims in *Maizel* were directed to a DNA vector comprising a sequence encoding a particular protein. The protein was defined in terms of molecular weight and amino acid sequence. The claimed DNA sequence encompassed any sequence that encoded such a protein or "any biologically functional equivalent" of that protein.[41] The Board found that the phrase "biologically functional equivalent thereof" covered any conceivable means, i.e., cell or DNA, which achieves the stated biological result, while the specification disclosed, at most, only a single specific DNA segment known to the inventor.[42]

The rejection of the claims under 35 U.S.C. § 112 was upheld on the grounds that they were far broader than what was enabled by the specification.[43] The Board further considered whether the nucleic acid sequence of the claimed vector could be corrected after filing, and held that it could not.[44]

***F. Ex parte DeCastro*[45]**

Ex parte DeCastro relates to the enablement of biotechnology method claims that reference the use of a broadly defined group of biological materials. The biological materials in the claims were broadly defined as "theophylline utilizing enzymes."[46] The specification described certain properties of three theophylline utilizing enzymes that could be used to identify other equivalent enzymes.[47] The specification did not include the microbial source of these enzymes, nor did it describe the enzymes by any physical characteristics. Properties possessed by the enzymes of oxidizing, dehydrating or demethylating theophylline were disclosed.[48]

***286** The Board affirmed the rejection of the claims under § 112, first paragraph, for failure to enable the scope of

"theophylline utilizing enzymes" of the claimed method.[49] The subsequent biological deposit of three microorganisms that made the particular "theophylline utilizing enzymes", listed in the application as "T-enzymes," was deemed non-persuasive on the issue of enablement as such failed to provide satisfaction of how to make and use the claimed method as of the date of filing.[50] Also viewed as non-persuasive was the availability of certain trademarked theophylline utilizing enzymes (T-040, T-060, T-090) to be sold by the assignee of the application "during the enforceable life of any patent."[51]

***G. In re Goodman*[52]**

In re Goodman relates to the enablement of biotechnology method claims for producing mammalian peptides in plant cells. The method called for integrating a DNA construct encoding a mammalian peptide into plant cells.[53] The specification described a single working example of the formation of an expression cassette with regulatory regions functional in tobacco plants and a structural gene coding for gamma interferon.[54] In the example, the expression cassette is joined to a selectable marker to simplify isolation of plant cells that successfully integrate the construct.[55] The selectable marker consisted of regulatory regions functional in tobacco plants and a DNA sequence coding for a tetracycline resistance gene.[56] The claims were broadly drawn to methods for producing any desired mammalian peptide produced in any plant cell.[57]

The Federal Circuit affirmed the rejection of the claims under § 112, first paragraph, because the specification was not considered sufficient to enable one skilled in biotechnology at the time the application was filed to practice the method for all plant cells encompassed by the scope of the claims.[58] The court noted that the contemporary art at the time the application was filed demonstrated the unpredictability and uncertainty of practicing the method with particular plant types, particularly with monocot plants.[59] The court also noted that the art showed the need for extensive experimentation to practice the claimed method for just a few plants, let alone all plant cells as broadly claimed in the application.[60]

The above review is not meant to suggest that generic biotechnology claims are *per se* nonenabled or foreclosed from broad patent protection. Instead, the guidelines provided in the case law suggest that when a claimed genus represents a diverse and relatively poorly understood group, the required disclosure to enable the claimed scope will be greater, compared to the disclosure needed to enable generic claims to an invention involving "predictable" factors, such as mechanical or electrical elements. However, broad claims to a genus or species of genetically engineered organisms may likely be found enabled under § 112 only when it can be successfully demonstrated or argued that the claimed genus represents a relatively non-diverse and well understood group of organisms.

***287** For claims directed to a DNA molecule *per se,* a sufficient description of a DNA molecule to establish conception and enablement has been found by disclosure of the actual DNA sequence. Disclosure of a method for obtaining a DNA molecule establishes conception of a DNA molecule claimed as a process. Generic claims to a DNA molecule of a less broad scope may be available where only a few "similar" sequences of a gene are disclosed. Broader generic claims to a DNA molecule will likely only be found sufficiently enabled where a larger representative group, i.e., more than "a few," DNA sequence analogs are described.

III. Utility

***A. Ex parte Aggarwal*[61]**

Ex parte Aggarwal relates to the enablement of claims directed to methods of therapeutic treatment. The claims were directed to methods for treating tumors using anti-cancer pharmaceutical agents, defined as lymphotoxins.[62] The specification included many broad statements of utility, and described the administration of lymphotoxin using virtually all known routes of administering anti-cancer substances.[63] However, the actual examples provided in the specification only demonstrated the activity of these agents by an *in vivo* tumor necrosis test in mice.[64]

The Board characterized the mouse *in vivo* example as not predictive of human anti-tumor activity.[65] The Board thus affirmed the combined rejection of the claims under 35 U.S.C. § 101 and § 112 as inoperative over the broad range of cancer/tumors set forth in the disclosure, as not useful to the scope claimed, and as not enabled.[66]

The Board acknowledged the need for an early filing date for applications in the biomedical field, but stated that such a filing is allowable only so long as the applicant, when challenged, "can provide evidence showing substantial activity in screening tests customarily used and accepted as predictive" of human activity for the type of chemical tested.[67] In addition, the Board stated that "the evidence must be commensurate with the scope of utility asserted and the subject matter claimed."[68]

In a broad sense, the *Aggarwal* holding means that non-human screening tests may be sufficient to demonstrate a therapeutic utility only where such a test has been characterized as predictive of the particular therapeutic utility in humans when viewed by one of skill in the art.

***B. Ex parte Balzarini*[69]**

Ex parte Balzarini relates to the enablement of claims directed to pharmaceutical compositions reciting a broad pharmacological activity.[70] The pharmacological activity recited in the claim was ***288** "effective to treat retroviral diseases in an animal or patient. . . . "[71] The Board found that the primary utility of the pharmaceutical compositions was in the treatment of humans who were HIV positive, who had retroviral disease, AIDS, or AIDS-related diseases. However, the specification disclosed only an *in vitro* anti-viral activity of the compounds.[72]

The court upheld the rejection of the claims under § 101 on the grounds that the applicant had failed to provide sufficient evidence that one of ordinary skill in the art would reasonably believe that the claimed compositions had the *in vivo* efficacy encompassed by the claims.[73] The declaration evidence submitted by the applicant was deemed non-persuasive on this issue, as the declaration only included the statement that the compositions claimed "may" have utility in combative diseases or syndromes causally related to HIV.[74]

The Board stated that "[w]hile we are not requiring human clinical trials, it may very well be that . . . those skilled in the art would not accept anything short of such human clinical trials."[75] The general rule of *Balzarini* is that in the case of a broad asserted scope of therapeutic utility in a claim, utility will be established only where the evidence is at least sufficient to satisfy those of skill in the art.[76]

***C. Ex parte Deuel*[77]**

Ex Parte Deuel relates to the requirement under § 101 that a statement of use of the invention be included in a specification.[78] The claims in *Deuel* were directed to a novel growth factor protein (prostate-derived mitogen) and a method of using it.[79] At issue was whether or not the specification or the art at the time the application was filed demonstrated any practical use of the claimed protein. The Board found that there was insufficient evidence that the invention satisfied the requirements of § 101, since there was no single statement of use or example of use for the growth factor in the specification or in any of the prior art cited by the examiner.[80]

Deuel stands for the proposition that even where a new composition is identified, there must exist some actual, i.e., practical, use for that composition stated in the specification, or established in the art contemporaneous with the date the application was filed to satisfy § 101.[81]

Rejections for lack of practical utility often arise where the defined biotechnology invention involves a therapeutic utility or encompasses numerous embodiments not demonstrated in the application. Consideration of the desired breadth of patent protection should therefore be tempered against a realistic evaluation of whether the scope of protection sought is commensurate not only with the scope of enablement, but also with the scope of utility of the invention.

*289 IV. Conclusion

The present selected review illustrates that, in a biotechnology case, consideration of an enabled practical utility commensurate with the scope of the claims involves a consideration of both 35 U.S.C. §§ 101 and 112. This review also demonstrates the essentially case-by-case basis by which the issues of enablement and utility are evaluated for inventions relating to this technology by the Patent Office and the courts. Ultimately, the scope of patent protection afforded the biotechnology invention will depend on the particular facts and circumstances of the case in view of the state of the art as of the date the application is filed.

Footnotes

a1 Arnold White & Durkee, Austin, Texas; B.A., Trinity University, 1979; M.S., The University of Texas, 1983; J.D., St. Mary's University, 1988. The author extends her appreciation to Gary Sertich, Ph.D., J.D., for his assistance in the preparation of this manuscript.

aa1 Felsman, Bradley, Gunter & Dillon, L.L.P., Ft. Worth, Texas; B.A., University of Texas at Austin, 1986; B.S.E.E., University of Texas at Dallas, 1993; J.D., University of Texas School of Law, 1989.

1 26 U.S.P.Q.2d (BNA) 1384 (Bd. Pat. App. & Int. 1991).

[2] *Tanksley,* 26 U.S.P.Q.2d (BNA) at 1385-86.

[3] *Id.* at 1386.

[4] *Id.* at 1387.

[5] *Id.* at 1386.

[6] *Id.* at 1387.

[7] *Id.* at 1387.

[8] *Id.* at 1389.

[9] *Id.*

[10] 24 U.S.P.Q.2d (BNA) 1255 (Bd. Pat. App. & Int. 1992).

[11] *Humphreys,* 24 U.S.P.Q.2d (BNA) at 1258.

[12] *Id.*

[13] *Id.* at 1260.

[14] *Id.* at 1259.

[15] *Id.* at 1260.

[16] Fiers v. Revel, 984 F.2d 1164, 25 U.S.P.Q.2d (BNA) 1601 (Fed. Cir. 1993).

[17] *See generally Fiers,* 984 F.2d 1164.

[18] *Id.* at 1167.

[19] *Id.* Human fibroblast beta - interferon is a protein that promotes viral resistance in human tissue.

[20] *Id.* at 1166.

[21] *Id.* at 1167.

[22] *Id.*

[23] *Id.*

[24] *Id.* at 1169.

[25] *Id.* The court, citing its decision in *Amgen,* stated that "irrespective of the complexity or simplicity of the method of isolation employed, conception of a DNA, like conception of any chemical substance, requires a definition of that substance other than by its functional utility." Amgen v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 U.S.P.Q.2d (BNA) 1016 (Fed. Cir.), *cert. denied,* 112 S. Ct. 169 (1991). The court also stated, "before reduction to practice, conception only of a process for making a substance, without a conception of a structural or equivalent definition of that substance, can at most constitute a conception of the substance claimed as a process." *Fiers,* 984 F.2d at 1169.

[26] *Fiers,* 984 F.2d at 1169.

[27] *Id.* at 1172.

[28] *Id.* at 1171.

[29] *Id.* at 1172.

[30] 999 F.2d 1557, 27 U.S.P.Q.2d (BNA) 1510 (Fed. Cir. 1993).

[31] *Id.* at 1558.

[32] *Id.* at 1559.

[33] *Id.* at 1559. The single working example of the vaccine was a recombinant vaccine that confers immunity in chickens against the RNA tumor virus known as Prague Avian Sarcoma Virus (PrASV), a member of the Rous Associated Virus (RAV) family. Claims directed to this particular RNA tumor virus vaccine were allowed.

[34] *Id.* at 1559.

[35] *Id.* at 1562 (emphasis in original).

[36] *Id.* at 1564.

[37] *Id.*

[38] *Id.*

[39] 27 U.S.P.Q.2d (BNA) 1662 (Bd. Pat. App. & Int. 1993).

[40] *Maizel,* 27 U.S.P.Q.2d (BNA) at 1644.

[41] *Id.* at 1664.

[42] *Id.* at 1665.

[43] *Id.*

[44] *Id.* at 1666; *But see Ex parte Marsili,* 214 U.S.P.Q. (BNA) 904 (Bd. Pat. App. & Int. 1979) (holding that changes in a chemical structure of a claimed compound are not new matter and are allowable after filing).

[45] 28 U.S.P.Q.2d (BNA) 1391 (Bd. Pat. App. & Int. 1993).

[46] *Castro,* 28 U.S.P.Q.2d (BNA) at 1392.

[47] *Id.*

[48] *Id.*

[49] *Id.* at 1394.

[50] *Id.*

[51] *Id.* at 1393.

[52] 11 F.3d 1046, 29 U.S.P.Q.2d (BNA) 2010 (Fed. Cir. 1993).

[53] *Goodman,* 11 F.3d at 1048.

[54] *Id.* at 1049.

[55] *Id.*

[56] *Id.*

[57] *Id.*

[58] *Id.* at 1052.

[59] *Id.*

[60] *Id.*

[61] 23 U.S.P.Q.2d (BNA) 1334 (Bd. Pat. App. & Int. 1992).

[62] *Aggarwal,* 23 U.S.P.Q.2d (BNA) at 1335.

[63] *Id.* at 1338.

[64] *Id.*

[65] *Id.* at 1338.

[66] *Id.* at 1339.

[67] *Id.* at 1339.

[68] *Id.*

[69] 21 U.S.P.Q.2d (BNA) 1892 (Bd. Pat. App. & Int. 1991).

[70] *Balzarini,* 21 U.S.P.Q.2d (BNA) at 1894.

[71] *Id.* at 1893.

[72] *Id.* at 1895.

[73] *Id.*

[74] *Id.* at 1897.

[75] *Id.*

[76] *Id.*

[77] 27 U.S.P.Q.2d (BNA) 1360 (Bd. Pat. App. & Int. 1993).

[78] *Deuel,* 27 U.S.P.Q.2d (BNA) at 1365.

[79] *Id.* at 1361. The invention related to a purified growth factor isolated from prostate tissue and to a method of stimulating the growth of fibroblast cells using the growth factor. The protein was described as having mitogenic activity, a molecular weight of 25,000 kDa, certain stability properties, and a particular amino acid content.

[80] *Id.* at 1365.

[81] *Id.*