

NOTE: This disposition is nonprecedential.

## United States Court of Appeals for the Federal Circuit

2006-1203, -1204, -1205

SYNGENTA SEEDS, INC.,

Plaintiff-Appellant,

v.

MONSANTO COMPANY and DEKALB GENETICS CORP.,

Defendants-Cross Appellants,

and

DOW AGROSCIENCES LLC, MYCOGEN PLANT SCIENCE, INC.  
and AGRIGENETICS, INC.

(Collectively doing business as Mycogen Seeds),

Defendants-Cross Appellants.

Donald R. Dunner, Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., of Washington, DC, argued for plaintiff-appellant. With him on the brief were Herbert H. Mintz, Barbara R. Rudolph, and Robert A. Pollock.

Richard G. Taranto, Farr & Taranto, of Washington, DC, argued for defendants-cross appellants Monsanto Company, et al. With him on the brief were Susan K. Knoll and Steven G. Spears, Howrey LLP, of Houston, Texas. Of counsel were Donald Hopkins Mahoney, III, Thomas A. Miller, and Melinda L. Patterson.

Daniel J. Thomasch, Orrick, Herrington & Sutcliffe LLP, of New York, New York, for defendants-cross appellants Dow Agrosiences LLC, et al. With him on the brief were Robert M. Isackson and Alex Verbin Chachkes of New York, New York, and Craig R. Kaufman and Elizabeth Ann Howard, of Menlo Park, California. Of counsel were Maura Eileen O'Connor, of New York, New York, and Hardip Passananti, of Irvine, California.

Appealed from: United States District Court for the District of Delaware

Chief Judge Sue L. Robinson

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DECIDED: May 3, 2007

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Before MAYER, SCHALL, and BRYSON, Circuit Judges.

BRYSON, Circuit Judge.

Syngenta Seeds, Inc., brought this patent infringement action in the United States District Court for the District of Delaware, alleging that the defendants, Monsanto Company, Dekalb Genetics Corp., Dow AgroSciences LLC, Mycogen Plant Science, Inc., and Agrigenetics, Inc., infringed three U.S. patents owned by Syngenta. The patents, U.S. Patent Nos. 6,403,865 (“the ’865 patent”), 6,075,185 (“the ’185 patent”),

and 6,320,100 (“the ’100 patent”), relate to a transgenic corn plant modified to produce an insecticidal protein. The district court held that the asserted claims of the ’185 patent and the ’100 patent were not infringed as a matter of law, and the jury found that the appealed claims of the ’865 patent were infringed but invalid. Syngenta now appeals. We affirm.

I

Bacillus thuringiensis (“Bt”) is a bacterium that produces a protein toxic to certain insects. In the 1980s, researchers began to experiment with genetically engineering plants to produce the Bt protein so that the genetically modified plants would in effect generate their own insecticide. When native Bt genes were inserted into the corn plant genome, scientists found expression of the Bt protein was sub-optimal. Syngenta (through its predecessor Ciba-Geigy Corp.) sought to increase expression of the Bt protein by modifying the Bt gene’s DNA sequence. Syngenta discovered that the genetically engineered plant would express greater amounts of Bt protein if the DNA sequence of the Bt gene were built with codons preferred by corn plants.

The codons of the native Bt gene are rich in the nucleotides adenine (“A”) and thymine (“T”). Only about 38 percent of the nucleotides in the native gene consist of guanine (“G”) and cytosine (“C”). Corn plants, however, tend to have codons that are rich in G and C nucleotides (“G+C”). In light of the apparent preference of the corn plant for codons rich in G+C, Syngenta designed its synthetic Bt gene by replacing certain codons containing A and T nucleotides (“A+T”) in the native Bt gene with codons that code for the same amino acids but contain more G+C nucleotides. After making further changes to aid in the assembly and manipulation of the synthetic gene,

Syngenta obtained a truncated Bt gene in which 65 percent of its nucleotides consisted of G+C.

Syngenta's work on the synthetic Bt gene led to an application that eventually matured into the '865, '100, and '185 patents. The pertinent claims of the '865 patent describe a transgenic corn plant that produces the Bt protein, "wherein the foreign DNA nucleic acid coding sequence has a G+C content of at least about 60%." The pertinent claims of the '100 and '185 patents similarly describe a transgenic corn plant that produces the Bt protein. Those claims require that the DNA sequence have a sufficient number of particular codons (known as "Murray maize-preferred codons"), so that the sequence contains at least about 60 percent G+C nucleotides.

Following the issuance of the Bt patents, Syngenta filed this action charging the defendants with infringement of all three patents. During the ensuing trial, the court granted the defendants' motion for judgment as a matter of law as to the '100 and '185 patents, holding that the defendants did not infringe those patents under the court's construction of the pertinent claims. The district court construed the claims to require that the change from 38 percent to 60 percent G+C content be attributable solely to the G+C nucleotides in the substituted Murray maize-preferred codons in the DNA sequence. Syngenta conceded that under that claim construction the accused products did not infringe. The jury found the asserted claims of the '865 patent to be infringed, but it then found those claims to be invalid for obviousness and for lack of an adequate written description. Syngenta then took this appeal, and the defendants cross-appealed from those aspects of the judgment unfavorable to them.

## II

Syngenta first challenges the sufficiency of the evidence to support the jury's verdict that the appealed '865 patent claims are invalid for obviousness. While "the ultimate judgment of obviousness is a legal determination," KSR Int'l Co. v. Teleflex Inc., No. 04-1350, slip op. at 23 (U.S. Apr. 30, 2007), that determination is necessarily based on underlying factual inquiries, see Winner Int'l Royalty Corp. v. Wang, 202 F.3d 1340, 1348 (Fed. Cir. 2000). When reviewing a jury verdict of obviousness, "[w]e first presume that the jury resolved the underlying factual disputes in favor of the verdict winner and leave those presumed findings undisturbed if they are supported by substantial evidence. Then we examine the legal conclusion de novo to see whether it is correct in light of the presumed jury fact findings." Jurgens v. McKasy, 927 F.2d 1552, 1557 (Fed. Cir. 1991) (citation omitted).

The principal prior art reference presented to the jury was a published patent application of Barton (U.S. Patent App. Pub. No. 2001/0003849). The Barton application describes a method for improving Bt expression in plant genes. It teaches that Bt expression is improved by selecting codons that are preferred by the native plant. It also teaches that Bt genes have a high proportion of codons that are rich in A+T, while plants generally display an opposite bias towards codons that are rich in G+C. Furthermore, as Syngenta's expert admitted at trial, it was well established at the time Syngenta began its experiments that the coding regions of corn genes tend to be high in G+C. Thus, the Barton application indicates that selecting codons rich in G+C would be likely to increase the expression of Bt in corn. That conclusion is consistent with the testimony of two experts at trial, who testified that it would have been obvious

to a person of skill in the art to make a Bt gene more closely resemble a corn gene by substituting codons that are rich in G+C for the codons of the native gene that code for the same amino acids.

Syngenta argues that while the general notion of substituting codons rich in G+C may have been obvious, the idea to modify the coding sequence of the Bt gene to increase the G+C content to more than 60 percent would not have been obvious. Syngenta relies on the following passage in the Barton application, which Syngenta characterizes as teaching away from modifying the entire coding sequence:

Since the [positive] results did not seem to vary greatly based on the length of the substituted codons, it is possible that the increased expressional efficiency is due principally to the substitutions at the amino-terminal, or 5', end of the coding sequence, perhaps those in the first 25 codons. . . . If true, this would suggest that entire coding regions need not be altered to gain a relatively significant increase in efficiency of expression, merely the amino-terminal end of the coding region, for perhaps about 25 codons. Performing such a codon substitution for the remaining portion of the coding region might still be expected to increase efficiency of expression, although perhaps less dramatically.

It is true, as Syngenta argues, that the quoted portion of the Barton application suggests that positive results could be achieved without modifying the entire DNA sequence. But the entire quoted statement, including the conclusion that a complete codon substitution “might still be expected to increase efficiency of expression,” plainly constitutes a suggestion that some increased efficiency of expression could be achieved by producing a synthetic Bt gene with a coding region consisting entirely of plant-preferred codons. In the case of corn, as the defendants’ expert in molecular biology testified, such a gene would necessarily have a G+C content of more than 60 percent. The jury was free to credit that testimony and thus to conclude that, in light of Barton, a person of

skill in the art would have found it obvious to produce a modified corn gene with a G+C content of more than 60 percent.

Syngenta argues that even if a gene modification resulting in a G+C content of more than 60 percent was obvious to try, there was no reasonable basis to expect that such a modification would lead to a significantly improved level of expression of the Bt protein, and thus no basis for the jury's finding of obviousness. See In re Merck & Co., 800 F.2d 1091, 1097 (Fed. Cir. 1986). Whether there was a reasonable expectation of success is a question of fact. See Medichem, S.A. v. Rolabo, S.L., 437 F.3d 1157, 1165 (Fed. Cir. 2006). The jury was properly instructed, and it concluded, with ample basis in the record, that the prior art gave rise to a reasonable expectation of success from the formulation found in the asserted claims.

In contending that there was no reasonable expectation of success from optimization of the entire genetic sequence, Syngenta argues that the Barton application provided no indication that modifications having the effect of increasing the G+C content to at least 60 percent would yield any additional benefit. That contention, however, is contrary to the portion of the disclosure in the Barton application suggesting that Bt expression is enhanced by the substitution of additional plant-preferred codons. The jury was entitled to rely on that portion of the Barton application in concluding that there was a reasonable expectation of success from such an increase in the G+C content of the codons in the genetic sequence.

Syngenta also argues that the Barton application dealt exclusively with tobacco plants and that the same strategy could not reasonably be expected to succeed in corn. The Barton application, however, specifically taught that the methodology and results it

described would be “equally applicable in other plant species.” Syngenta attempts to offset the force of that statement by noting that we have upheld a decision of the Board of Patent Appeals and Interferences that found similar language in a patent application to “merely contemplate[] future success” and not to be enabling. Adang v. Fischhoff, 286 F.3d 1346 (Fed. Cir. 2002). The issue in Adang, however, was whether the Board’s decision was supported by substantial evidence. In addition to other evidence suggesting non-enablement, the application in Adang contained statements pointing in opposite directions: There was language suggesting the applicability of the patent’s methodology to other plant species, but there was also language teaching that the transformation of other plant species was not predictable. In light of the conflicting teachings, we held that the Board’s finding that the reference “merely contemplate[d] future success” was supported by substantial evidence. Adang, 286 F.3d at 1357. Here, by contrast, the Barton application did not back away from the statement that its methodology and results “will be equally applicable in other plant species.” Moreover, and significantly, the issue in this case is not whether there is substantial evidence to support a conclusion of non-enablement, but whether there is substantial evidence to support the jury’s verdict that the invention would have been obvious. In light of the difference in the evidence in the two cases and the difference in the applicable standard of review, our decision in Adang does not require that we overturn the jury’s verdict in this case.

Additionally, Syngenta points to numerous other prior art references that fail to suggest a G+C content of greater than 60 percent. Those references do little to offset the clear suggestion in the Barton application that complete codon substitution would



lead to improved results. To be sure, Syngenta identifies one reference, U.S. Patent No. 5,500,365 to Fischhoff, which affirmatively teaches the avoidance of sequences containing more than five A or T nucleotides, or more than five G or C nucleotides, in succession. Although that reference cuts against a finding of obviousness, the jury was entitled to weigh Fischhoff against the other evidence and conclude, as a factual matter, that there was a reasonable expectation of success from substituting plant-preferred codons in place of the codons found in the native Bt gene.

Finally, Syngenta argues that Bt coding sequences having a G+C content of at least 60 percent resulted in an unexpected degree of success and that the G+C range of at least 60 percent was patentable based on the absence of any suggestion in the prior art that the 60 percent range would produce exceptionally good results. Whether the degree of success is unexpected in light of suggestions in the prior art is a factual question. CFMT, Inc. v. Yieldup Int'l Corp., 349 F.3d 1333, 1342 (Fed. Cir. 2003). In this case, the jury had sufficient evidence, in the form of expert testimony, from which it could conclude that the degree of success at the 60 percent level was not substantially different from what could reasonably have been expected based on the prior art. Because the jury's verdict was supported by substantial evidence, we uphold the district court's judgment holding the '865 patent claims invalid for obviousness, and we uphold the district court's ruling denying Syngenta's motion for a new trial on obviousness.

### III

Syngenta appeals from the district court's ruling, based on the court's claim construction, that the '100 and '185 patents are not infringed as a matter of law. Syngenta concedes that the accused products do not infringe under the district court's

claim construction, but argues that the district court erroneously construed a key term that is common to all the asserted claims.

Both the '100 and '185 patents are directed to transgenic corn DNA sequences that code for the Bt protein. The appealed claims of the '100 patent all depend from claim 18, which describes a Bt-encoding DNA sequence obtained by reverse-translating a Bt protein into a “synthetic DNA coding sequence comprising a sufficient number of the following codons: [the Murray maize-preferred codons]; such that said synthetic DNA coding sequence has at least about 60% G+C content.” The appealed claims of the '185 patent all depend from claim 1, which similarly describes a sequence obtained by reverse-translating a particular Bt protein into a “maize-optimized nucleic acid coding sequence comprising a sufficient number of the single codons that most frequently encode each amino acid in maize, wherein said maize-optimized nucleic acid coding sequence has at least about 60% G+C content.” The appealed claims also depend from claim 2, which recites a sequence “wherein the single codons determined to most frequently encode each amino acid in maize are” the Murray maize-preferred codons. Thus, all of the '100 and '185 patent claims require a sufficient number of the Murray maize-preferred codons to produce a sequence having a G+C content of at least about 60 percent.

The parties dispute the meaning of the claim term “sufficient number” in this context. In its opening claim construction brief in the district court, Syngenta argued that the number of Murray maize-preferred codons in a sequence would be “sufficient” “as long as there are enough maize preferred codons such that the overall sequence has at least about 60% G+C content.” In a subsequent oral argument before the district

court, Syngenta appeared to offer a narrower view, suggesting that if the total G+C content of a sequence was at least about 60 percent, the number of Murray maize-preferred codons would be sufficient as long as the “majority” of the change from 38 percent (the percent of G+C nucleotides in the native Bt gene) to 60 percent was due to G+C nucleotides contributed by substituted Murray maize-preferred codons.

The district court adopted a different construction. It construed the claims to require that all of the change from 38 percent to 60 percent G+C content be attributable to the substitution of Murray maize-preferred codons. To the extent that the original claim construction order is ambiguous, the court’s subsequent order granting judgment of noninfringement for the defendants makes clear that, under the court’s construction, the G+C nucleotides in codons other than the Murray maize-preferred codons cannot be counted towards the 60 percent.

Syngenta now argues that the number of substituted Murray maize-preferred codons should be regarded as sufficient as long as the G+C content of the modified gene would not be more than 60 percent without those substitutions. Syngenta did not offer that proposed claim construction in the court below. Neither in its brief nor at oral argument did Syngenta ever articulate to the district court that the sufficiency of the number of Murray maize-preferred codon substitutions should be determined by whether or not those substitutions are necessary to reach 60 percent. Instead, the closest Syngenta came to that proposed construction in its presentations to the district court was to argue that the number of Murray maize-preferred codon substitutions would be sufficient if the G+C content of the coding sequence, including the Murray

maize-preferred codons, were at least 60 percent, a construction that is subtly, but significantly, different.

The doctrine of waiver precludes a party from advocating a new theory of claim construction on appeal. Conoco, Inc. v. Energy & Env'tl. Int'l, L.C., 460 F.3d 1349, 1359 (Fed. Cir. 2006); Interactive Gift Express, Inc. v. CompuServe Inc., 256 F.3d 1323, 1346 (Fed. Cir. 2001). Because Syngenta never raised its present proposed construction before the district court, its proposed construction is waived. As Syngenta has not challenged the construction of the '100 and '185 patent claims on any other ground, we affirm the judgment of noninfringement.

In light of our affirmance of the judgment with respect to the obviousness of the '865 patent, we need not address Syngenta's challenge to the jury's verdict on the written description issue or defendant Mycogen's challenge to the jury's verdicts of infringement of the claims of the '865 patent.

Each party shall bear its own costs for this appeal and cross-appeal.